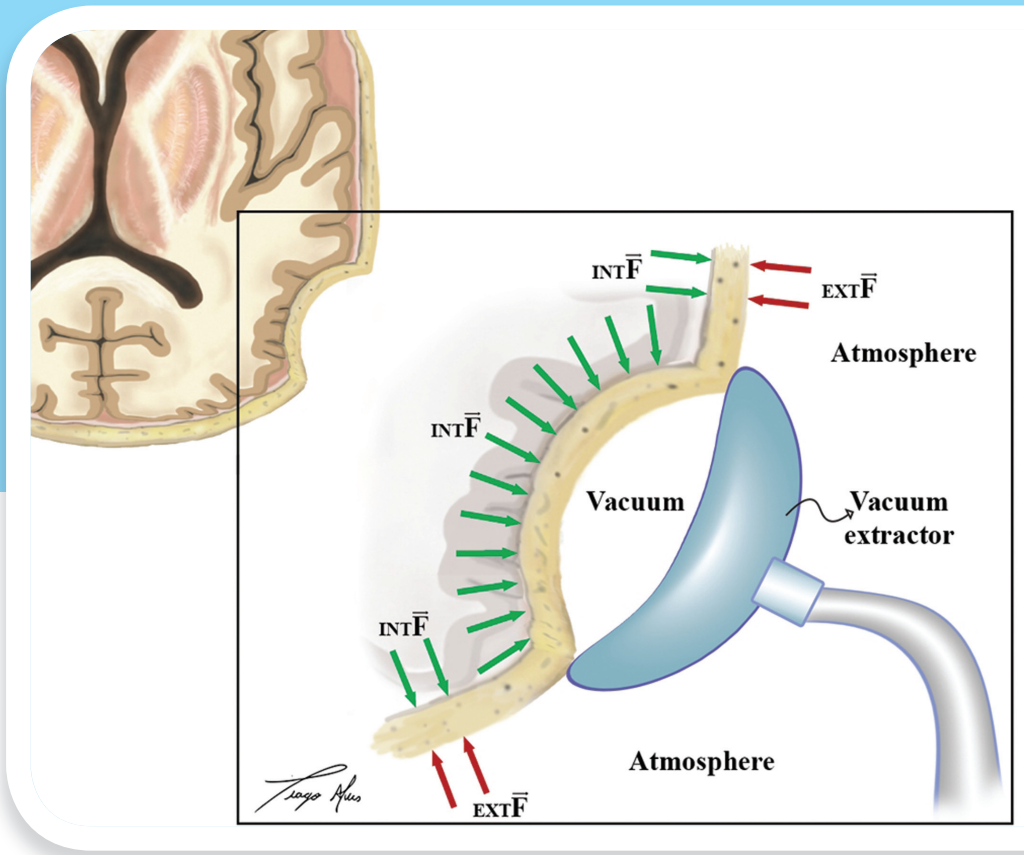
ISSN 0103-5355

Brazilian Neurosurgery

Arquivos Brasileiros de Neurocirurgia

Number 3 • Volume 40 • Pages 207–296 • September 2021



SBN
Sociedade Brasileira de Neurocirurgia

OPEN ACCESS

CELEBRATING 40 VOLUMES

Thieme

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Volume 40, Number 3/2021

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Original Articles | Artigos Originais

207 Terson Syndrome: Assessment of 53 Patients with Subarachnoid Hemorrhage by a Ruptured Aneurysm
Síndrome de Terson: avaliação de 53 pacientes com hemorragia subaracnóidea por ruptura de aneurisma
Roney Mendonça Santos, Walter Fagundes

210 Surgical Treatment of Carotid-cavernous Fistula Performed through the Brazilian Unified Health System
Tratamento cirúrgico de fístula carotídeo-cavernosa realizado por meio do Sistema Único de Saúde
Ilanna Sobral de Luna, Airan Lobo da Costa

215 Epidemiological Profile of Surgically-Treated Peripheral-Nerve Diseases
Perfil epidemiológico das doenças de nervos periféricos tratadas cirurgicamente
Helen Kerlen Bastos Fuzari, Armèle Dornelas de Andrade, Renata Janaina Pereira de Souza, Silvya Nery Bernardino, Fernando Henrique Moraes de Souza, Antonio Sarmento, Daniella Araújo de Oliveira

222 Hypoglossal-Facial Anastomosis for Facial Nerve Reconstruction: Outcomes using the Side-to-End Surgical Technique
Anastomose Hipoglosso-Facial para reanimação do nervo facial: Resultados da técnica término-lateral
Leonardo Gilmone Ruschel, Joel Sanabria Duarte, Jonathan De La Cruz, Kristel Back Merida, Gustavo Fabiano Nogueira, Matheus Fernandes de Oliveira, Ricardo Ramina

Review Article | Artigo de Revisão

229 Dorsal Root Entry Zone Lesioning: Systematic Review
Lesionamento da zona de entrada da raiz dorsal: Revisão sistemática
Giovanna Zambo Galafassi, Paulo Henrique Pires Aguiar, André Akira Takahashi, Jorge Roberto Pagura

238 Surgical Treatment for Spasticity: Selective Dorsal Rhizotomy – Technique and Literature Review
Tratamento cirúrgico para espasticidade: Rizotomia dorsal seletiva – Técnica e revisão da literatura
Marcos Paulo dos Santos Teixeira, Bernardo Assumpção de Monaco, Jessie Medeiros de Navarro, Emmanuel Alejandro Vazquez, Arthur José Maia Lopes, Thais Cristina de Souza Melo, Manoel Jacobsen Teixeira

245 Traumatic Dissection of Arterial Cervical Vessels: Report of Two Cases and Literature Review
Dissecção arterial traumática de vasos craniocervicais: Relato de casos e revisão da literatura
Guilherme Finger, Tobias Ludwig do Nascimento, Julia Carolina Lusa Tessaro, Eduarda Tanus Stefani, Maria Eduarda Conte Gripa, Eduardo Ekman Tisbierek, Luiz Carlos Porcello Marrone, Carla Bittencourt Rynkowski

253 Brain Tumor Heterogeneity
Heterogeneidade dos tumores cerebrais
Telmo Augusto Barba Belsuzarri, Maick Willen Fernandes Neves, Otávio Augusto da Costa, Diego Alves Soares, Fernando Antônio de Melo Filho, Mariana Mazzuia Guimarães, Tiago Fernandes Gonçales, Wolnei Marques Zeviani, João Flávio Mattos Araújo

Case Reports | Relatos de Caso

257 Rare Case of Young Patient with Intraventricular Angiomatous Meningioma
Caso raro de paciente jovem com meningioma angiomatoso intraventricular
Gabriel Carvalho Heemann, Rafael Silva Paglioli, Ricardo Chmelnitsky Wainberg

Thieme Revinter Publicações Ltda

online www.thieme-connect.com/products

263 Use of Vacuum-suction in Depressed Skull Fractures – Case Report and Technical Nuances of Nonoperative Treatment
Uso da vácuo-sucção nas fraturas em afundamento – Relato de caso e aspectos técnicos do tratamento não-operatório
Rodrigo Moreira Faleiro, Sérgio Cavalheiro, João Tiago Alves Belo, Vítor Vieira de Souza Moraes, Aieska Kellen Dantas dos Santos, Ellano de Brito Pontes, Rodrigo de Oliveira Teixeira, Aretha Miranda Silva, Nathalia Lacerda Eller Costa

268 Remarkable Clinical Improvement Following Microsurgical Resection of Left Lingual Gyrus Cerebral Cavernous Malformation: A Case Report
Samer S. Hoz, Zahraa F. Al-Sharshahi, Mustafa M. Altaweel, Saja A. Albanaa

272 Progressive Cerebral Arteriopathy – Moyamoya Disease: A Report of Two Cases with Different Clinical Presentation
Arteriopatia progressiva cerebral – Doença de moyamoya: Relato de dois casos com apresentações clínicas distintas
Marx Lima de Barros-Araújo, Tibério Silva Borges dos Santos, Irapuá Ferreira Ricarte, Guilherme Victor Sousa Medeiros, Joemir Jabson da Conceição Brito, Stephany Vargas Guindani, Larissa Clementino Leite de Sá Carvalho

277 Sarcoidosis Mimicking Skull Base Meningioma
Sarcoidose mimetizando meningioma na base do crânio
Jennyfer Paulla Galdino Chaves, Carlos Alberto Mattozo, Adriano Keijiro Maeda, Luciane Filla, Aline Kelly de Cezaro Piva, Thiago Suzuki, Larissa Luvison Gomes da Silva, Alexandre Novicki Francisco

280 Brain Abscess Caused by Nocardia: Case Report and Literature Review
Abscesso Cerebral causado por Nocardia: Relato de Caso e Revis –ao da Literatura
Guilherme Finger, Maria Eduarda Conte Gripa, Tiago Paczko Bozko Cecchini, Tobias Ludwig do Nascimento

284 Microsurgical Resection of Glioblastoma in a Patient Infected with Covid-19: A Case Report
Ressecção microcirúrgica de glioblastoma em um paciente infectado com COVID-19: Relato de caso
Lívio Pereira de Macêdo, Kauê Franke, Auricélio Batista Cezar-Junior, Igor Vilela Faquini, Eduardo Vieira de Carvalho Júnior, Nivaldo S. Almeida, Hildo Rocha Cirne Azevedo-Filho

Technical Note | Nota Técnica

288 Minimally Invasive Mini-orbitozygomatic Approach for Clipping an Anterior Communicating Artery Aneurysm: Virtual Reality Surgical Planning
Abordagem mini-orbitozigomático minimamente invasiva para clipagem de um aneurisma da artéria comunicante anterior: planejamento cirúrgico de realidade virtual
Nicolás González Romo, Franco Ravera Zunino

Letters to the Editor | Cartas para o editor

294 Author university affiliation
Apio Antunes

295 Cavernous sinus triangles – correlation between cranial and endonasal visualization
Gustavo Rassier Isolan, Francisco Braga, Ricardo Lopes de Araújo

The colored content of this issue is available online at www.thieme.com/bns.

Cover design: © Thieme
Cover image source: © Sociedade Brasileira de Neurocirurgia
(Faleiro RM, Cavalheiro S, Belo JTA, Moraes VVS, Santos AKD, Pontes EB, Teixeira RO, Silva AM, Costa NLE. Use of Vacuum-suction in Depressed Skull Fractures – Case Report and Technical Nuances of Nonoperative Treatment Arq Bras Neurocir 2021; 40(3):263–267)

 Arquivos Brasileiros de Neurocirurgia is published four times a year in March, June, September, and December by Thieme-Revinter Publicações Ltda, Rua do Matoso, 170, Rio de Janeiro, 20270-135, Brazil.

Editorial comments should be sent to **journals@thieme.com**. Articles may be submitted to this journal on an open-access basis. For further information, please send an e-mail to openaccess@thieme.com. The content of this journal is available online at **www.thieme-connect.com/products**. Visit our Web site at **www.thieme.com** and the direct link to this journal at w**ww.thieme.com/bns**.

Arquivos Brasileiros de Neurocirurgia is an official publication of the Brazilian Neurosurgery Society (Sociedade Brasileira de Neurocirurgia) and the Portuguese Language Neurosurgery Societies. It is listed in LILACS and LILACS-Express (Latin-American and Caribbean Center on Health Sciencies Information), and Latindex (Regional Cooperative Online Information System for Scholarly Journals from Latin America, the Caribbean, Spain and Portugal). Thieme Medical Publishers is a member of the CrossRef initiative.

ISSN 0103-5355

Terson Syndrome: Assessment of 53 Patients with Subarachnoid Hemorrhage by a Ruptured Aneurysm

Síndrome de Terson: avaliação de 53 pacientes com hemorragia subaracnóidea por ruptura de aneurisma

Roney Mendonça Santos[1] Walter Fagundes[1]

[1] Multivix, Vitória, ES, Brazil

Arq Bras Neurocir 2021;40(3):e207–e209.

Address for correspondence Roney Mendonça Santos, Multivix, rua José Alves, 301, Goiabeiras, Vitória, ES, Brazil. CEP: 29075-053 (e-mail: roneymendonca@outlook.com).

Abstract

Objective Terson syndrome (TS), also known as vitreous hemorrhage, is reported in patients with subarachnoid hemorrhage caused by a ruptured aneurysm. This study aims to evaluate the presence of ocular hemorrhage in such patients, trying to identify those who could benefit from the specific treatment for visual deficit recovery.

Methods Prospective study of 53 patients with spontaneous subarachnoid hemorrhage (SSAH) due to ruptured aneurysm. The patients were evaluated for vitreous hemorrhage through indirect fundoscopy with 6 to 12 months of follow-up.

Results The ages of the patients ranged from 17 to 79 years-old (mean age, 45.9 ± 11.7); 39 patients were female (73%) and 14 were male (27%). Six patients (11%) presented TS, and 83.3% had a transient loss of consciousness during ictus.

Conclusions An ophthalmologic evaluation must be routinely performed in subarachnoid hemorrhage patients, especially in those with worse neurological grade. Moreover, prognosis was bad in TS patients.

Keywords
- spontaneous subarachnoid hemorrhage
- aneurysm
- vitreous hemorrhage

Resumo

Objetivo A síndrome de Terson (ST), também conhecida como hemorragia vítrea, tem sido relatada em pacientes com hemorragia subaracnóidea por ruptura de aneurisma. O presente estudo tem por objetivo avaliar a presença de hemorragia ocular em tais pacientes, visando identificar os que se beneficiariam com o tratamento específico para recuperação do déficit visual.

Métodos Foram estudados, prospectivamente, 53 pacientes com hemorragia subaracnóidea espontânea (HSAE) por ruptura de aneurisma, em relação à presença de hemorragia vítrea, através de fundoscopia indireta, com seguimento de 6 a 12 meses.

Resultados As idades dos pacientes variaram de 17 a 79 anos (média 45,9 ± 11,7), sendo que 39 pacientes (73%) eram mulheres, e 14, homens (27%). Observou-se que 6 pacientes (11%) apresentavam ST, sendo que 83,3% tiveram perda de consciência transitória durante o íctus.

Conclusão A avaliação oftalmológica deve ser realizada rotineiramente nos pacientes portadores de HSAE, especialmente naqueles com pior grau neurológico. Além disso, os pacientes portadores da ST apresentaram pior prognóstico.

Palavras-chave
- hemorragia subaracnóidea espontânea
- aneurisma
- hemorragia vítrea

received
November 28, 2016
accepted
March 16, 2017
published online
May 8, 2017

DOI https://doi.org/10.1055/s-0037-1603105.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

The first case reported in the literature showing an association between vitreous hemorrhage and subarachnoid hemorrhage occurred in 1881, and it was described by a German ophthalmologist.[1] In 1900, French ophthalmologist Albert Terson reported a case of vitreous hemorrhage associated with spontaneous subarachnoid hemorrhage (SSAH).[2,3] Dupuy-Dutemps (1926) named the bleeding of the vitreous body following SSAH by a ruptured cerebral aneurysm Terson syndrome (TS).[4]

The incidence of TS in several studies can range from 3 to 33% of SSAH cases.[3] However, up to 1950, only 16 cases of this syndrome were reported in the literature.[2] Therefore, we believe that it is reasonable to assume that this condition has been underdiagnosed.

According to statistics from the United States, the mean incidence of SSAH from a ruptured aneurysm is 30,000 cases per year.[5] Based on an average ST incidence of 10%, there would be around 3,000 cases per year. Projecting such numbers to Brazil, there would be ~15,000 cases of SSAH annually and 1,500 cases of TS per year. The objective of the present study is to evaluate the incidence of vitreous hemorrhage in patients with SSAH due a ruptured aneurysm, its evolution and relation to prognosis, as well as the evolution from an ophthalmological point of view, especially regarding the need for specific treatment.

Casuistry and Methods

Fifty-three consecutive patients with SSAH due a ruptured aneurysm were evaluated; all patients were treated at the neurology and neurosurgery department of Santa Casa, Belo Horizonte, Brazil, from March 1997 to December 2003. Patients with SSAH without angiographic evidence of aneurysm and those who died prior to the ophthalmologic evaluation were excluded from the study.

All patients underwent a computed tomography (CT) of the head and/or a lumbar puncture followed by cerebral angiography with four vessels visualization. The neurological evaluation included Fischer, Hunt-Hess and Glasgow scales. The ophthalmologic examination consisted of indirect fundoscopy performed by an ophthalmologist and an ocular ultrasound in selected cases. Follow-up ranged from 6 months to 1 year, evaluating the presence or absence of unilateral or bilateral focal deficit and visual complaints.

Statistical analysis was performed using the Student *t*-tests and chi-square tests with a Cornfield confidence limit of 95%.

Results

From the 53 studied patients, 39 were women (73%) and 14 were men (27%). Vitreous hemorrhage occurred in 6 cases (11%), retinal hemorrhage in 6 (11%), and other alterations in fundoscopy were observed in 15 patients (28%). As for the loss of consciousness during ictus, 83.3% of the patients with vitreous hemorrhage presented a period of unconsciousness against 56.2% of the patients from the general group ($p < 0.05$).

The amount of blood at head CT, assessed with the Fischer scale, and the clinical neurological score, based on the Glasgow and Hunt-Hess coma scales, did not differ statistically between the groups with or without vitreous hemorrhage. Regarding the location of the aneurysms in the general group, 44 cases were at the anterior circulation (93.6%), and three at posterior circulation (6.4%). All patients with vitreous hemorrhage had an anterior circulation aneurysm.

Morbidity, that is, presence of focal deficits, was 21% in the general group and 33% in the TS group, while mortality was 15% and 17%, respectively ($p < 0.05$). Five of the TS cases were unilateral, whereas one was bilateral. Only four patients (67%) had visual complaints. Five patients presented spontaneous resolution of vitreous hemorrhage, and only one required specific treatment, a vitrectomy, with visual deficits recovery.

Discussion

Terson syndrome is common, occurring in 20% of SSAH cases.[6] However, the pathophysiology of TS is not fully understood.[1] Subarachnoid hemorrhage was initially thought to accompany the optic nerve, rupturing the cryptic lamina and reaching the vitreous body.[5] Electron microscopy studies negate this hypothesis by demonstrating that there is no continuity relationship between the subarachnoid space and the vitreous body.[2] Another theory on the cause of vitreous hemorrhage states that it occurs due to blood infusion through the subarachnoid space, compressing the central retinal vein, resulting in its engorgement and rupture.[7] Anatomical studies have shown that when the cavernous sinus or even the central retinal vein is occluded, there is no significant increase in venous pressure or rupture, because there are communicating venous branches, choroidal anastomoses, which drain the venous circulation of the eye.[2] More recent theories postulate that the sudden increase in intracranial pressure, both in SSAH and some other conditions, would cause an infusion of cerebrospinal fluid (CSF) through the optic nerve sheath, with consequent compression of the central retinal vein and its anastomoses, resulting in their rupture and vitreous hemorrhage.[1] This theory would explain the higher incidence of ictal loss of consciousness in SSAH in patients with TS, since this loss of consciousness seems to be associated with a greater increase in intracranial pressure and a transient interruption of the cerebral blood flow during bleeding.

It has also been shown that patients with worse clinical status after SSAH have an increased incidence of TS.[8] Despite this, there appears to be no difference in the amount of blood at head CT between the two groups or in Glasgow and Hunt-Hess coma scales scores, contrary to the literature.[7] This suggests that the main mechanism of injury is the sudden intracranial pressure increase, not blood.[9]

Regarding the evolution of vitreous hemorrhage, most cases (80%) improve spontaneously, not requiring specific treatment, which may vary from vitrectomy to laser use.[7]

Conclusion

Based on the presented data, we suggest the routine performance of an ophthalmologic evaluation in patients with SSAH, especially those with severe neurological status, with or without visual complaints, since they have a worse prognosis and a higher mortality rate.

There was no relationship between the location of the aneurysm, the amount of blood at head CT and vitreous hemorrhage.

In addition, patients with TS should be observed for at least 6 months prior to vitrectomy, since most of them present spontaneous resolution of the condition.

Conflict of Interest

The authors have no conflicts of interest to report.

References

1 Medele RJ, Stummer W, Mueller AJ, Steiger HJ, Reulen HJ. Terson's syndrome in subarachnoid hemorrhage and severe brain injury accompanied by acutely raised intracranial pressure. J Neurosurg 1998;88(05):851–854

2 Garfinkle AM, Danys IR, Nicolle DA, Colohan AR, Brem S. Terson's syndrome: a reversible cause of blindness following subarachnoid hemorrhage. J Neurosurg 1992;76(05):766–771

3 van Rens GH, Bos PJ, van Dalen JT. Vitrectomy in two cases of bilateral Terson syndrome. Doc Ophthalmol 1983;56(1-2):155–159

4 Terson A. Le syndrome de l'hematome du corps vitrè et de l'hèmorragia intracranienne spontanès. Ann Ocul (Paris) 1926; 163:663–673

5 Frizzell RT, Kuhn F, Morris R, Quinn C, Fisher WS III. Screening for ocular hemorrhages in patients with ruptured cerebral aneurysms: a prospective study of 99 patients. Neurosurgery 1997;41 (03):529–533, discussion 533–534

6 Muller PJ, Deck JHN. Intraocular and optic nerve sheath hemorrhage in cases of sudden intracranial hypertension. J Neurosurg 1974;41(02):160–166

7 Clarkson JG, Flynn HW Jr, Daily MJ. Vitrectomy in Terson's syndrome. Am J Ophthalmol 1980;90(04):549–552

8 Terson A. l'hemorrhagie dans le corps vitrè au cours de l'hèmorrhagie cèrèbrale. La Clinique Ophtalmologique 1900;22:309–312

9 Ballantyne AJ. The ocular manifestations of spontaneous subarachnoid hemorrhage. Br J Ophthalmol 1943;27(09):383–414

Surgical Treatment of Carotid-cavernous Fistula Performed through the Brazilian Unified Health System

Tratamento cirúrgico de fístula carotídeo-cavernosa realizado por meio do Sistema Único de Saúde

Ilanna Sobral de Luna[1] Airan Lobo da Costa[2]

[1] Departament of Neurology, Faculdade de Medicina, Universidade do Oeste Paulista, Presidente Prudente, São Paulo, Brazil
[2] Departament of Neurology, Faculdade de Medicina, Universidade do Oeste Paulista, São Paulo, São Paulo, Brazil

Address for correspondence Ilanna Sobral de Luna, Faculdade de Medicina, Departament of Neurology, Universidade do Oeste Paulista, Rua José Bongiovani, 700 - Cidade Universitária, Presidente Prudente, São Paulo, Brazil (e-mail: ilaanna_sobral@hotmail.com).

Arq Bras Neurocir 2021;40(3):e210–e214.

Abstract

Introduction The carotid-cavernous fistula (CCF) is an abnormal communication between the arterial carotid system and the cavernous sinus. In most cases, spontaneous fistulas are due to the rupture of intracavernous carotid artery aneurisms. Traumatic fistulas occur in 0.2% of head injuries, and 75% of all CCFs are caused by automobile accidents or penetrating traumas.

Objective To identify the data regarding the number of annual procedures, hospital expenses, length of hospital stay, and the number of deaths of patients admitted by the Brazilian Unified Health System (SUS, in the Portuguese acronym), in the period between 2007 and 2017, using the surgical code of the surgical treatment for CCF.

Methods The present was an ecological study whose data were obtained by consulting the database provided by the Department of Computer Sciences of the Brazilian Unified Health System (Datasus, in Portuguese).

Results A total of 85 surgical procedures were performed for the treatment of CCFs from January 2007 to October 2017 through the Unified Health System (SUS, in Portuguese), and there was a reduction of 71.42% in this period. The annual incidence of patients undergoing this surgical treatment during the period observed remained low, with 1 case per 13,135,714 in 2007, and 1 case per 51,925,000 in 2017.

Conclusion Despite the low annual incidence of the surgical treatment of CCFs performed by the SUS in Brazil in the period of 2007–2017, based on the data obtained on the average length of stay and expenditures in hospital services, it is necessary that we develop an adequate health planning.

Keywords
- carotid-cavernous fistula
- Brazilian unified health system
- health care

Resumo

Introdução A fístula carotídeo-cavernosa (FCC) é uma comunicação anormal entre o sistema carotídeo e o seio cavernoso. Na maioria dos casos, as fístulas espontâneas ocorrem por ruptura de aneurismas intracavernosos da artéria carótida interna. As fístulas traumáticas ocorrem em cerca de 0,2% dos traumatismos cranioencefálicos,

received
January 5, 2017
accepted
April 24, 2017
published online
June 21, 2018

DOI https://doi.org/10.1055/s-0038-1657775.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

sendo que 75% de todas as FCCs são causadas por traumas penetrantes ou acidentes automobilísticos.

Objetivo Identificar os dados a respeito do número de procedimentos anuais, os gastos hospitalares, o tempo de internação, e o número de óbitos dos pacientes admitidos pelo Sistema Único de Saúde (SUS), no período de 2007 a 2017, utilizando o código cirúrgico de tratamento cirúrgico de FCC.

Métodos Trata-se de um estudo ecológico, cujos dados foram obtidos por meio de consulta à base de dados disponibilizada pelo Departamento de Informática do SUS (Datasus).

Resultados Foram realizados 85 procedimentos cirúrgicos para tratamento de FCC de janeiro de 2007 a outubro de 2017 por meio do SUS, e ocorreu uma redução de 71,42% neste período. A incidência anual dos pacientes submetidos a este tratamento cirúrgico durante o período observado continuou baixa, apresentando 1 caso para cada 13.135.714 em 2007, e 1 caso para cada 51.925.000 em 2017.

Conclusão Apesar da incidência anual do tratamento cirúrgico de FCC realizado pelo SUS no Brasil no período de 2007 a 2017 ter sido baixa, a partir dos dados obtidos sobre a média de permanência e gastos em serviços hospitalares, é necessário um planejamento adequado em saúde.

Palavras-chave
- fístula carotídeo-cavernosa
- sistema único de saúde
- assistência à saúde

Introduction

Carotid-cavernous fistula (CCF) is an abnormal communication between the carotid system and the cavernous sinus.[1] It is classified according to the etiology as traumatic or spontaneous; according to hemodynamic characteristics, it is classified as high- or low-flow; and depending on the angioarchitecture, it is classified as direct or indirect.[2] In most cases, spontaneous fistulas occur by rupture of intracavernous aneurysms of the internal carotid artery. Traumatic fistulas occur in $\sim$ 0.2% of cranioencephalic traumas, and 75% of all CCFs are caused by penetrating traumas or automobile accidents.[3,4]

The signs and symptoms often associated with CCFs vary in installation speed and severity.[5,6] They are: pulsatile exophthalmos, pulsatile proptosis, Dandy triad, which consists of blowing and venular dilation with chemosis, diplopia, and dysfunctions of cranial nerve pairs III and V; and, in 85% of the cases, dysfunction of cranial nerve pair IV.[7]

For the initial imaging diagnosis when there is suspicion of CCF, computed tomography (CT), magnetic resonance imaging (MRI), angiography by CT, angiography by MRI, or Doppler are requested.[8,9] However, cerebral angiography is presented as a gold standard for the diagnosis, classification and definitive planning of the endovascular intervention due to the identification of the type, location and size of the connection, as well as the analysis of the arteriovenous environment and the presence of coexistent deviations, mainly ischemic repercussions on the cortex. The differential diagnosis encompasses a vast field of pathologies, including intraorbital lesions such as osteoma, hemangioma, fibrous dysplasia, frontal sinus mucocele and ocular neoplasms.[10]

The management of the patient with CCF depends on the risks, and can be performed conservatively, consisting of drug treatment and manual compression therapy, surgical treatment, stereotactic radiosurgery, and transarterial or transvenous endovascular repair.[11] The surgical approaches are limited because of the associated morbidity of cranial nerve deficits and residual fistulae communications, but are indicated when the proximal arterial access is compromised, preventing endovascular repair, or when failures occur by this method.[12] The approaches may be: ligature of the common carotid artery, surgical segmental isolation of the fistula, and surgical transvenous tamponade. Currently, endovascular therapy is the procedure of choice for CCFs.[13] Some authors advocate treatment at an early stage, especially with the emergence of intracranial hemorrhage, epistaxis, increased intraocular pressure, reduction of visual acuity or progressive proptosis. Carotid-cavernous fistulas may evolve to complications such as amaurosis, intracerebral hemorrhage, hypertension, cranial nerve palsy, and subarachnoid hemorrhage.[14,15]

Objective

The goal of the present study is to identify epidemiological data regarding the number of annual procedures, hospital expenses, length of stay and number of deaths of patients admitted by the Brazilian Unified Health System (SUS, in Portuguese) in the period from 2007 to 2017 using the surgical code of surgical treatment for CCF.

Methods

This is an ecological study, whose data were obtained by consulting the database provided by the Department of Computer Sciences of the SUS (Datasus) (http://www.datasus.gov.br), which was accessed from October to December 2017. The study sample consisted of all cases of patients undergoing surgical treatment for CCF (code 0403070090) from January 2007 to October 2017. New tables were made based on the data obtained through the Datasus using the

Table 1 Total distribution of the number of surgeries for the treatment of carotid-cavernous fistula from 2007 to 2017 in the Unified Health System

Processed year	Total AHs	%
2007	14	16.47
2008	16	18.82
2009	6	7.06
2010	9	10.59
2011	4	4.71
2012	10	11.76
2013	2	2.35
2014	11	12.94
2015	3	3.53
2016	6	7.06
2017	4	4.71
Total	85	100

Abbreviation: AHs, authorizations for hospitalization.
Note: Source: Ministério da Saúde - Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH/SUS).

Table 2 Annual Incidence of patients who underwent surgical treatment for carotid-cavernous fistula from 2007 to 2017 in the Unified Health System

Processed year	Total AHs	Brazilian population (millions)	Incidence
2007	14	183.9	1: 13,135,714
2008	16	189.6	1: 11,850,000
2009	6	190.7	1: 31,783,333
2010	9	191.4	1: 21,266,666
2011	4	192.3	1: 48,075,000
2012	10	193.9	1: 19,390,000
2013	2	201.1	1: 19,390,000
2014	11	202.7	1: 18,427,272
2015	3	204.4	1: 68,133,333
2016	6	206.0	1: 34,333,333
2017	4	207.7	1: 51,925,000

Abbreviation: AHs, authorizations for hospitalization.
Note: Source: Ministério da Saúde - Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH/SUS).

Microsoft Word (Microsoft Corporation, Redmond, WA, US) software. Since a public domain bank was used to obtain the data, submission of the project to the Research Ethics Committee was not necessary.

Results

►**Table 1** presents the data referring to the surgical treatment of CCF from January 2007 to October 2017. Out of 85 surgeries, 16 occurred in 2008, the year that had the highest number of cases, representing 18.82% of the total. Comparing the years 2007 and 2017, a decrease of 10 procedures was observed.

In a comparative analysis between the number of procedures in this same period and the Brazilian population, it was possible to notice that, even with the population increase, the annual incidence of patients undergoing this surgical treatment remained low: 1 case for each 13,135,714 in 2007, and 1 case for each 51,925,000 in 2017, as represented in ►**Table 2**.

Regarding the analysis by region, quantitatively, most surgeries occurred in the Southeastern region of Brazil. There were 33 procedures, representing 44.71% of the total. As observed in ►**Table 3**, the Northern region presented the smallest number of surgeries in the period, with 1 procedure, totaling 1.18%.

As evidenced in ►**Table 4**, the mean value of the procedure in 2007 was R$3,078.32, and R$2,463.61 in 2017, representing a decrease of 19.9%. In the same period, the value of hospital and professional services suffered a reduction in expenses of 25.43% and 58.77% respectively.

Table 3 Distribution by region of the number of surgeries for the treatment of carotid-cavernous fistula from 2007 to 2017 in the Unified Health System

Region	Number	%
Northern	1	1.18
Northeastern	16	18.82
Southern	16	18.82
Southeastern	38	44.71
Midwestern	14	16.47
Total	85	100

Note: Source: Ministério da Saúde - Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH/SUS).

In turn, ►**Table 5** highlights the data regarding the average length of stay in the hospital, as well as the number of deaths. The year with the highest average length of stay was 2014, and there was a variation of 9.8 days between 2007 and 2017. In relation to the number of deaths, they were only reported in 2008, 2012 and 2016.

Discussion

In total, 85 surgical procedures were performed for the treatment of CCF from January 2007 to October 2017 through the SUS, and there was a 71.42% reduction in the number of procedures performed in this period. The endovascular emergency treatment of CCF is reserved for some specific situations, such as in the presence of pseudoaneurysms and increased intracranial pressure. The neuroendovascular

Table 4 Distribution of costs in *reais* (R$) resulting from surgeries for the treatment of carotid-cavernous fistulas from 2007 to 2017 in the Unified Health System

Processed year	Total value (R$)	Mean value (R$)	Value of hospital services (R$)	Value of professional services (R$)
2007	43,096.48	3,078.32	23,116.00	6,760.84
2008	47,783.37	2,986.46	37,318.15	10,465.22
2009	21,628.94	3,604.82	17,097.56	4,531.38
2010	21,768.00	2,418.67	15,273.93	6,494.07
2011	12,587.41	3,146.85	8,880.99	3,706.42
2012	38,547.97	3,854.80	27,847.95	10,700.02
2013	6,189.88	3,094.94	4,222.48	1,967.40
2014	33,170.38	3,015.49	22,707.86	10,462.52
2015	7,641.86	2,547.29	4,811.61	2,830.25
2016	28,954.33	4,825.72	22,022.78	6,931.55
2017	9,854.46	2,463.61	5,880.63	3,973.83

Note: Source: Ministério da Saúde - Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH/SUS).

Table 5 Average distribution of days of hospital stay and number of deaths related to surgeries for the treatment of carotid-cavernous fistula from 2007 to 2017 in the Unified Health System

Processed year	Mean stay (days)	Deaths
2007	14.3	–
2008	13.6	1
2009	11.7	–
2010	5.2	–
2011	8.3	–
2012	10.4	1
2013	7.0	–
2014	18.3	–
2015	18.0	–
2016	12.0	1
2017	4.5	–

Note: Source: Ministério da Saúde - Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH/SUS).

treatment is reserved for cases in which the conservative management is ineffective, or before ocular surgical procedures.[16,17] The endovascular (arterial or venous) approach is the current procedure of choice.

The annual incidence of patients undergoing this surgical treatment during the observed period remained low: 1 case for each 1.3135.714 in 2007, and 1 case for each 51,925,000 in 2017. Although it is not a common pathology in the clinical practice, CCF is a diagnostic hypothesis that should be mandatorily proposed when the clinical picture suggestive of it, since it can develop with important complications, such as intracranial hypertension and cerebral hemorrhage.[18,19]

In a quantitative analysis according to the Brazilian geographic regions, most surgeries occurred in the Southeastern region, with a total of 44.71%. The Northern region presented the smallest number of surgeries, with a total of 1.18%. The population density, the type of work activity, the patient's access to health services, and the ability of the health professional to recognize the pathology are some of the factors responsible for the differences observed among the Brazilian regions, which have socioeconomic characteristics that distinguish the reality of health care.[20]

Comparatively, between 2007 and 2017, there was a reduction in expenditure in SUS services. There was a decrease of 19.9% in the mean value, and a reduction in expenses with hospital services and professionals of 25.43% and 58.77% respectively. The surgical correction of arteriovenous fistulas frequently required large procedures, such as occipital or temporal craniotomy in cases of involvement of the carotid and vertebral arteries. However, with the recent development of catheters and balloons for the treatment of CCFs, the surgeries had their size reduced. Large surgeries are costly for health services, and there is a high probability of fluid and blood loss.[21] With the expansion of the use of new technologies for CCF treatment, the length of hospitalization was minimized, decreasing the treatment costs when compared with open interventions as well as the resulting complications, which also explains the reduction in the number of days in the average length of stay.

Regarding the number of deaths, which was null in most years, the data evidenced that the additional information arising from the evolution and solvability of neuroimaging techniques increase the accuracy and anticipation of the topographic diagnosis and facilitate the therapeutic access, resulting in greater success in the treatment approach.[22]

Conclusion

Despite the low annual incidence of surgical treatment of CCFs performed by the SUS in Brazil in the period from 2007 to 2017, the data obtained on the mean length of stay and

expenses regarding hospital services evidenced the need for a health planning suitable for the Brazilian regions that have the poorest health care indicators regarding this issue, since early diagnosis and neurosurgical intervention in a timely manner promote the reduction of morbidity and mortality.

Conflict of Interests
The authors have none to declare.

References

1 Kim J-W, Kim S-J, Kim M-R. Traumatic carotid-cavernous sinus fistula accompanying abducens nerve (VI) palsy in blowout fractures: missed diagnosis of 'white-eyed shunt'. Int J Oral Maxillofac Surg 2013;42(04):470–473
2 Shinohara Y, Kashima T, Akiyama H, Kishi S. Alteration of choroidal thickness in a case of carotid cavernous fistula: a case report and a review of the literature. BMC Ophthalmol 2013;13(01):75
3 Carneiro JT Jr, Paschoal EHA, Carreira ASD, Real RPV. Carotid cavernous fistula after surgically assisted rapid maxillary expansion with a bone anchored appliance. Int J Oral Maxillofac Surg 2013;42(03):326–328
4 Vilela MAP. Carotid-cavernous fistula. Rev Bras Oftalmol 2013;72 (01):70–75
5 Tanweer O, Raz E, Brunswick A, et al. Cavernous carotid aneurysms in the era of flow diversion: a need to revisit treatment paradigms. AJNR Am J Neuroradiol 2014;35(12):2334–2340
6 Kashiwazaki D, Kuwayama N, Akioka N, Kuroda S. Delayed abducens nerve palsy after transvenous coil embolization for cavernous sinus dural arteriovenous fistulae. Acta Neurochir (Wien) 2014;156(01):97–101
7 Chi CT, Nguyen D, Duc VT, Chau HH, Son VT. Direct traumatic carotid cavernous fistula: angiographic classification and treatment strategies. Study of 172 cases. Interv Neuroradiol 2014;20 (04):461–475
8 Turfe ZA, Brinjikji W, Murad MH, Lanzino G, Cloft HJ, Kallmes DF. Endovascular coiling versus parent artery occlusion for treatment of cavernous carotid aneurysms: a meta-analysis. J Neurointerv Surg 2015;7(04):250–255
9 Linfante I, Lin E, Knott E, Katzen B, Dabus G. Endovascular repair of direct carotid-cavernous fistula in Ehlers-Danlos type IV. J Neurointerv Surg 2015;7(01):e3
10 Barnwell SL, O'Neill OR. Endovascular therapy of carotid cavernous fistulas. Neurosurg Clin N Am 1994;5(03):485–495
11 Xu X-Q, Liu S, Zu Q-Q, et al. Follow-up of 58 traumatic carotid-cavernous fistulas after endovascular detachable-balloon embolization at a single center. J Clin Neurol 2013;9(02):83–90
12 Korchi AM, Cuvinciuc V, Caetano J, Becker M, Lovblad KO, Vargas MI. Imaging of the cavernous sinus lesions. Diagn Interv Imaging 2014;95(09):849–859
13 Chin OY, Ghosh R, Fang CH, Baredes S, Liu JK, Eloy JA. Internal carotid artery injury in endoscopic endonasal surgery: A systematic review. Laryngoscope 2016;126(03):582–590
14 Rodrigues T, Willinsky R, Agid R, TerBrugge K, Krings T. Management of dural carotid cavernous fistulas: a single-centre experience. Eur Radiol 2014;24(12):3051–3058
15 Gölitz P, Struffert T, Lücking H, et al. Parametric color coding of digital subtraction angiography in the evaluation of carotid cavernous fistulas. Clin Neuroradiol 2013;23(02):113–120
16 Chen C-J, Lee C-C, Ding D, et al. Stereotactic radiosurgery for intracranial dural arteriovenous fistulas: a systematic review. J Neurosurg 2015;122(02):353–362
17 Ducruet AF, Albuquerque FC, Crowley RW, McDougall CG. The evolution of endovascular treatment of carotid cavernous fistulas: a single-center experience. World Neurosurg 2013;80(05): 538–548
18 Luo C-B, Teng MM-H, Chang F-C, Lin C-J, Guo W-Y, Chang C-Y. Transarterial detachable coil embolization of direct carotid-cavernous fistula: immediate and long-term outcomes. J Chin Med Assoc 2013;76(01):31–36
19 Lin L-M, Colby GP, Jiang B, Pero G, Boccardi E, Coon AL. Transvenous approach for the treatment of direct carotid cavernous fistula following Pipeline embolization of cavernous carotid aneurysm: a report of two cases and review of the literature. J Neurointerv Surg 2015;7(08):e30
20 Tomasi E, Facchini LA, Piccini RX, et al. Perfil sócio-demográfico e epidemiológico dos trabalhadores da atenção básica à saúde nas regiões Sul e Nordeste do Brasil. Cad Saude Publica 2008;24(01): 193–201
21 Kim MJ, Shin YS, Ihn YK, et al. Transvenous embolization of cavernous and paracavernousdural arteriovenous fistula through the facial vein: report of 12 cases. Neurointervention 2013;8(01):15–22
22 Borba R, Sonda I, Dini LI, Calcagnotto FN, Marchett N, Cobalchini PC. Fístula carótido-cavernosa com epistaxe letal: relato de caso. Arq Neuropsiquiatr 2001;59(2-A):276–279

Epidemiological Profile of Surgically-Treated Peripheral-Nerve Diseases

Perfil epidemiológico das doenças de nervos periféricos tratadas cirurgicamente

Helen Kerlen Bastos Fuzari[1,2] Armèle Dornelas de Andrade[2] Renata Janaina Pereira de Souza[2] Silvya Nery Bernardino[3] Fernando Henrique Moraes de Souza[4] Antonio Sarmento[2] Daniella Araújo de Oliveira[1,2]

[1] Programa de Neuropsiquiatria e Ciências do Comportamento (POSNEURO), Universidade Federal de Pernambuco (UFPE), Recife, PE, Brazil
[2] Department of Physiotherapy, Universidade Federal de Pernambuco (UFPE), Recife, PE, Brazil
[3] Hospital Getúlio Vargas, Recife, PE, Brazil
[4] Hospital da Restauração, Recife, PE, Brazil

Address for correspondence Helen Kerlen Bastos Fuzari, Departmento de Fisioterapia, Universidade Federal de Pernambuco, Av. Jornalista Aníbal Fernandes s/n - Cidade Universitária, Recife, PE, 50740-560, Brazil (e-mail: helen.fisio@uol.com.br).

Arq Bras Neurocir 2021;40(3):e215–e221.

Abstract

Objective To outline the epidemiological profile of surgical patients treated at the peripheral-nerve outpatient clinic of a public hospital in the state of Pernambuco, Brazil, from 2008 (the year this service was implemented in the hospital) to 2016.

Material and Methods A cross-sectional study with data collection from the medical records. A descriptive analysis was performed with the qualitative variables presented as relative and absolute frequencies, and the quantitative variables, as means and standard deviations. The studied variables were gender, age, diagnosis, and surgical techniques.

Results In total, 506 medical records were analyzed. Of these, 269 were of male patients (53%), and 238 were of female patients (46%). The age of the sample ranged from 5 to 84 years (41 $\pm$ 14 years). The most prevalent diagnoses were: carpal tunnel syndrome (38.9%) followed by traumatic brachial plexus injury (33.2%). The first diagnosis was more frequent among women, while the second, among men. This collaborates with the predominant findings of upper-limb lesions (91%), in which men accounted for 52,75% (244) and women, for 47,25% (217).

Conclusion The present study provided relevant information regarding the reality of peripheral-nerve surgeries performed at a public hospital in the state of Pernambuco, Brazil. Public health issues increasingly require the continuity of public policies and government incentive.

Keywords
- epidemiology
- brachial plexus
- carpal tunnel syndrome

received
May 13, 2020
accepted
August 24, 2020
published online
November 26, 2020

DOI https://doi.org/10.1055/s-0040-1719001.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Objetivo O presente estudo buscou delinear o perfil epidemiológico dos pacientes cirúrgicos atendidos no ambulatório de nervos periféricos de um hospital público de Pernambuco no período de 2008 (ano de implantação deste serviço no hospital) a 2016.

Material e métodos Estudo transversal com coleta de dados em prontuários. Foi realizada análise descritiva, com as variáveis qualitativas apresentadas como frequências relativas e absolutas, e as variáveis quantitativas numéricas, como médias e desvios padrão. As variáveis estudadas foram sexo, idade, diagnóstico, e técnicas cirúrgicas.

Resultados No total, 506 prontuários foram analisados, sendo 269 de pacientes homens (53%) e 238 de pacientes mulheres (46%). A faixa etária variou de 5 a 84 anos (41 ± 14 anos). Os diagnósticos mais prevalentes foram: síndrome do túnel do carpo (38%), seguida por lesão traumática do plexo braquial (33%). O primeiro diagnóstico foi mais frequente entre as mulheres, e o segundo, entre os homens. Isto colabora com os achados predominantes das lesões dos membros superiores (91%), em que os homens representaram 52.75% (244), e as mulheres, 47.25% (217).

Conclusão O presente estudo forneceu informações relevantes sobre a realidade das cirurgias de nervos periféricos realizadas em um hospital público em Pernambuco. Tais problemas de saúde pública precisam cada vez mais da continuidade das políticas públicas e do incentivo do governo.

Palavras-chave

- epidemiologia
- plexo braquial
- síndrome do túnel do carpo

Introduction

Peripheral-nerve lesions have been extensively studied in recent years;[1] however, the diagnosis and treatment are still a challenging problem that requires an appropriate approach, adequate electrodiagnostic and imaging studies, and adequate time for early diagnosis.[2]

Peripheral-nerve diseases range from traumatic lesions (that is, stretching, avulsion, crushing, or compression) to degenerative-infectious conditions. Once damaged, the peripheral nerves may suffer an interruption in the transmission of signals, affecting limb function directly through sensory and motor deficits, or both. In some cases, compression may lead to a better prognosis (such as in cases of radial nerve compression), or surgical interventions, such as in more severe cases (compartmental syndromes in which the nerve is compressed considerably, for example).[3] Moreover, the incidence of individuals with injury to the brachial plexus after automobile accidents has increased considerably, and is considered a public health problem, since it aggravates hospitalization costs and treatments, as well as the labor licenses for those in full working activity.[4]

Rehabilitation after nerve decompression takes time, since it depends on axon regeneration ($\sim$ 1 mm to 5 mm/day in adults).[5] It should also be noted that many factors are determinants in rehabilitation, such as age, cause of the injury, the degree of compression, the time of onset of the problem, and the most appropriate surgery for each case. Notwithstanding, in most cases, referral to a specialist is time-consuming, making some types of procedures impossible.[6] In this sense, outpatient clinics must present sufficient subsidies for accurate semiology and establish the best course of action for each patient. Nevertheless, there is still a lack of complementary tests and continuous rehabilitation to guarantee the success of the procedure in hospital and clinical services.

It is also important to point out that peripheral-nerve outpatient clinics in Brazil are still in development and expansion; thus, a lot must improve.[7] Although the state of Pernambuco (located in Noertheastern Brazil) has one of the main reference centers for peripheral nerve surgery in the Northeast, there is no literature describing its reality. Thus, the present study aimed to trace an epidemiological profile of patients undergoing peripheral-nerve surgeries from 2008 to 2016 in a public hospital in the state of Pernambuco, Brazil.

Materials and Methods

The present is a retrospective study conducted within the confines of the World Medical Association Declaration of Helsinki, and approved by the Ethics and Research Committee of our institution (under number 59986616.9.0000.5208).

The present study was based on a secondary database, and data was collected from the medica records in the second half of 2017 at the Medical and Statistical Archive Service of the peripheral-nerve outpatient clinic of Hospital da Restauração, located in the city of Recife. The inclusion criteria were: medical records containing the description of the clinical diagnosis and the assessments that confirmed it (that is, magnetic resonance imaging and electromyography) from patients of any age submitted to any peripheral-nerve surgery.

The following sociodemographic and clinical data were obtained: age, gender, diagnosis, surgical technique, and the

prevalence of the affected limbs (upper or lower) in each year. For didactic purposes, carpal tunnel syndrome was considered a unique separate group, despite being considered a compressive neuropathy. In addition, the following surgeries were grouped into microsurgery for compressive upper-limb neuropathy because they represented a very small percentage of the sample: interdigital nerve, ulnar in the Guyon canal, and median nerve of the proximal forearm.

Regarding age, normality was conducted using the Kolmogorov-Smirnov test, and the Mann-Whitney test was applied using the Statistical Paclage for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 22. For the qualitative variables, descriptive statistics were conducted and expressed as relative (percentages) and absolute frequencies (n), while for the quantitative variables, means and standard deviations were used.

Results

The sample consisted of 506 records, 268 (52.9%) of which were from male, and 238 (47.1%), from female patients. The age of the sample ranged from 5 to 84 years (41 ± 14 years), and was significantly different regarding gender (male patients: 35 ± 14 years; female patients: 48 ± 12 years; $p < 0.01$). The patients who sought the most care in the peripheral-nerve outpatient clinic were men aged 20 to 29 years (17%) without health insurance. On the other hand, the age range with the highest number of patients was between 30 and 39 years (13.% - 125 patients) (►**Fig. 1**).

Carpal tunnel syndrome was the most diagnosed lesion (38.9% - 197), and it affected more female (34.3% - 174) than male (4.5% - 23) patients. On the other hand, male patients were more affected by traumatic brachial plexus injury (33.2% - 168), followed by compression of the ulnar nerve (9.3% - 47) and sural nerve tumor (4.6% - 23) (►**Table 1**).

An essential point of the present study is related to the large diversity of surgical techniques (►**Table 2**). It can be noted that the diagnoses of 47 patients were listed as compression injury of the ulnar nerve on ►**Table 1**. However, in ►**Table 2**, only 1 submuscular transposition of the ulnar nerve was reposted. As the other 46 (17.9%) cases underwent simple decompression, the patients were classified as microsurgery for compressive upper-limb neuropathy (►**Table 2**). Thus, microsurgery for compressive upper-limb neuropathy (45.67% - 248 of all surgeries; 35.72% - 194 performed in female patients) followed by brachial plexus microsurgery (31.% - 170; 29.28% - 159 performed in male patients) were the most used surgical techniques probably because the only specialized and reference hospital in the state of Pernambuco, for these types of surgery was located in the city of Recife. It is also essential to note that some of the microneurolysis and nerve biopsies were performed due to chronic infectious leprosy disease, with the following main affected nerves: radial, median and ulnar, and facial nerves. From 2008 to 2012, there was an increase in the number of surgeries for carpal tunnel syndrome, followed by a gradual decrease in the subsequent years. On the other hand, the number of traumatic brachial plexus surgeries increased almost 5-fold from 2008 to 2016 (►**Table 3**). It is suggested that other hospitals in the state also absorbed these surgeries.

Given the data, it was possible to calculate the total and partial brachial plexus surgeries performed per year. Out of 18 surgeries (47%), 11 (59%) were for partial plexus lesion and 7 (41%) were for whole plexus lesion. It is worth mentioning that these are medium-sized surgeries that require general anesthesia and are performed according to the demand of the service (►**Table 3**).

As shown in ►**Table 4**, most surgeries were performed in patients between the ages of 20 and 69 years, with the age group of 30 to 39 years presenting a higher number of surgeries. However, the age group of 20 to 29 years presented the highest number of traumatic brachial plexus injuries (61 subjects; 12%), while those with ages between 50 and 59 years presented the highest number of cases of carpal tunnel syndrome (65 subjects; 12.8%). The predominance of upper-limb lesions (91%) was also observed, with males accounting for 52.75% (244), and females, 47.25 (217).

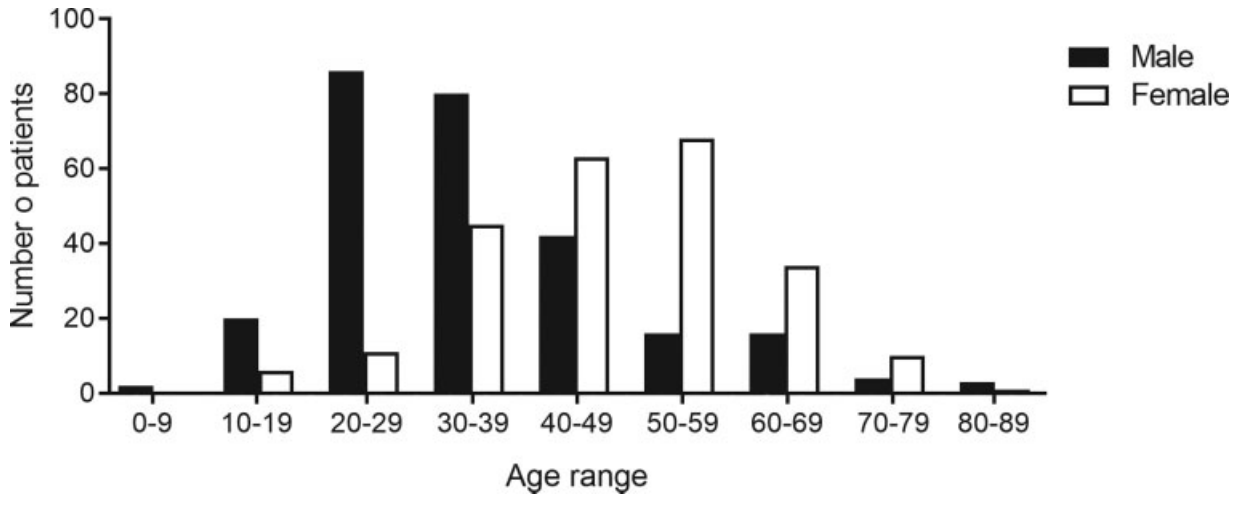


Fig. 1 Distribution by age group and gender of the surgical patients at the peripheral-nerve outpatient clinic from 2008 to 2016.

Table 1 Diagnoses of the study sample according to gender

Diagnosis	ALL	GENDER	
		MALE	FEMALE
	n (%)	n (%)	n (%)
Compressive lesions			
Carpal tunnel syndrome	197 (38.9)	23 (4.5)	174 (34.3)
Compression injury of the ulnar nerve	47 (9.3)	28 (5.5)	19 (3.7)
Compression of the radial nerve	9 (1.8)	7 (1.4)	2 (0.4)
Compressive neuropathy of the median nerve	2 (0.4)	1 (0.2)	1 (0.2)
Traumatic lesions			
Traumatic brachial plexus injury	168 (33.2)	157 (31)	11 (2.2)
Traumatic injury of the tibial nerve	11 (2.2)	6 (1.2)	5 (1)
Facial nerve injury	8 (1.6)	7 (1.4)	1 (0.2)
Fibular nerve injury	8 (1.6)	6 (1.2)	2 (0.4)
Traumatic injury of the median nerve	7 (1.4)	5 (1)	2 (0.4)
Traumatic radial nerve injury	6 (1.2)	5 (1)	1 (0.2)
Traumatic axillary nerve injury	4 (0.8)	2 (0.4)	2 (0.4)
Tumor of the vagus nerve	3 (0.6)	–	3 (0.6)
Traumatic sciatic nerve injury	2 (0.4)	2 (0.4)	–
Traumatic injury by electrical shock of the median nerve	1 (0.2)	1 (0.2)	–
Traumatic ulnar neuroma	1 (0.2)	1 (0.2)	–
Neoplastic lesions			
Sural nerve tumor	23 (4.6)	13 (2.6)	10 (2)
Median nerve tumor on the forearm	4 (0.8)	1 (0.2)	3 (0.6)
Accessory nerve tumor	2 (0.4)	2 (0.4)	–
Median nerve tumor	2 (0.4)	–	2 (0.4)
Supraclavicular lipoma	1 (0.2)	1 (02)	–
TOTAL	**506**	**268 (52.9)**	**238 (47.1)**

Discussion

According to the epidemiological profile of the patients in our sample, there was a predominance of men with traumatic brachial plexus injury and women with carpal tunnel syndrome. In addition, the former affects more subjects between the ages of 20 to 39 years, while the latter, between the ages of 30 and 59 years.

According to the present study, the largest age group seeking peripheral nerve service was between 20 and 29 years (17%). This corroborates the study performed by Flores,[8] which evidenced a predominance of this age group since it is the period in which individuals are in full labor activity. This entails high costs for the health system and a significant socioeconomic impact.[9,10]

Table 2 Types of surgeries performed in Hospital da Restauração according to gender between the years 2008 and 2016

Type of Surgery	ALL	GENDER	
		MALE	FEMALE
	n (%)	n (%)	n (%)
Simple decompression			
Microsurgery for compressive upper-limb neuropathy	248 (45.67)	54 (9.94)	194 (35.72)
Microsurgery of the fibular nerve	8 (1.47)	6 (1.10)	2 (0.37)
Nerve transfer			
Brachial plexus microsurgery	170 (31.3)	159 (29.28)	11 (2.2)
Motor neurotransfer for the lower limbs	4 (0.73)	–	4 (0.73)
Neurotransference from the brachial branch to anterior interosseous nerve	2 (0.37)	2 (0.37)	–
Nerve transposition			
Submuscular transposition of the ulnar nerve	1 (0.18)	1 (0.18)	–
Biopsy			
Sural nerve biopsy for diagnosis	29 (5.34)	19 (3.49)	10 (1.84)
Ulnar dorsal cutaneous nerve biopsy for diagnosis	25 (4.60)	8 (1.47)	17 (3.4)
External neurolysis			
Microneurolysis of the radial nerve	15 (2.76)	15 (2.76)	–
Microneurolysis of the median and ulnar nerves	9 (1.65)	8 (1.47)	1 (0.18)
Femoral nerve microneurolysis	2 (0.37)	–	2 (0.37)
Brachial plexus microneurolysis	1 (0.18)	1 (0.18)	–
Tumor resection			
Microsurgery for median nerve tumor	5 (0.92)	2 (0.37)	3 (0.55)
Microsurgery for accessory nerve tumor	2 (0.37)	2 (0.37)	–
Microsurgery for vagus nerve tumor	2 (0.37)	–	2 (0.37)
Microsurgery for sural nerve tumor by schwannoma	2 (0.37)	1 (0.18)	1 (0.18)
Microsurgery for nerve tumor - malignant lesion	2 (0.37)	–	2 (0.37)
Lipoma resection	1 (0.18)	1 (0.18)	–
Microsurgery for brachial plexus tumor	1 (0.18)	1 (0.18)	–
Reconstruction with graft			
Reconstruction of the axillary nerve with sural graft	4 (0.73)	2 (0.37)	2 (0.37)
Reconstruction of the radial nerve with sural graft	2 (0.37)	1 (0.18)	1 (0.18)
Microneurolysis of the facial nerve	8 (1.47)	6 (1.10)	2 (0.37)
TOTAL	**543**	**289 (53.22)**	**254 (46. 78)**

Table 3 Distribution of diagnoses per year (2008–2016) among the study sample

Diagnosis	Year of Diagnosis								
	2008	2009	2010	2011	2012	2013	2014	2015	2016
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Compressive lesions									
Carpal tunnel syndrome	12 (2.4)	23 (4.5)	31 (6.1)	29 (5.7)	32 (6.3)	29 (5.7)	11 (2.2)	13 (2.6)	17 (3.4)
Compression injury of the ulnar nerve	1 (0.2)	4 (0.8)	7 (1.4)	9 (1.8)	4 (0.8)	7 (1.4)	6 (1.2)	1 (0.2)	8 (1.6)
Compression of the radial nerve	2 (0.4)	–	–	1 (0.2)	2 (0.4)	–	1 (0.2)	2 (0.4)	1 (0.2)
Compressive neuropathy of the median nerve	–	–	–	–	1 (0.2)	–	1 (0.2)	–	–
Traumatic lesions									
Traumatic brachial plexus injury	5 (1.0)	17 (3.4)	17 (3.4)	19 (3.7)	14 (2.8)	22 (4.3)	25 (4.9)	25 (4.9)	24 (4.7)
Total plexus lesion	1(0.2)	7(1.4)	7(1.4)	7(1.4)	5(1.0)	7(1.4)	7(1.4)	7(1,3)	7(1.4)
Partial plexus lesion	4(0.8)	10(2.0)	10(2.0)	12(2.3)	9(1.8)	15(2.9)	18(3.5)	18(3,6)	17(3.3)
Traumatic injury of the tibial nerve	–	–	–	–	2 (0.4)	2 (0.4)	1 (0.2)	3 (0.6)	3 (0.6)
Facial nerve injury	–	–	–	–	–	–	6 (1.2)	2 (0.4)	–
Fibular nerve injury	1 (0.2)	1 (0.2)	2 (0.4)	–	–	–	–	2 (0.4)	2 (0.4)
Traumatic injury of median nerve	1 (0.2)	–	–	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	–
Traumatic radial nerve injury	1 (0.2)	1 (0.2)	–	1 (0.2)	–	1 (0.2)	2 (0.4)	–	–
Traumatic axillary nerve injury	–	–	–	–	–	2 (0.4)	1 (0.2)	–	1 (0.2)
Tumor of the vagus nerve	–	–	–	–	1 (0.2)	1 (0.2)	–	–	1 (0.2)
Traumatic sciatic nerve injury	–	–	–	–	–	–	–	1 (0.2)	1 (0.2)
Traumatic injury by electrical shock of the median nerve	–	–	1 (0.2)	–	–	–	–	–	–
Traumatic ulnar nerve neuroma	–	–	–	–	–	–	1 (0.2)	–	–
Neoplastic lesion									
Sural nerve tumor	–	–	2 (0.4)	4 (0.8)	2 (0.4)	4 (0.8)	8 (1.6)	1 (0.2)	2 (0.4)
Median nerve tumor forearm	–	–	–	1 (0.2)	1 (0.2)	1 (0.2)	–	–	1 (0.2)
Accessory nerve tumor	–	–	–	–	–	–	–	2 (0.4)	–
Median nerve tumor	–	–	1 (0.2)	1 (0.2)	–	–	–	–	–
Supraclavicular lipoma	–	–	–	–	–	–	–	–	1 (0.2)
TOTAL	**23 (4.53)**	**46 (9.1)**	**61 (12)**	**67 (13.2)**	**60 (11.8)**	**70 (13.82)**	**64 (12.6)**	**53 (10.4)**	**62 (12.2)**

Table 4 Main types of surgeries performed from 2008 to 2016 in the study sample according to the age group of the patients

Surgeries	Age Group (years)								
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Compressive									
Carpal tunnel syndrome	–	–	–	28 (5.5)	55 (10.8)	65 (12.8)	32 (6.3)	13 (2.6)	4 (0.8)
Compression injury of the ulnar nerve	1 (0.2)	–	7 (1.4)	17 (3.4)	7 (1.4)	7 (1.4)	7 (1.4)	1 (0.2)	–
Compression of the radial nerve	–	–	4 (0.8)	2 (0.4)	3 (0.6)	–	–	–	–
Compressive neuropathy of the median nerve	–	–	1 (0.2)	–	–	1 (0.2)	–	–	–
Neurolysis									
Traumatic Brachial Plexus Injury	1 (0.2)	20 (3.9)	61 (12)	55 (10.8)	24 (4.7)	3 (0.6)	4 (0.8)	–	–
Traumatic injury of the tibial nerve	–	1 (0.2)	2 (0.4)	4 (0.8)	1 (0.2)	2 (0.4)	2 (0.4)	–	–
Fibular nerve injury	–	1 (0.2)	2 (0.4)	3 (0.6)	1 (0.2)	–	1 (0.2)	–	–
Traumatic radial nerve injury	–	1 (0.2)	4 (0.8)	1 (0.2)	–	–	–	–	–
Traumatic axillary nerve injury	–	–	1 (0.2)	2 (0.4)	1 (0.2)	–	–	–	–
Traumatic sciatic nerve injury	–	1 (0.2)	–	–	1(0.2)	–	–	–	–
Traumatic injury by electrical shock of the median nerve		–	–	–	1 (0.2)	–	–	–	–
Tumor resection									
Sural nerve tumor	–	–	3 (0.6)	7 (1.4)	7 (1.4)	4 (0.8)	2 (0.4)	–	–
Median nerve tumor on the forearm	–	–	1 (0.2)	1 (0.2)	2 (0.4)	–	–	–	–
Tumor of the vagus nerve	–	–	1 (0.2)	1 (0.2)	1 (0.2)	–	–	–	–
Accessory nerve tumor	–	–	1 (0.2)	1 (0.2)	–	–	–	–	–
Arm median nerve tumor	–	–	1 (0.2)	–	1 (0.2)	–	–	–	–
Supraclavicular Lipoma	–	–	–	–	–	1 (0.2)	–	–	–
Reconstruction with graft									
Facial nerve injury	–	–	5 (1.0)	1 (0.2)	–	1 (0.2)	1 (0.2)	–	–
Traumatic injury of median nerve	–	2 (0.4)	3 (0.6)	1 (0.2)	–	–	1 (0.2)	–	–
TOTAL	**2 (0.4)**	**26 (5.2)**	**98 (19.4)**	**124(24.4)**	**105 (20.7)**	**84(16.6)**	**50(9.8)**	**14(2.7)**	**4 (0.8)**

In this context, the present study showed that 157 (31%) men had brachial plexus injury throughout the 9 years of follow-up (2008 to 2016), and that 174 (34%) were women diagnosed with carpal tunnel syndrome. In the study by Faglioni et al.,[7] which was developed in the Department of Neurosurgery of Universidade de São Paulo, a higher prevalence of male patients was observed, with 384 (94.6%) patients with brachial plexus lesions having a mean age of 28 years. Regarding women, the highest carpal tunnel syndrome prevalence was also recorded in the studies by Chammas et al.[11] and Kouyoumdjian et al.[3]

In the study by Narakas,[12] neurolysis was used 43 times in 36 patients, mainly to relieve pain, while an autologous nerve graft was used in 100 patients. The present study showed that the highest prevalence was of brachial plexus microsurgery among men (159; 31%). Among the techniques used in men, we can cite the Oberlain technique, the Sonsak technique, and the phrenic nerve transfer. Among women, microsurgery for compressive neuropathy in carpal tunnel syndrome occurred 174 times (34%).

The present study also collaborated in proving the annual increase in the number of patients with traumatic brachial plexus lesions due to the increasing rates of traffic accidents in the country,[3,7] as well as a decrease in patients with carpal tunnel syndrome cared for at Hospital da Restauração, which we believe was due to the services provided at other specialized centers in the state.

Conclusion

According to the epidemiological profile outlined in the present study for surgical patients at Hospital da Restauração between 2008 and 2016, there was a predominance of young men in active working age with a diagnosis of traumatic brachial plexus injury, and of adult women diagnosed with carpal tunnel syndrome, emphasizing the predominance of upper-limb lesions.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Patel NP, Lyon KA, Huang JH. An update-tissue engineered nerve grafts for the repair of peripheral nerve injuries. Neural Regen Res 2018;13(05):764–774
2 Siqueira MG, Martins RS. Surgical treatment of adult traumatic brachial plexus injuries: an overview. Arq Neuropsiquiatr 2011; 69(03):528–535
3 Kouyoumdjian JA, Graça CR, Ferreira VFM. Peripheral nerve injuries: A retrospective survey of 1124 cases. Neurol India 2017;65(03):551–555
4 Reichenheim MEet al. Violência e Lesões no Brasil: efeitos, avanços alcançados e desafios futuros. Saúde no Brasil 2011; 5:75–89
5 Jacobson S, Guth L. An electrophysiological study of the early stages of peripheral nerve regeneration. Exp Neurol 1965;11:48–60
6 Robinson LR. How electrodiagnosis predicts clinical outcome of focal peripheral nerve lesions. Muscle Nerve 2015;52(03):321–333
7 Faglioni W Jr, Siqueira MG, Martins RS, Heise CO, Foroni L. The epidemiology of adult traumatic brachial plexus lesions in a large metropolis. Acta Neurochir (Wien) 2014;156(05):1025–1028
8 Flores LP. Estudo epidemiológico das lesões traumáticas de plexo braquial em adultos. Arq Neuropsiquiatr 2006;64(01):88–94
9 Midha R. Epidemiology of brachial plexus injuries in a multitrauma population. Neurosurgery 1997;40(06):1182–1188, discussion 1188–1189
10 Dubuisson AS, Kline DG. Brachial plexus injury: a survey of 100 consecutive cases from a single service. Neurosurgery 2002;51 (03):673–682, discussion 682–683
11 Chammas M, Boretto J, Burmann LM, Ramos RM, Santos Neto FC, Silva JB. Síndrome do túnel do carpo – Parte I (anatomia, fisiologia, etiologia e diagnóstico). Rev Bras Ortop 2014;49(05):429–436
12 Narakas AO. The surgical treatment of traumatic brachial plexus lesions. Int Surg 1980;65(06):521–527

Hypoglossal-Facial Anastomosis for Facial Nerve Reconstruction: Outcomes using the Side-to-End Surgical Technique

Anastomose Hipoglosso-Facial para reanimação do nervo facial: Resultados da técnica término-lateral

Leonardo Gilmone Ruschel[4] Joel Sanabria Duarte[1] Jonathan De La Cruz[1] Kristel Back Merida[2] Gustavo Fabiano Nogueira[3] Matheus Fernandes de Oliveira[4,5] Ricardo Ramina[1]

[1] Neurosurgery Department, Instituto de Neurologia de Curitiba (INC), Curitiba, Paraná, Brazil
[2] Neurology Department, Instituto de Neurologia de Curitiba (INC), Curitiba, Paraná, Brazil
[3] Otorhinolaryngology Department, Instituto de Neurologia de Curitiba (INC), Curitiba, Paraná, Brazil
[4] DFV Neuro Neurology and Neurosurgery Service, São Paulo, Brazil
[5] Neurosurgery Department, Hospital do Servidor Público Estadual de São Paulo, São Paulo, Brazil

Address for correspondence Matheus Fernandes de Oliveira, MD, PhD, Av. Loefgren, 700, apto 103, Vila Mariana, São Paulo, São Paulo, 04040-000, Brazil (e-mail: mafernoliv@yahoo.com.br).

Arq Bras Neurocir 2021;40(3):e222–e228.

Abstract

Introduction The side-to-end hypoglossal-facial anastomosis (HFA) technique is an excellent alternative technique to the classic end-terminal anastomosis, because it may decrease the symptoms resulting from hypoglossal-nerve transection.

Methods Patients with facial nerve palsy (House-Brackmann [HB] grade VI) requiring facial reconstruction from 2014 to 2017were retrospectively included in the study.

Results In total, 12 cases were identified, with a mean follow-up of 3 years. The causes of facial paralysis were due to resection of posterior-fossa tumors and trauma. There was improvement in 91.6% of the patients (11/12) after the HFA. The rate of improvement according to the HB grade was as follows: HB III - 58.3%; HB IV - 16.6%; and HB II - 16.6%. The first signs of improvement were observed in the patients with the shortest time between the paralysis and the anastomosis surgery (3.5 months versus 8.5 months; $p = 0.011$). The patients with HB II and III had a shorter time between the diagnosis and the anastomosis surgery (mean: 5.22 months), while the patients with HB IV and VI had a longer time of paresis (mean: 9.5 months; $p = 0.099$). We did not observe lingual atrophy or changes in swallowing.

Discussion and Conclusion Hypoglossal-facial anastomosis with the terminolateral technique has good results and low morbidity in relation to tongue motility and swallowing problems. The HB grade and recovery appear to be better in patients operated on with a shorter paralysis time.

Keywords
- facial-nerve trauma
- facial nerve
- hypoglossal nerve
- facial paralysis
- surgical anastomosis

received
March 23, 2020
accepted
August 5, 2020
published online
October 16, 2020

DOI https://doi.org/10.1055/s-0040-1718431.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Introdução A técnica de Anastomose Hipoglosso-Facial término-lateral é uma técnica excelente alternativa à clássica Anastomose Término-Terminal, pois pode diminuir os sintomas resultantes da transecção do nervo hipoglosso.

Métodos Pacientes com paralisia do nervo facial (grau VI de House-Brackmann) com necessidade de reconstrução facial foram incluídos retrospectivamente de 2014 a 2017.

Resultados Doze casos foram identificados com um seguimento médio de 3 anos. As causas da paralisia facial foram devido à ressecção de tumores da fossa posterior e trauma. Houve melhora em 91,6% dos pacientes (11/12) após a cirurgia. A maioria dos pacientes apresentou melhora com HB III, 58,3%, grau IV 16,6%, grau II 16,6%. Os primeiros sinais de melhora foram nos pacientes com menor tempo entre a cirurgia de paralisia e anastomose (3,5 meses vs. 8,5 meses) ($p = 0,011$). Pacientes com HB II e III tiveram menor tempo entre o diagnóstico e a cirurgia da anastomose (média de 5,22 meses), enquanto os pacientes com HB IV e VI tiveram um tempo maior de paresia (média de 9,5 meses) ($p = 0,099$). Não observamos atrofia lingual ou alterações na deglutição.

Discussão e Conclusão A Anastomose Hipoglosso-Facial término-lateral apresenta bons resultados e baixa morbidade em relação à motilidade da língua e problemas de deglutição. O grau (HB) e a recuperação parecem ser melhores em pacientes operados com menor tempo de paralisia.

Palavras-chave

- trauma do nervo facial
- nervo facial
- nervo hipoglosso
- paralisia facial
- anastomose cirúrgica

Introduction

Despite the remarkable development of microsurgical techniques and advances in intraoperative facial-nerve monitoring, facial paralysis remains a feared drawback and a major challenge for the neurosurgeon.[1,2] Paralysis of facial-expression muscles is a debilitating and psychologically devastating condition for the patient, leading to a degree of emotional disability related to self-esteem.[3] To reduce this social impact, several techniques for facial-nerve restoration have been described, including nerve anastomosis, free-muscle transplantation, and lengthening temporalis myoplasty.[4,5]

Despite the development of new microsurgical techniques, facial-nerve rehabilitation remains challenging. It is known that end-to-end primary facial-nerve repair, with or without graft interposition, offers the best hope for recovery in intracranial and extracranial facial-nerve transection.[4,5] Occasionally, this anastomosis cannot be performed as readily, especially in cases in which the proximal stump of the facial nerve in the brainstem is not available, as well as in cases of facial-nucleus destruction, or even after degenerative nerve alterations.[6–8] In these cases, hypoglossal-facial neurorrhaphy is one of the best techniques available to restore the dynamic expression of the face, and is probably the most used technique after total facial-nerve rupture in the cerebellopontine angle (CPA).[5,6,8–10]

The favorable outcomes in facial-nerve recovery do not hide the side effects of the end-to-end anastomosis that are associated with the inevitable hypoglossal-nerve atrophy, mass movements of the face and speech, and chewing and swallowing difficulties that interfere with daily life.[7,9–11] Variations of this technique have been described since 1991, with May's technique using cable graft.[12] A side-to-end hypoglossal-facial neurorrhaphy with translocation of the intratemporal facial nerve to the lateral portion of the hypoglossal nerve was described in 1997 by Darrouzet with similar results, minimizing tongue atrophy and speech disorders.[13–15] Recently, an hemihypoglossal facial-anastomosis technique has been described with minimal tongue atrophy.[16]

In the present article, we describe our experience and results with a case series of 12 patients with facial paralysis submitted to hypoglossal-facial anastomosis (HFA) by the side-to-end technique, regarding the assessment of the preoperative and postoperative factors and recovery of facial-nerve function.

Methods

The clinical, surgical and hospital records of the patients who underwent surgery for facial hypoglossal-anastomosis due to secondary facial paralysis were reviewed from 2014 to 2017 at Instituto de Neurologia de Curitiba (INC). All surgeries were performed by a single skull-base neurosurgeon (Ramina R).

Preoperatively and postoperatively, we recorded data from the medical records regarding demographics (age, sex, economic stratum), the examination of the cranial nerves (facial mimic, facial tonicity, tongue atrophy and swallow disorders). The clinical follow-up was performed at 3, 6 and 12 months. The patients lost to follow up were excluded. Other recorded information included etiology of the facial paralysis, the House-Brackmann (HB) facial grading system, and electromyography. A total of 12 patients met these criteria. The time of facial paralysis was counted as the onset of paresis until the day

of surgery; in addition, if it presented some type of recovery after surgery, it was called recovery time. The study was approved by the Ethics and Research Committee of INC.

Statistical Analysis

The data was analyzed using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 21.0. The qualitative variables are described as frequency and percentages; the quantitative variables are presented as mean values. In order to find differences between the quantitative variables, the non-parametric Mann-Whitney U test was used, as the numerical variables were not normally distributed. The statistical significance was set at a $p < 0.05$.

Surgical Anatomy and the Technique (Side-to-End HFA)

The patient is placed in the supine position with the head turned 45° to the contralateral side. A retroauricular-arch incision is made 2 cm from the ear, exposing the mastoid, extending it caudally along the anterior border of the sternocleidomastoid muscle (SCM) until just above the angle of the mandible. The greater auricular nerve that runs in the subcutaneous fat tissue is dissected and preserved to avoid transient sensitive disorders of the pinna and mandibular angle. The mastoid tip is exposed by removing the muscle attachments.

The facial nerve must be identified where it leaves the skull in the stylomastoid foramen, anterior to the SCM at the mastoid process (►**Fig. 1**). The styloid process is an important anatomical reference when locating the main trunk of the facial nerve, which is lateral from this slender bone, leading the surgeon to the stylomastoid foramen, where the nerve can be identified. It is possible to expose and mobilize the nerve trunk with or without mastoidectomy (►**Fig. 1**).

The hypoglossal nerve is found deep in the posterior belly of the digastric muscle at the caudal end of the incision. It is confirmed with a nerve stimulator, followed and dissected proximally (►**Fig. 1**).

Partial mastoidectomy of the anterior triangle-shaped part of the mastoid process is performed with a diamond drill, leaving only a thin layer of bone over the facial nerve, which is then removed using a microdissector. The facial nerve is exposed up to its external genu and geniculate ganglion, the stylomastoid foramen is opened, and the nerve is released from the connective tissue and to the parotid gland. The facial nerve is sectioned near its external genu and then displaced caudally toward the previously isolated hypoglossal nerve. The anastomosis point is defined between the proximal portion of the facial nerve and the lateral portion of the hypoglossal nerve. A longitudinal neurotomy is performed, and the facial nerve is attached to the suture. The facial nerve passes beneath the digastric muscle without any tension in order for us to perform a suture with a 10.0 nylon suture. Then, a thin layer of fibrin glue is placed at the anastomosis site. Cautiously, hemostasis is performed, as we do not leave the suction drain at closing (►**Fig. 2**).

Results

In total, 12 patients were submitted to this procedure from 2014 to 2017, with an average follow-up of 3 years (►**Table 1**); 8 patients were men (66.6%), and 4 were women (33.4%). Their ages ranged from 7 to 65 years, and the average age was 46 years among men, and 55 years among women. The facial paresis occurred at the left side in 6 subjects (50%), and at the right side in the other 6 subjects (50%).

Among the 12 cases, in 9 (75%) patients the procedure was secondary to surgery for skull-base tumors. Vestibular schwannoma (VS) larger than 3.5 cm was the cause in 7 cases; 1 case was a patient with a CPA meningioma, and there was another patient with jugular glomus tumor. The three remaing patients had brainstem cavernoma, facial trauma and congenital paralysis.

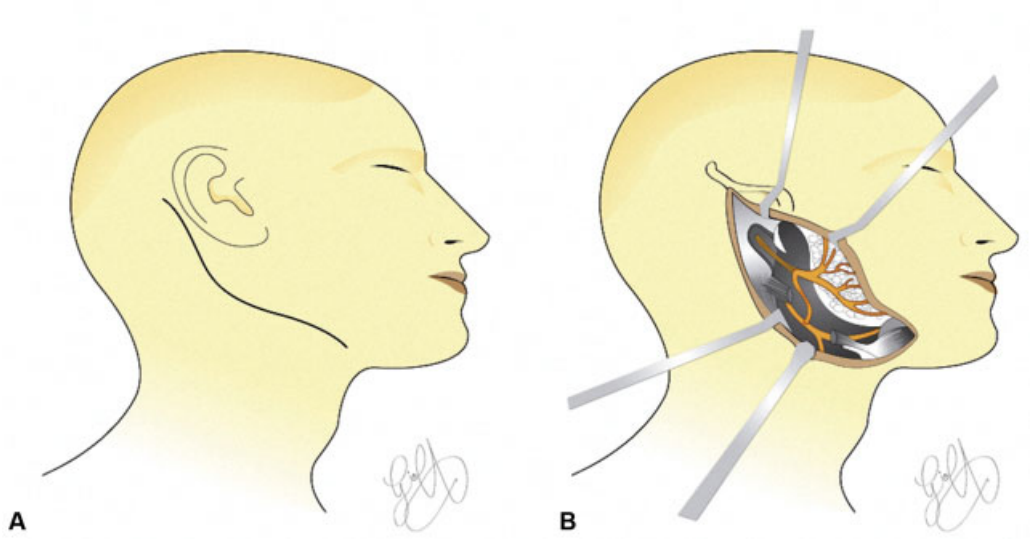


Fig. 1 Schematic demonstration of the side-to-end reconstruction technique. (**A**) Skin incision; (**B**) subcutaneous and muscular dissection displaying a branch of the hypoglossal nerve reinervating the facial nerve.

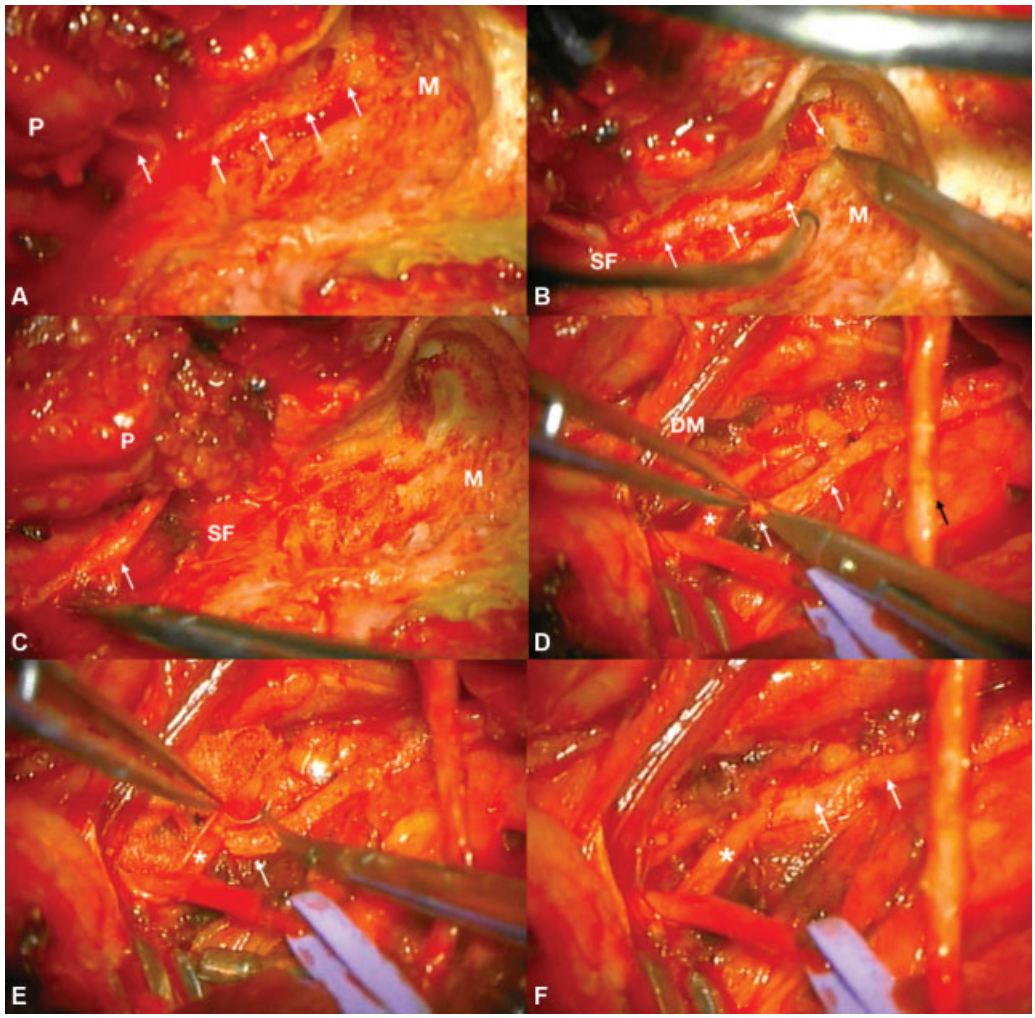


Fig. 2 Anatomical details of the side-to-end reconstruction technique. (**A**) Partial mastoidectomy of the anterior part of the mastoid process. (**B and C**) The facial nerve is sectioned near its external genu and then displaced caudally stylomastoid foramen. (**D**) A longitudinal neurotomy is performed on the hypoglossal nerve, and the distal stump of the facial nerve is prepared; (**E**) Suture performed with a 10.0 nylon suture of the lateral portion of the hypoglossal nerve with the distal stump of the facial nerve. (**F**) Final aspect of the anastomosis. White arrow: facial nerve; black arrow: greater auricular nerve; asterisk: hypoglossal nerve; M, mastoid; P, parotid gland; SF, stylomastoid foramen; DM, digastric muscle.

Improvement of the facial paresis was observed in 91.6% of the patients (11/12). Most patients showed improvement: HB grade III - 58.3% (7/12); HB grade IV - 16.6% (2/12); HB grade II - 16.6% (2/12); and 1 patient (HB grade VI - 8.4%; 1/12) did not recover.

The variables evaluated in the Mann-Whitney U test were postoperative HB and time of paresis until surgery. Patients with HB II and III had an average time interval between diagnosis and reconstruction surgery of 5.22 months, while patients with HB IV and VI had an average time of paresis of 9.5 months ($p = 0.099$). Although not significant ($p = 0.099$), we observed a tendency for better postoperative HB related to the shorter time of intervention (►**Table 2**).

All patients were evaluated after surgery, and the average time until nerve recovery was of 5.09 months (range: 3 to 12 months). The onset of nerve recovery was also related to the lower mean time of facial paresis ($p = 0.011$). Patients who were operated early, with an average facial paralysis time of 3.5 months, showed signs of nerve recovery in 3 months ($p = 0.011$). Patients with an average of 8.5 months of facial paralysis showed the first signs of recovery in 6 months. (►**Table 3**).

The only patient who did not have any improvement was the one submitted to a resection surgery due to a brainstem cavernoma. Among the patients who had mild improvement (HB grade IV), one of them had congenital paralysis, and another was submitted to a resection of VS T4B (vestibular schwannoma grade T4b, in Hannover Classification of Vestibular Schwanomas). No patient had lingual atrophy or swallowing dysfunction after surgery.

The side-to-end anastomosis technique favored the recovery of the facial nerve in 91.6% of the cases, and in 75% of them the recovery was significant, with variation in minimal facial movement and symmetry (HB II, III).

Discussion

Facial-nerve injury is a major concern, mainly regarding the surgical removal of vestibular schwannomas. The consequence of the lesion, in addition to its serious functional

Table 1 Data and results of 12 patients who underwent side-to-end hypoglossal-facial anastomosis

Cases	Gender	Age	Side	HB Pre	HB Post	Paresis Cause	Hypoglossal Paresis	Paresis time
1	M	63	Right	VI	II	VS	N	4 d
2	M	37	Right	VI	IV	VS	N	15 m
3	M	55	Left	VI	VI	BCA	N	14 m
4	F	65	Left	VI	III	VS	N	18 m
5	F	59	Left	VI	III	VS	N	4 m
6	M	7	Right	VI	IV	CONG	N	7 y
7	M	49	Right	VI	III	TR	N	3 m
8	M	61	Left	VI	III	MEN	N	2 m
9	F	58	Right	VI	II	PARAG	N	6 m
10	F	39	Left	VI	III	VS	N	11 m
11	M	42	Right	VI	III	VS	N	10 m
12	M	55	Left	VI	III	VS	N	7 m

Abbreviations: BCA, brainstem cavernoma; CONG, congenital; d, days; F, female; HB, House-Brackmann facial grading system; m, months; M, male; MEN, meningioma; PARAG, paraganglioma; TR, trauma; VS, vestibular schwannoma; y, years.

Table 2 Facial nerve recovery by average paresis time – 11 patients*

HB Post	N	Average paresis time
II and III	9	5.22 months
IV and VI	2	9.50 months
Total	11	$p = 0.099$

Abbreviation: HB, House-Brackmann facial grading system.
Note: * Table showing two groups of patients with facial paresis after skull-base-tumor surgery with worse (IV and VI) and better (II and III) outcomes regarding facial-nerve reconstruction. The mean time of paresis until the reconstruction surgery was related to the postoperative result ($p = 0.099$). The patient (number 6) with congenital facial paresis (with a paresis time of 7 years) was excluded from this sample.

Table 3 Postoperative facial nerve improvement by time of paresis – 10 patients*

Facial nerve outcomes	N	Average time from facial nerve injury to surgery
Onset of improvement in 3 months	6	3.5 months
Onset of improvement in 6 months	4	8.5 months
Total	10	$p = 0.011$

Note: *The mean time from the paresis to the reconstruction surgery was related to the onset of nerve recovery ($p = 0.011$). The patient (number 6) with congenital facial paresis (with a paresis time of seven years) was excluded. Patient number 3 was not included in this evaluation, because he did not improve.

deficits, can cause psychological trauma due to facial asymmetry that has been less accepted nowadays.[1–3] Regarding the different etiologies, the neurosurgeon is more likely to deal with traumatic[17] and neoplasic lesions.[17,18] Facial paralysis is one of the main complications in cases of vestibular-schwannoma surgery. Even with microsurgical techniques and advances in facial-nerve intraoperative monitoring, facial paralysis remains a feared result, with an incidence of 3% to 19% in the main modern series.[19–21]

A wide variety of reconstructive techniques have been described for reconstruction, using muscle transfers, free-muscle grafts, shortening or plication of weakened muscles, dermal transplants, fascial transplants, and redundant-skin removal.[22] When the the proximal stump of the facial nerve is not available, a neural anastomosis can be performed. The most used donor nerve is the hypoglossus, which is connected to the facial nerve at the level of the stylomastoid foramen.

Facial-nerve reinnervation surgery with HFA is indicated when direct nerve repair is not possible and the facial muscles are viable. The three main indications are loss of the proximal part of the facial nerve at the brainstem in the CPA, destruction of the facial motor nucleus (as in pontine hemorrhages due to cavernomas) and internal axonotmesis. Additionally, as may be presumed, it is also indicated in cases in which, during a CPA operation, the nerve appears to be anatomically preserved, but functional recovery does not occur after 12 months.[8]

The facial and hypoglossal nerves have a cortical topographic proximity in the motor cortex. Both nerves receive afferent input from the trigeminal reflex, and act synergistically in the coordination of some mimic and prandial functions; furthermore, both contain myelinated motor fibers with similar fascicular anatomy.[23,24]

Reinnervation occurs in 4 to 12 months. Approximately 70% of the patients obtain good results, with the function of the facial nerve classified as “good”, or as HB grade III.[18,24] Although some authors initially reported that the onset of facial-nerve remission can occur up to 2 years after tumor resection, the reconstruction operation did not show a

difference between the early and late treatments.[7] Therefore, the performance of nerve reconstruction procedures is recommended within six months to one year after the paralysis. After this first year, the results are uncertain and less satisfactory.[8,18] According to a recent independent meta-analysis of types of techniques, cases within 1 year after facial paralysis had better recovery.[5] In the present series, we observed that the earlier facial reconstruction was performed, the earlier was the onset of improvement. In the present study, we observed a statistically significant association ($p = 0.011$) between the time from facial-nerve injury to reinnervation surgery lower than 4 months, and an onset of improvement within 6 months. This could mean that early surgery would improve the outcome. We examined 12 cases and found a statistically significant result, but we know that a larger sample is needed to corroborate the results of the present study.

Several degenerative phenomena occur during facial-nerve injury, such as muscular atrophy, nerve fibrosis, degeneration of the pontine nucleus, and degeneration and loss of information plasticity in the facial area of the motor cortex. Therefore, the reconstruction procedure must be performed before the degenerative mechanisms can evolve, making recovery of facial-nerve function more difficult.[8]

Some studies[7] have demonstrated a relationship between the improvement in nerve function and the interval until the reconstruction surgery. Patients with delayed surgery did not have a functional improvement as good as that of the patients submitted to surgery before 6 months of the diagnosis.[7]

In the present study, we observed a trend towards a better postoperative HB related to the shorter paresis time (►**Table 2**). Although without statistical significance ($p = 0.099$), due to the small sample size, we observed a favorable postoperative evolution in most cases, especially in those patients operated with shorter time of paresis after the diagnosis.

The recovery time of the nerve was also related to a longer interval between the injury and the nerve reconstruction surgery.[10] In these cases, complete recovery, according to Rebol et al[16] and Catli et al,[5] can be observed after 2 years of the nerve reconstruction surgery.[14,25] Radiotherapy was also associated to delayed nerve recovery, including a recommendation for these cases of more aggressive resection with early hypoglossal-facial anastomosis, rather than a more conservative resection with partial tumor excision and facial paralysis.[10]

Regarding the causes of the paresis, our results show worst outcomes in one patient after a resection of a cavernous angioma in the brainstem, one case of congenital facial paralysis, and another case of vestibular schwannoma. Studies[10] show that patients with facial paralysis after resection of a vestibular schwannoma obtained better results than those with meningiomas or other tumors, regardless of the anastomosis technique.[10] These results were also indicated by other authors[5,26]; they state that even with a short interval between the neural damage and the reconstruction surgery, histopathological findings of greater nerve fibrosis were found.[26] A meta-analysis of 293 patients operated using the end-to-end HFA technique showed that cases with facial paralysis due to traumatic events or facial neuroma had a worse outcome than those with vestibular schwannomas.[5]

The classic end-to-end HFA technique is an effective procedure with excellent facial tonicity in the postoperative control.[11] However, complete transection of the hypoglossal nerve causes ipsilateral hypoglossal atrophy, with speech and swallowing changes. In addition, the axonal load between the hypoglossal nerve and the facial nerve leads to dyskinesia and spasms.[7,9,10]

A comparison between the classic end-to-end and the side-to-end techniques presented equivalent results in terms of facial-nerve recovery.[9,10] However, the side-to-end technique minimized tongue atrophy and speech disorders.[13,14,26] Furthermore, the classic technique is more restricted to patients who already have deficits related to the lower cranial nerves. Hemihypoglossal-facial and masseteric-facial anastomosis are also options to improve facial-nerve function with lesser complications.[27–31] Both techniques present decreased morbidity and average outcomes compared with classic HFA.[27–31] In many studies in the literature,[27–31] there is wide evidence to support their application. Although the masseteric-facial anastomosis technique seems to be technically easier, the outcomes tend to be equal or worse than those of the HFA.[27–32]

Regarding the complications of side-to-end HFA, few articles with a low number of patients have been published. In a study conducted by Samii et al,[10] 1 out of 17 patients developed lingual hypotrophy. Two other studies describe a patient with tongue-movement weakness[32] and another with motility alteration.[14] In the present study ,we used the side-to-end anastomosis technique, and no complications or major drawbacks, such as tongue atrophy or other swallowing disorders, related to the hypoglossal-nerve section were found.

Conclusion

Postoperative peripheral facial palsy in skull-base surgery is a condition that can be treated with facial nerve reconstruction techniques such as the HFA. The side-to-end anastomosis technique has significantly favored the recovery of facial-nerve function in most cases, with slight changes in symmetry and facial movements. The cases with greater paralysis time were those that had the worst results. In addition, no operated patients had alterations in tongue motility or atrophy, swallowing disorders, or even other complaints related to the hypoglossal-nerve damage.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Asaoka K, Sawamura Y, Nagashima M, Fukushima T. Surgical anatomy for direct hypoglossal-facial nerve side-to-end “anastomosis”. J Neurosurg 1999;91(02):268–275
2 Atlas MD, Lowinger DS. A new technique for hypoglossal-facial nerve repair. Laryngoscope 1997;107(07):984–991

3 Campero A, Socolovsky M. Facial reanimation by means of the hypoglossal nerve: anatomic comparison of different techniques. Neurosurgery 2007;61(03):41–49, discussion 49–50
4 Cardoso AC, Fernandes YB, Ramina R, Borges G. Acoustic neuroma (vestibular schwannoma): surgical results on 240 patients operated on dorsal decubitus position. Arq Neuropsiquiatr 2007;65 (3A):605–609
5 Catli T, Bayazit YA, Gokdogan O, Goksu N. Facial reanimation with end-to-end hypoglossofacial anastomosis: 20 years' experience. J Laryngol Otol 2010;124(01):23–25
6 Cross T, Sheard CE, Garrud P, Nikolopoulos TP, O'Donoghue GM. Impact of facial paralysis on patients with acoustic neuroma. Laryngoscope 2000;110(09):1539–1542
7 Cusimano MD, Sekhar L. Partial hypoglossal to facial nerve anastomosis for reinnervation of the paralyzed face in patients with lower cranial nerve palsies: technical note. Neurosurgery 1994;35(03):532–533, discussion 533–534
8 Darrouzet V, Guerin J, Bébéar JP. New technique of side-to-end hypoglossal-facial nerve attachment with translocation of the infratemporal facial nerve. J Neurosurg 1999;90(01):27–34
9 Dziedzic TA, Kunert P, Marchel A. Hemihypoglossal-Facial Nerve Anastomosis for Facial Nerve Reanimation: Case Series and Technical Note. World Neurosurg 2018;118:e460–e467
10 Yvens FB, Ramina R, Cyrino HS, Proa F Jr, Silva M. Facial reconstruction by hypoglossal-facial neurorrhaphy. Arq Bras Neurocir 2014;33:17–21
11 Koerbel A, Gharabaghi A, Safavi-Abbasi S, Tatagiba M, Samii M. Evolution of vestibular schwannoma surgery: the long journey to current success. Neurosurg Focus 2005;18(04):e10
12 May M, Sobol SM, Mester SJ. Hypoglossal-facial nerve interpositional-jump graft for facial reanimation without tongue atrophy. Otolaryngol Head Neck Surg 1991;104(06):818–825
13 Moubayed SP, Labbé D, Rahal A. Lengthening temporalis myoplasty for facial paralysis reanimation: an objective analysis of each surgical step. JAMA Facial Plast Surg 2015;17(03):179–182
14 Odebode TO, Ologe FE. Facial nerve palsy after head injury: Case incidence, causes, clinical profile and outcome. J Trauma 2006;61 (02):388–391
15 Pitty LF, Tator CH. Hypoglossal-facial nerve anastomosis for facial nerve palsy following surgery for cerebellopontine angle tumors. J Neurosurg 1992;77(05):724–731
16 Rebol J, Milojković V, Didanovic V. Side-to-end hypoglossal-facial anastomosis via transposition of the intratemporal facial nerve. Acta Neurochir (Wien) 2006;148(06):653–657, discussion 657
17 Rosenwasser RH, Liebman E, Jiménez DF, Buchheit WA, Andrews DW. Facial reanimation after facial nerve injury. Neurosurgery 1991;29(04):568–574
18 Samii M, Alimohamadi M, Khouzani RK, Rashid MR, Gerganov V. Comparison of direct side to end and end to end hypoglossal-facial anastomosis for facial nerve repair. World Neurosurg 2015; 84(02):368–375
19 Samii M, Matthies C. Indication, technique and results of facial nerve reconstruction. Acta Neurochir (Wien) 1994;130(1-4): 125–139
20 Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): surgical management and results with an emphasis on complications and how to avoid them. Neurosurgery 1997;40(01):11–21, discussion 21–23
21 Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): the facial nerve–preservation and restitution of function. Neurosurgery 1997;40(04):684–694, discussion 694–695
22 Sampath P, Holliday MJ, Brem H, Niparko JK, Long DM. Facial nerve injury in acoustic neuroma (vestibular schwannoma) surgery: etiology and prevention. J Neurosurg 1997;87(01):60–66
23 Sawamura Y, Abe H. Hypoglossal-facial nerve side-to-end anastomosis for preservation of hypoglossal function: results of delayed treatment with a new technique. J Neurosurg 1997;86 (02):203–206
24 Slattery WH III, Cassis AM, Wilkinson EP, Santos F, Berliner K. Side-to-end hypoglossal to facial anastomosis with transposition of the intratemporal facial nerve. Otol Neurotol 2014;35(03):509–513
25 Yetiser S, Karapinar U. Hypoglossal-facial nerve anastomosis: a meta-analytic study. Ann Otol Rhinol Laryngol 2007;116(07): 542–549
26 Ylikoski J, Hitselberger WE, House WF, Sanna M. Degenerative changes in the distal stump of the severed human facial nerve. Acta Otolaryngol 1981;92(3-4):239–248
27 Jandali D, Revenaugh PC. Facial reanimation: an update on nerve transfers in facial paralysis. Curr Opin Otolaryngol Head Neck Surg 2019;27(04):231–236
28 Venail F, Sabatier P, Mondain M, Segniarbieux F, Leipp C, Uziel A. Outcomes and complications of direct end-to-side facial-hypoglossal nerve anastomosis according to the modified May technique. J Neurosurg 2009;110(04):786–791
29 Socolovsky M, Martins RS, di Masi G, Bonilla G, Siqueira M. Treatment of complete facial palsy in adults: comparative study between direct hemihypoglossal-facial neurorrhaphy, hemihipoglossal-facial neurorrhaphy with grafts, and masseter to facial nerve transfer. Acta Neurochir (Wien) 2016;158(05):945–957, discussion 957
30 Martins RS, Socolovsky M, Siqueira MG, Campero A. Hemihypoglossal-facial neurorrhaphy after mastoid dissection of the facial nerve: results in 24 patients and comparison with the classic technique. Neurosurgery 2008;63(02):310–316, discussion 317
31 Kim MJ, Kim HB, Jeong WS, Choi JW, Kim YK, Oh TS. Comparative Study of 2 Different Innervation Techniques in Facial Reanimation: Cross-face Nerve Graft-Innervated Versus Double-Innervated Free Gracilis Muscle Transfer. Ann Plast Surg 2019;84(02): 188–195
32 Murphey AW, Clinkscales WB, Oyer SL. Masseteric Nerve Transfer for Facial Nerve Paralysis: A Systematic Review and Meta-analysis. JAMA Facial Plast Surg 2018;20(02):104–110

Dorsal Root Entry Zone Lesioning: Systematic Review

Lesionamento da zona de entrada da raiz dorsal: Revisão sistemática

Giovanna Zambo Galafassi[1] Paulo Henrique Pires Aguiar[2,3,4] André Akira Takahashi[1] Jorge Roberto Pagura[5]

[1] Faculdade de Medicina do ABC, Santo André, SP, Brazil
[2] Department of Research and Innovation, Laboratório de Biologia Celular e Molecular, Faculdade de Medicina do ABC, Santo André, SP, Brazil
[3] Department of Neurosurgery, Hospital Santa Paula, São Paulo, SP, Brazil
[4] Department of Neurology, Pontifícia Universidade Católica de São Paulo, Sorocaba, SP, Brazil
[5] Department of Neurology and Neurosurgery, Faculdade de Medicina do ABC, Santo André, SP, Brazil

Address for correspondence Giovanna Zambo Galafassi, Faculdade de Medicina do ABC, Rua Pirassununga, 190, apto 42, Valparaíso, Santo André, SP, 09060020, Brazil (e-mail: giovannagalafassi@gmail.com).

Arq Bras Neurocir 2021;40(3):e229–e237.

Abstract

Introduction Dorsal root entry zone (DREZ) leasioning (DREZ-otomy) is considered an effective treatment for chronic pain due to spinal cord injuries, brachial and lumbosacral plexus injuries, postherpetic neuralgia, spasticity, and other conditions. The objective of the technique is to cause a selective destruction of the afferent pain fibers located in the dorsal region of the spinal cord.

Objective To identify and review the effectiveness and the main aspects related to DREZ-otomy, as well as the etiologies that can be treated with it.

Methods The PubMed, MEDLINE and LILACS databases were used as bases for this systematic review, having the impact factor as the selection criteria. The 23 selected publications, totalizing 1,099 patients, were organized in a table for systematic analysis.

Results Satisfactory pain control was observed in 70.1% of the cases, with the best results being found in patients with brachial/lumbosacral plexus injury (70.8%) and the worst, in patients with trigeminal pain (40% to 67%).

Discussion Most of the published articles observed excellent results in the control of chronic pain, especially in cases of plexus injuries. Complications are rare, and can be minimized with the use of new technologies for intraoperative monitoring and imaging.

Conclusion DREZ-otomy can be considered a great alternative for the treatment of chronic pain, especially in patients who do not tolerate the side effects of the medications used in the clinical management or have refractory pain.

Keywords
- neuropathic pain
- dorsal root entry zone
- radiculopathy
- spinal cord

Resumo

Introdução O lesionamento da zona de entrada da raiz dorsal (*dorsal root entry zone*, DREZ), ou DREZ-otomia, é considerado um tratamento eficaz para a dor crônica decorrente de lesões medulares, lesão dos plexos braquial e lombossacro, neuralgia

received
May 4, 2020
accepted
August 24, 2020
published online
November 26, 2020

DOI https://doi.org/10.1055/s-0040-1719003.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

pós-herpética, espasticidade, entre outras lesões. O objetivo da técnica é causar uma destruição seletiva das fibras localizadas na região dorsal da medula espinal, entre elas as fibras aferentes de dor.

Objetivo Identificar a efetividade da DREZ-otomia e as principais etiologias que podem ser tratadas por este procedimento, e revisar os principais aspectos relacionados à técnica.

Métodos As bases de dados do PubMed, MEDLINE e Lilacs foram utilizadas na realização desta revisão sistemática, tendo o impacto como critério de seleção. As 23 publicações selecionadas, totalizando 1.099 pacientes, foram organizadas numa tabela para análise sistemática.

Resultados Controle satisfatório da dor foi observado em 70,1% dos casos, sendo que os melhores resultados foram encontrados em pacientes com lesão dos plexos braquial/lombossacro (70,8%), e os piores, em pacientes com dor neuropática do nervo trigêmeo (40% a 67%).

Discussão A maioria dos artigos publicados encontrou ótimos resultados no controle da dor crônica, principalmente na dor relacionada à lesão de plexos. As complicações são raras, podendo ser minimizadas com o emprego das novas tecnologias de monitoração intraoperatória e imagem existentes.

Conclusão A drezotomia pode ser considerada uma ótima alternativa para o tratamento da dor crônica, especialmente em pacientes que não toleram os efeitos colaterais das medicações utilizadas no manejo clínico ou apresentam dor refratária.

Palavras-chave
- dor neuropática
- zona de entrada da raiz dorsal
- radiculopatia
- medula espinal

Introduction

Neurosurgical procedures should be considered as a possible treatment for chronic pain refractory to pharmacotherapy and other treatments.[1] Over 100 million adults in the United States are afflicted with chronic pain conditions by different causes (chronic diseases, peripheral nerve disorders and primary pain disorders) that play an important role in the patient's quality of life.[2,3]

Chronic neuropathic pain seems like a disease in itself, without any benefit or protective significance that characterizes the role of nociceptive pain in the human body. This illness imposes economic burdens to individuals and society, which can be observed in studies that suggest that patients with chronic pain experience worse health-related quality of life than the general population.[4–6] Moreover, some epidemiological studies have also reported the negative effect that chronic pain has on health conditions, since it can be associated with more symptoms of anxiety and depression, and poorer sleep quality.[7]

The lesion of the dorsal root entry zone (DREZ) is considered an effective procedure to treat this type of pain. The goal of DREZ lesioning is to create a selective destruction of neurons and fibers that enter the DREZ and, by this mean, cut off the pain circuit and relieve the symptoms.[8] The idea for the DREZ operation came to be in the early 1970's, after the introduction of the gate-control theory by Melzack and Wall in 1965. It was discovered that electrical stimulation was able to reduce certain types of pain. Thus, it became clear that the modulation of DREZ was important to understand the pain mechanisms.[9] The first surgical attempts were made in 1972 to determine whether a destructive procedure in the DREZ was feasible, safe and effective. This procedure was described as microsurgical DREZ-otomy (MDT), and it consisted of an incision and bipolar coagulations performed ventrolaterally at the entrance of the rootlets into the dorsolateral sulcus. The lesion penetrates the lateral part of the DREZ and the medial part of the tract of Lissauer, extending down to the apex of the dorsal horn. The latter is recognized under the surgical microscope by its brownish-gray color. The typical lesion is 2 mm deep, and it is made at a 45° angle medially and ventrally.[10]

Recently, other types of DREZ-lesioning techniques have been described to better achieve the expected results regarding the symptoms of the patient symptoms. Hence, the aim of the present study is to clarify, by a literature review, the results with different DREZ operation techniques to treat conditions involving neuropathic pain.

Methods

The PubMed, MEDLINE and LILACS databases were searched for manuscripts related to the DREZ operation. All relevant articles were included in the present review. Additionally, the reference sections of these articles were evaluated, and papers that provided important information regarding the subject were included. The results and conclusion of these articles were summarized in a chart. All types of studies were accepted, including other literature reviews. Articles that did not provide data regarding the effectiveness of the technique were not included. The selection protocol followed the flowchart in ►**Fig. 1**.

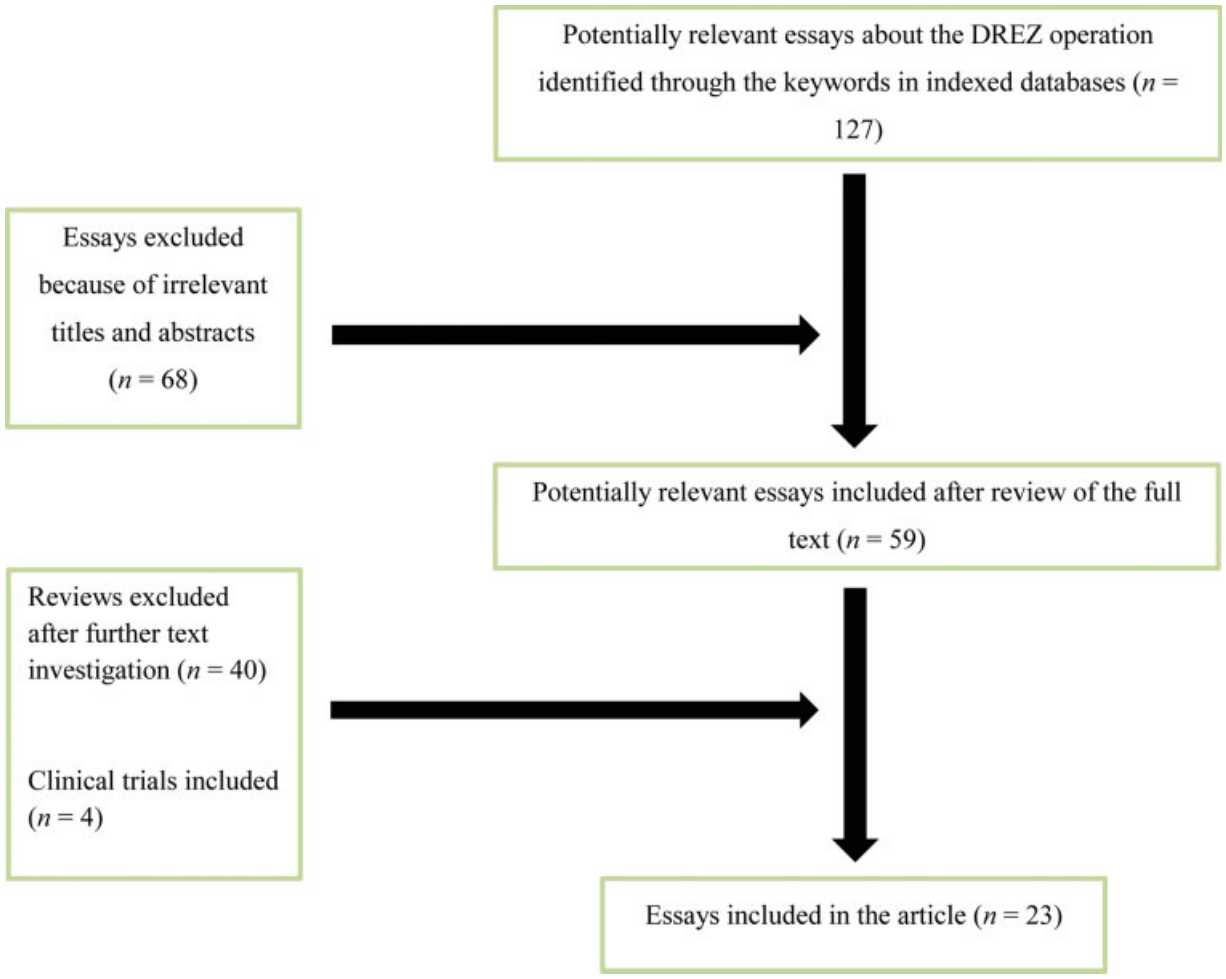


Fig. 1 Selection of articles.

Results

In total, 23 articles were included in the present review, totalizing 1,099 patients. The articles retrieved were written between 1986 and 2017. All data collected was summarized in ►**Table 1**, including the conclusion, year and number of patients evaluated.

Out of the 23 articles, 10 performed the procedure for the improvement of chronic pain related to spinal cord injury, 4, due to phantom pain, 13, due to lesion of the brachial or lumbosacral plexuses, 4, due to postherpetic neuralgia, 2, due to cauda equina lesion, 3, due to hyperspastic states, 3, due to facial pain of multiple causes, 3, due to peripheral nerves, 1, due to deafferentation pain syndromes, and 2 for the control of cancer pain (►**Table 1**).

For cervical DREZ lesioning, the highest percentage of good or excellent pain relief was found regarding cancer pain, hyperspastic states and cervical root avulsion. Plexus injuries, spinal cord injury, peripheral nerve injury and hyperspastic states were the etiologies related to the best results with conus medullaris DREZ lesion (►**Table 1**).

Nucleus caudalis DREZ lesion was the technique with the fewer number of patients ($n = 41$). All of them underwent surgery due to facial pain. The median percentage of good or excellent pain relief was of 60% (range: 40% to 73%). Due to the small sample, these results may not show the actual effectiveness (►**Table 1**).

Discussion

Considerations Regarding the Nonsurgical Management of Pain

There is a vast range of pharmacological and nonpharmacological treatments available, including different mechanisms to control the pain pathway. In general, the pharmacological treatment is well tolerated by the patients; nevertheless, some of those treatments have potentially complicated side effects.[11]

Antiepileptics, such as gabapentin and pregabalin, can be considered the most popular drugs to treat neuropathic pain. Pregabalin is approved for the management of pain due to diabetic peripheral neuropathy, postherpetic neuralgia, fibromyalgia, and neuropathic pain due to spinal cord injuries.[11,12] Recently, the combination of intravenous ketamine and oral gabapentin was evaluated in a double-blinded, randomized, controlled trial on complicated neuropathic pain. This study showed an important improvement in pain scores in comparison to the placebo group.[13] Anticonvulsants, like phenytoin

Table 1 Systematic review of studies on lesioning of the dorsal root entry zone (DREZ)

Study	DREZ lesioning methods	Target	Etiology	Patients (n)	Pain relief
Friedman and Nashold, 1986[29]	Radiofrequency thermocoagulation	Cervix or conus medullaris	Spinal cord injury	56	50%
Saris et al., 1988[30]	Radiofrequency thermocoagulation, probe withe 0.5 mm of diameter, and 2 mm in depth	Conus medullaris	Phanton pain	9	67%
Young, 1990[31]	Radiofrequency method using a 0.5–2-mm stainless steel electrode with control of electric currentand duration	Cervix or conus medullaris	Brachial or lumbosacralplexuses injuries, spinal cord injury, phanton pain, postherpetic neuralgia,and cauda equina injury	21	67%
	CO2 Laser			20	45%
	Radiofrequency method usinga 0.25–2-mm stainless steel electrode with control of the electrodetemperature and duration			37	68%
Sindou, 1995[20]	Microsurgical DREZ-otomy, 45° ventromedially, and 2–3-mm deep	Cervix	Cancer pain	46	87%
		Conus medullaris	Cancer pain	35	78%
		Cervix or conus medullaris	Brachialplexus injuries, spinal cord injury, peripheral nerve lesion, phanton pain, postherpetic neuralgia	139	87%
		Cervix	Hyperspastic states	42	82%
		Conus medullaris	Hyperspastic states	93	
Bullard and Nashold, 1997[32]	Radiofrequency thermocoagulation	Nucleus caudalis	Facial pain	25	67%
Rath et al., 1997[33]	2-mm bare-tipped thermocontrolled electrode	Cervix	Cervical root avulsion	23	82%
		Cervix or conus medullaris	Spinal cord injury	23	48%
Samii et al., 2001[34]	Radiofrequency thermocoagulation	Cervix	Brachial plexus injuries	47	63%
Sindou et al., 2001[35]	Microsurgical DREZ-otomy, 3 mm in depth on average, with 35° of ventromedial obliquity	Cervix or conus medullaris	Spinal cord and/or cauda equina injuries	44	60%
Delgado-López et al., 2003[36]	Radiofrequency	Nucleus caudalis	Facial pain	5	40%
Sindou et al., 2005[37]	2-mm deep and made at a 45° angle medially and ventrally	Cervix	Brachial plexus injuries	55	66%
Spaic et al., 2005[38]	Microsurgical DREZ-otomy, 2-mm deep, and made at a 45° angle medially and ventrally	Thorax or conus medullaris	Spinal cord injuries	24	77%
				14	85%

Table 1 (*Continued*)

Study	DREZ lesioning methods	Target	Etiology	Patients (n)	Pain relief
	Microsurgical DREZ-otomy modifiedwith the dorsal horn suction				
Prestor, B. 2006[39]	Radiofrequency thermocoagulation	Cervix	Brachial plexus avulsion	26	96%
Chen and Tu, 2006[40]	Radiofrequency thermocoagulation	Cervix	Brachial plexus injuries	60	60%
Teixeira et al., 2007[41]	Radiofrequency lesions using a thermo-couple electrode spaced by 2 mm along the DREZ	Cervix	Radiation-induced brachial plexopathy	8	75%
Zhang et al., 2008[42]	Radiofrequency thermocoagulation	Cervix or conus medullaris	Deafferentation pain syndromes	23	74%
Hong et al., 2008[43]	2.5-mm deep radiofrequency electrode at in the Lissauer tract and obliquely oriented at 45°	Cervix	Upper-extremity spasticity	9	67%
Kanpolat et al., 2008[44]	Radiofrequency electrode at 45° and 2-mm depth to the spinal cord	Cervix or conus medullaris	Brachial plexus avulsion, phantom limb pain, painful spasticity after spinal cord injury, tumor and postherpetic neuralgia	44	77%
		Nucleus caudalis	Facial pain	11	73%
Ruiz-Juretschke et al., 2011[45]	Radiofrequency thermocoagulation	Cervix	Spinal cord injury, brachial plexus avulsion and other peripheral nerve injuries	13	77%
		Thorax and conus medullaris		6	50%
Awad et al., 2013[46]	Radiofrequency thermocoagulation	Cervical	Brachial plexus injuries, spinal cord injuries	19	69%
Haninec et al., 2014[47]	Radiofrequency electrode with a tip 2 mm deep	Cervix	Brachial plexus injury	48	70.8%
Liu et al., 2015[48]	Microsurgical DREZ-otomy assisted with spinal cord stimullation	Thorax and conus medullaris	Postherpetic neuralgia	6	83%
Chivukula et al., 2015[49]	Radiofrequency thermocoagulation	Nucleus caudalis	Facial pain	16	68.75%
		Cervix	Brachial plexus injury and postherpetic neuralgia	25	44%
		Thorax and conus medullaris	Postherpetic neuralgia, spinal cord injury, phantom limb and pelvic pain	42	71.40%
Takai and Taniguchi, 2017[23]	Microsurgical tumor forceps with ablunt dissection technique at a depth of 4–5 mm from thesurface of the DREZ.	Cervix	Brachialplexus injuries	10	90%

and carbamazepine, and other older-generation antiepileptic drugs (phenobarbital and valproic acid) have unfavorable metabolic and interaction profiles; thus, they are being less and less prescribed nowadays.[14]

Tricyclic antidepressants can modulate afferent pain pathways by increasing the levels of serotonin and norepinephrine in the central nervous system. Tricyclics have proven to be effective in the treatment of several chronic pain conditions, and can also be considered a first-line treatment in patients with neuropathic pain. Although these medications tend to be well-tolerated, various side effects are described, which are caused by the serotonergic, noradrenergic, and anti-histaminergic properties of these drugs. These adverse effects include: bladder retention, prolonged QT interval, sedation etc.[15]

Cannabinoids have received a lot of attention in recent years. This is due to studies that have shown their analgesic effects for non-cancerous pain. While cannabinoids tend to be well-tolerated with mild, transient side effects, more studies are required to prove the effectiveness and security of these drugs for the treatment of neuropathic pain.[16,17]

Surgical Treatment

Lesioning of the DREZ is a well-established surgical treatment for neuropathic pain. This procedure can be considered effective, safe and well-tolerated by most patients, justifying its frequent use.

Since the first description, DREZ lesioning evolved considerably. Created as a method for pain control for patients with chronic pain following brachial plexus avulsion, it can be used for many conditions, such as deafferentation pain, postparaplegia pain, painful spasticity, facial pain, cancer pain, postherpetic neuralgia, and brachial and sacral plexus avulsions.

The effectiveness of DREZ lesioning is based on the physiopathology of these diseases. They have in common neuropathic pain, which can be caused by imbalances between excitatory and inhibitory somatosensory signaling, alterations in ion channels, and variability in the way that pain messages are modulated in the central nervous system.[18]

The dorsal root of the spinal cord contains the axons from the primary afferent fibers originated in nociceptive receptors, which are responsible for the connection between the peripheral nervous system and the central nervous system. These neurons can ascend or descend a few vertebral levels through the tract of Lissauer. They enter the spinal cord through the dorsal root, where neurotransmitters are liberated, activating the second-order neurons located in the dorsal root. The second-order neurons ascend in the spinal cord through the lateral spinothalamic tract and spinal lemniscus until they reach the primary somatosensory cortex, where the information is processed. Considering these anatomophysiological aspects, it is simpler to understand why the destruction of the dorsal root has the potential to modulate neuropathic pain.

However, DREZ lesioning does not affect only pain fibers. The procedure has the ability of interrupting the unmyelinated and small myelinated fibers (considered tonigenic by their nociceptive input), as well as the large myelinated fibers going to the ventral horn, which are situated laterally and centrally in the DREZ respectively. At the end, the targets for lesioning are the central portion of the dorsal rootlets, the lateral part of the tract of Lissauer, and mainly the first five dorsal layers of the dorsal horn, where the (deafferented) hyperactive neurons are located (which are involved in the physiopathology of neuropathic pain) or where the excitatory segmental circuitry of tone is situated (which is involved in spasticity) .

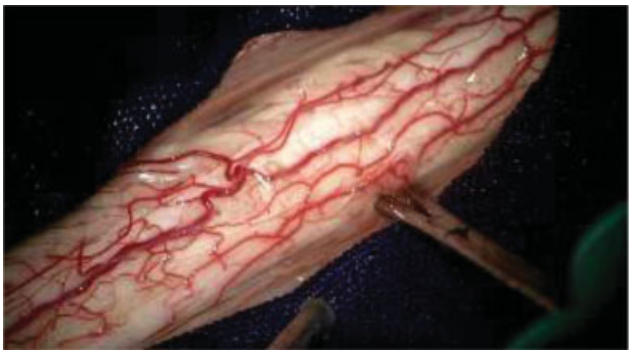


Fig. 2 Vessels along the sulcus.

The procedure is performed in prone position, and, depending on the level of the spinal cord, it may require a three-point cranial fixation device to align and immobilize the spine and skull.[19] The laminectomy level should be determined based on the symptomatology, which generally follows specific dermatomes, demanding the bilateral destruction of fibers. Hemilaminectomies can be used for postherpetic neuralgia, or less frequently for single-dermatome pain or unstable spine. Patients undergoing a conus medullaris DREZ generally have laminectomies from levels D10 to L1, while patients undergoing nucleus caudalis or solitarius lesions undergo a small suboccipital craniectomy and Cl-C2 laminectomies.[19]

The dura mater and arachnoid are opened in the midline. Some structures, like the serpiginous vessels (►**Fig. 2**), may be present along the sulcus, so they must be retracted to enable a proper visualization of the region. Once the DREZ is located (►**Fig. 3**), the electrode can be introduced. Radiofrequency lesions are generally made at 75°C for 15 seconds, at 1 mm intervals along the intermediolateral sulcus, including the entire altered zone. The electrode should penetrate 2.0 mm deep and be held at a 25° angle into the dorsal nerve rootlet (►**Fig. 4**). The

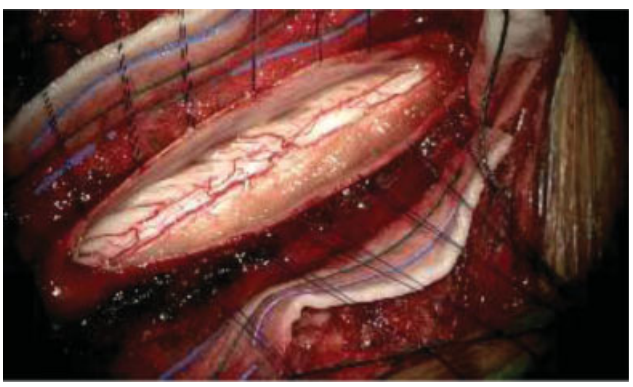


Fig. 3 Delimitation of the posterior medial sulcus (PMS).

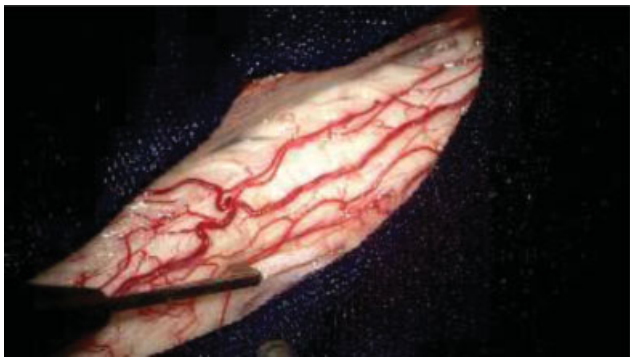


Fig. 4 DREZ lesioning using the electrode.

procedure is extended to the segments corresponding to the pain territory, including one level above and one below.[20]

Takai and Taniguchi[23] described a posterior horn lesion using a microsurgical tumor forceps with a dissection technique at a depth of 4 mm to 5 mm from the surface of the DREZ. This new technique is based on recent findings regarding neuropathic pain suggesting the involvement of deeper layers of the gray matter of the spinal cord in pain conduction.[22] This justifies the performance of deeper lesions on the posterior horn.

Another interesting fact regarding DREZ lesioning is the worse results found in conditions with diffuse pain. This seems to be related to the delimitation of the appropriate lesion level, which can be difficult depending on the case. Chun et al.[21] described a modified DREZ lesioning procedure performed on both the complete injury zone (directly-injured cord level following spine injury) and the incomplete injury zone (indirectly-injured cord level identified on magnetic resonance imaging by signal change). This technique showed better results for diffuse pain than the original one, so they concluded that DREZ lesioning should be performed from the injured level up, including all abnormal rootlets above the level of the injury.

Sindou and Jeanmonod[24] reported a series of 53 patients with harmful spasticity in one or both lower limbs. These patients underwent MDT for their painful state or abormal postures (either hyperextention or flexion). Spasticity and spasms decreased or were abolished in most patients, 75% and 88.2% of them respectively. Abolition of sensation was found in less than 10% of the patients. This study showed that MDT has the potential to significantly improve the quality of life of the patients. In 2017, Sitthinamsuwan et al.[25] Published a study comparing DREZ lesioning and selective dorsal rhizotomy in fifteen spasticity patients. They concluded that DREZ lesioning is more effective to reduce spasticity, but more destructive than selective dorsal rhizotomy. Due to this, they suggested that DREZ lesioning should be preferred for bed-ridden patients, white selective dorsal rhizotomy, for ambulatory patients.

In 2016, Sindou and Georgoulis[26] published a case series of 3 patients with focal dystonia who underwent cervical microsurgical DREZ-otomy. They noticed that all patients maintained the relief of hypertonia, the sustained abnormal dystonic postures remained absent, and most of the functional benefit was still present at the last follow-up. No patient suffered total loss of tactile sensation and proprioception. However, thermal and nociceptive sensations almost disappeared in all three patients. Moreover, patients did not develop neuropathic pain.[26]

The complications associated with DREZ lesioning can be separated into two different groups: over-lesioning and under-lesioning. The most common complications regarding over-lesioning are paralysis and dysesthesia, due to the destruction of adjacent pathways in the spinal cord (the lateral corticospinal, rubrospinal and spinocerebellar tracts, and the dorsal fasciculus). Genito-sphincterian deficits are another possible complication.[19] On the other hand, ineffective pain control represents the under-lesioning complications.

To minimize the complications, it is imperative to choose the right spinal cord level, size of the lesion and angle of insertion. Henssen at al.[27] conducted a study in 2019 to measure the angle between the DREZ and the posterior median sulcus (PMS). They made 11.7-T post-mortem magnetic resonance images and compared them to polarized light imaging microscopy to determine the fiber orientation of the dorsal horn tracts. The median angles between the DREZ and the PMS were of 40.1° (left hemicord) and 39.8° (right hemicord). With these results, they concluded that an insertion angle of 25° should be recommended for DREZ lesioning.

Another study, conducted in 2019 by Monaco et al.,[28] described a real-time imaging technique to optimize DREZ lesioning using intraoperative ultrasound (US), which can determinate the exact location of the gray matter and dorsal horn. The US enables a correct positioning of the needle during the puncture, a proper angular adjustment, and a controlled depth.

Conclusion

Lesioning of the DREZ is an effective and safe procedure that should be considered a treatment for neuropathic pain due to diverse etiologies. Even though the pharmacological treatment is a possibility for the non-complicated cases, the surgical procedure is related to better results and fewer side effects. Thus, the treatment must be individualized, considering the quality of life and the decision of the patient.

Conflict of Interests
The authors have no conflicts of interest to declare.

References

1 Teixeira MJ, Haman C, Teixeira WGJ. Tratamento cirúrgico funcional da dor. Rev Med (São Paulo) 2001;80:276–289
2 Chivukula S, Tomycz ND, Moossy JJ. Paddle lead cervical spinal cord stimulation for failed neck surgery syndrome. Clin Neurol Neurosurg 2013;115(10):2254–2256
3 Deer TR, Skaribas IM, Haider N, et al. Effectiveness of cervical spinal cord stimulation for the management of chronic pain. Neuromodulation 2014;17(03):265–271, discussion 271
4 Jensen MP, Chodroff MJ, Dworkin RH. The impact of neuropathic pain on health-related quality of life: review and implications. Neurology 2007;68(15):1178–1182

5 Smith BH, Torrance N, Bennett MI, Lee AJ. Health and quality of life associated with chronic pain of predominantly neuropathic origin in the community. Clin J Pain 2007;23(02):143–149
6 Inoue S, Taguchi T, Yamashita T, Nakamura M, Ushida T. The prevalence and impact of chronic neuropathic pain on daily and social life: A nationwide study in a Japanese population. Eur J Pain 2017;21(04):727–737
7 Attal N, Lanteri-Minet M, Laurent B, Fermanian J, Bouhassira D. The specific disease burden of neuropathic pain: results of a French nationwide survey. Pain 2011;152(12):2836–2843
8 Konrad P. Dorsal root entry zone lesion, midline myelotomy and anterolateral cordotomy. Neurosurg Clin N Am 2014;25(04): 699–722
9 Nashold BS Jr. Current status of the DREZ operation: 1984. Neurosurgery 1984;15(06):942–944
10 Sindou M. 1972Study of the dorsal root - spinal cord junction. A target for pain surgery. *These Doctorat Medecine*, Lyon182
11 Hatch MN, Cushing TR, Carlson GD, Chang EY. Neuropathic pain and SCI: Identification and treatment strategies in the 21st century. J Neurol Sci 2018;384:75–83
12 Cardenas DD, Nieshoff EC, Suda K, et al. A randomized trial of pregabalin in patients with neuropathic pain due to spinal cord injury. Neurology 2013;80(06):533–539
13 Amr YM. Multi-day low dose ketamine infusion as adjuvant to oral gabapentin in spinal cord injury related chronic pain: a prospective, randomized, double blind trial. Pain Physician 2010;13(03):245–249
14 Finnerup NB, Gottrup H, Jensen TS. Anticonvulsants in central pain. Expert Opin Pharmacother 2002;3(10):1411–1420
15 Dworkin RH, O'Connor AB, Audette J, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. Mayo Clin Proc 2010;85(03):S3–S14). Elsevier.
16 Lynch ME, Campbell F. Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials. Br J Clin Pharmacol 2011;72(05):735–744
17 Karst M, Salim K, Burstein S, Conrad I, Hoy L, Schneider U. Analgesic effect of the synthetic cannabinoid CT-3 on chronic neuropathic pain: a randomized controlled trial. JAMA 2003;290 (13):1757–1762
18 Colloca L, Ludman T, Bouhassira D, et al. Neuropathic pain. Nat Rev Dis Primers 2017;3:17002. Doi: 10.1038/nrdp.2017.2
19 Rawlings CE III, el-Naggar AO, Nashold BS Jr. The DREZ procedure: an update on technique. Br J Neurosurg 1989;3(06):633–642. Doi: 10.3109/02688698908992686
20 Sindou M. Microsurgical DREZotomy (MDT) for pain, spasticity, and hyperactive bladder: a 20-year experience. Acta Neurochir (Wien) 1995;137(1-2):1–5
21 Chun H-J, Kim YS, Yi H-J. A modified microsurgical DREZotomy procedure for refractory neuropathic pain. World Neurosurg 2011;75(3-4):551–557. Doi: 10.1016/j.wneu.2010.12.005
22 Yang F, Zhang C, Xu Q, et al. Electrical stimulation of dorsal root entry zone attenuates wide-dynamic-range neuronal activity in rats. Neuromodulation 2015;18(01):33–40, discussion 40
23 Takai K, Taniguchi M. Modified dorsal root entry zone lesioning for intractable pain relief in patients with root avulsion injury. J Neurosurg Spine 2017;27(02):178–184. Doi: 10.3171/2017.1.spine16234
24 Sindou M, Jeanmonod D. Microsurgical DREZ-otomy for the treatment of spasticity and pain in the lower limbs. Neurosurgery 1989; 24(05):655–670. Doi: 10.1227/00006123-198905000-00002
25 Sitthinamsuwan B, Phonwijit L, Khampalikit I, Nitising A, Nunta-Aree S, Suksompong S. Comparison of efficacy between dorsal root entry zone lesioning and selective dorsal rhizotomy for spasticity of cerebral origin. Acta Neurochir (Wien) 2017;159 (12):2421–2430. Doi: 10.1007/s00701-017-3322-x
26 Sindou M, Georgoulis G. Focal Dystonia in Hemiplegic Upper Limb: Favorable Effect of Cervical Microsurgical DREZotomy Involving the Ventral Horn - A Report of 3 Patients. Stereotact Funct Neurosurg 2016;94(03):140–146. Doi: 10.1159/000446078
27 Henssen DJHA, Weber RC, de Boef J, et al. Post-mortem 11.7 Tesla Magnetic Resonance Imaging vs. Polarized Light Imaging Microscopy to Measure the Angle and Orientation of Dorsal Root Afferents in the Human Cervical Dorsal Root Entry Zone. Front Neuroanat 2019;13:66. Doi: 10.3389/fnana. 2019.00066
28 Monaco BA, Lopes AJM, Teixeira MJ. Ultrasound-Guided DREZotomy: Technical Note. Stereotact Funct Neurosurg 2019;97(02): 127–131. Doi: 10.1159/000500491
29 Friedman AH, Nashold BS Jr. DREZ lesions for relief of pain related to spinal cord injury. J Neurosurg 1986;65(04):465–469
30 Saris SC, Iacono RP, Nashold BS Jr. Successful treatment of phantom pain with dorsal root entry zone coagulation. Appl Neurophysiol 1988;51(2-5):188–197
31 Young RF. Clinical experience with radiofrequency and laser DREZ lesions. J Neurosurg 1990;72(05):715–720
32 Bullard DE, Nashold BS Jr. The caudalis DREZ for facial pain. Stereotact Funct Neurosurg 1997;68(1-4 Pt 1):168–174
33 Rath SA, Seitz K, Soliman N, Kahamba JF, Antoniadis G, Richter HP. DREZ coagulations for deafferentation pain related to spinal and peripheral nerve lesions: indication and results of 79 consecutive procedures. Stereotact Funct Neurosurg 1997;68(1-4 Pt 1):161–167
34 Samii M, Bear-Henney S, Lüdemann W, Tatagiba M, Blömer U. Treatment of refractory pain after brachial plexus avulsion with dorsal root entry zone lesions. Neurosurgery 2001;48(06): 1269–1275, discussion 1275–1277
35 Sindou M, Mertens P, Wael M. Microsurgical DREZotomy for pain due to spinal cord and/or cauda equina injuries: long-term results in a series of 44 patients. Pain 2001;92(1-2):159–171
36 Delgado-López P, García-Salazar F, Mateo-Sierra O, Carrillo-Yagüe R, Llauradó G, López E. Trigeminal nucleus caudalis dorsal root entry zone radiofrequency thermocoagulation for invalidating facial pain. Neurocirugia (Astur) 2003;14(01):25–32, discussion 32
37 Sindou MP, Blondet E, Emery E, Mertens P. Microsurgical lesioning in the dorsal root entry zone for pain due to brachial plexus avulsion: a prospective series of 55 patients. J Neurosurg 2005; 102(06):1018–1028. Doi: 10.3171/jns.2005.102.6.1018
38 Spaic M, Markovic N, Mikicic D, Ilic S, Milosavljevic I. The DREZ Surgical Treatment of chronic pain in traumatic paraplegia. Indian Journal of Neurotrauma 2005;2(02):111–116
39 Prestor B. Microcoagulation of junctional dorsal root entry zone is effective treatment of brachial plexus avulsion pain: long-term follow-up study. Croat Med J 2006;47(02):271–278
40 Chen HJ, Tu YK. Long term follow-up results of dorsal root entry zone lesions for intractable pain after brachial plexus avulsion injuries. Acta Neurochir Suppl (Wien) 2006;99:73–75
41 Teixeira MJ, Fonoff ET, Montenegro MC. Dorsal root entry zone lesions for treatment of pain-related to radiation-induced plexopathy. Spine 2007;32(10):E316–E319
42 Zhang XH, Li YJ, Hu YS, Tao W, Zheng Z. Dorsal root entry zone coagulation for treatment of deafferentation pain syndromes. Chin Med J (Engl) 2008;121(12):1089–1092
43 Hong JC, Kim MS, Chang CH, Kim SW, Kim OL, Kim SH. Long term results of microsurgical dorsal root entry zonotomy for upper extremity spasticity. J Korean Neurosurg Soc 2008;43(04): 182–185
44 Kanpolat Y, Tuna H, Bozkurt M, Elhan AH. Spinal and nucleus caudalis dorsal root entry zone operations for chronic pain. Neurosurgery 2008;62(03, Suppl 1):235–242, discussion 242–244
45 Ruiz-Juretschke F, García-Salazar F, García-Leal R, et al. Treatment of neuropathic deafferentation pain using DREZ lesions; long-term results. Neurologia 2011;26(01):26–31

46 Awad AJ, Forbes JA, Jermakowicz W, Eli IM, Blumenkopf B, Konrad P. Experience with 25 years of dorsal root entry zone lesioning at a single institution. Surg Neurol Int 2013;4:64
47 Haninec P, Kaiser R, Mencl L, Waldauf P. Usefulness of screening tools in the evaluation of long-term effectiveness of DREZ lesioning in the treatment of neuropathic pain after brachial plexus injury. BMC Neurol 2014;14(01):225
48 Liu MX, Zhong J, Zhu J, Xia L, Dou NN. Treatment of postherpetic neuralgia using DREZotomy guided by spinal cord stimulation. Stereotact Funct Neurosurg 2015;93(03):178–181
49 Chivukula S, Tempel ZJ, Chen CJ, Shin SS, Gande AV, Moossy JJ. Spinal and nucleus caudalis dorsal root entry zone lesioning for chronic pain: efficacy and outcomes. World Neurosurg 2015;84 (02):494–504

Surgical Treatment for Spasticity: Selective Dorsal Rhizotomy – Technique and Literature Review

Tratamento cirúrgico para espasticidade: Rizotomia dorsal seletiva – Técnica e revisão da literatura

Marcos Paulo dos Santos Teixeira[1] Bernardo Assumpção de Monaco[2] Jessie Medeiros de Navarro[3] Emmanuel Alejandro Vazquez[4] Arthur José Maia Lopes[5] Thais Cristina de Souza Melo[6] Manoel Jacobsen Teixeira[7]

[1] Foundation of Beneficence, Hospital de Cirurgia, Aracaju, SE, Brazil
[2] Department of Neurosurgery, Hospital das Clínicas, Faculty of Medicine, Universidade de São Paulo, São Paulo, SP, Brazil
[3] Department of Neurophysiology, Hospital das Clínicas, Faculty of Medicine, Universidade de São Paulo, São Paulo, SP, Brazil
[4] Department of Neurosurgery, Hospital Aleman de Bueno Aires, Argentina; Hospital das Clínicas, Faculty of Medicine, University of São Paulo, São Paulo, SP, Brazil
[5] Neurosurgery Residency, Faculty of Medicine, University of São Paulo, São Paulo, SP, Brazil
[6] Medical School Graduation, Universidade Federal de Sergipe Aracaju, SE, Brazil
[7] Neurosurgery Discipline, Hospital das Clínicas, Faculty of Medicine University of São Paulo, São Paulo, SP, Brazil

Address for correspondence Marcos Paulo dos Santos Teixeira, MD, Fundação de Beneficência Hospital de Cirurgia, Av. General Djenal Tavares de Queiroz, 310, apto 502, Luzia, Aracaju, Sergipe, Brazil (e-mail: marcosp_med@hotmail.com).

Arq Bras Neurocir 2021;40(3):e238–e244.

Abstract

Spasticity is a motor disorder that leads to a resistance to passive joint movement. Cerebral palsy is the most important cause of spasticity and can be caused by several factors, including multiple gestations, alcoholism, infections, hemorrhages, drowning, and traumatic brain injuries, among others. There are many scales that help to measure and monitor the degree of impairment of these patients. The initial treatment should focus on the causal factor, such as tumors, inflammation, degenerative diseases, hydrocephalus, etc. Subsequently, the treatment of spastic musculature includes oral or intrathecal myorelaxants, spinal cord electrostimulation, neurotomies, Lissauer tract lesion, dentatotomy and selective dorsal rhizotomy. The latter is a safe technique, possible to be performed in most centers with neurosurgical support, and it is effective in the treatment of severe spasticity. In this article, the authors describe the surgical technique and conduct a review the literature.

Keywords
- spasticity
- rhizotomy
- cerebral palsy
- electrical stimulation
- surgery

Resumo

A espasticidade é um distúrbio motor que leva a um quadro de resistência ao movimento articular passivo. A paralisia cerebral é a mais importante causa de espasticidade e pode ser causada por diversos fatores, tais como gestações múltiplas, alcoolismo, infecções, hemorragias, afogamento, lesões cerebrais traumáticas, entre

received
October 27, 2017
accepted
December 4, 2017
published online
May 10, 2018

DOI https://doi.org/10.1055/s-0038-1623514.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Palavras-chave
- espasticidade
- rizotomia
- paralisia cerebral
- monitorização intraoperatória
- cirurgia

outros. Existem muitas escalas que ajudam a mensurar e acompanhar o grau de acometimento desses pacientes. O tratamento inicial deve focar no fator causal, como tumores, inflamação, doenças degenerativas, hidrocefalia etc. Posteriormente, o tratamento da musculatura espástica inclui miorrelaxantes orais, intratecais, eletroestimulação medular, neurotomias, lesão do trato de Lissauer, dentatotomia e a rizotomia dorsal seletiva. Esta última é uma técnica segura, possível de ser realizada na maioria dos centros com suporte neurocirúrgico, e eficaz no tratamento da espasticidade grave. No presente, artigo, os autores descrevem a técnica cirúrgica e fazem uma revisão da literatura.

Introduction

Spasticity is a motor disorder characterized by increased muscle tone, leading to a frame of resistance to passive articular movement. In the clinical practice, spasticity is one of the positive signs of upper motor neuron syndrome, which may be accompanied by stiffness, hyperreflexia, primitive reflexes, hypertonia of antigravitary muscles, increased reflexogenic areas, bladder hyperreflexia and clasp knife spasticity. Negative signs can also accompany the clinic examination in these patients, such as paresis, incoordination, fatigue, reduction of tissue elasticity, among others. These signs, under extreme conditions, impair posture, ambulation and self-care. As a direct consequence, we can cite pain, fractures and decubitus ulcers. The worsening of these patients also worsens the quality of life of their respective caregivers. However, the degree of spasticity may help some patients in the maintenance of posture and gait.

Cerebral palsy (CP) is considered one of the most important causes of spasticity, especially in children in whom, when associated with other symptoms such as dystonia, ataxia or stiffness, it leads to a serious disability condition. Even with the advances in care in the neonatal period, an increase in the incidence of CP cases has been observed, which may be related to an increase in the survival of children with very low weight.[1,2]

Etiologically, CP is associated with prenatal events (multiple pregnancies, maternal alcoholism, infections), perinatals (hemorrhages, infections, bradycardia, fetal anoxia) and postnatal (drowning, traumatic brain injury, among others).[3]

To objectively evaluate spasticity, we use quantitative and qualitative indicators that measure the degree and functional repercussion of patients.

The modified Ashworth scale is the most widely used to assess muscle tone. It is a qualitative scale that evaluates the degree of spasticity, measured according to the degree of resistance to passive movement of a segment moved rapidly by an examiner[4] (►**Table 1**). The Penn scale, also widely used in the clinical practice, evaluates the occurrence of spasms (►**Table 1**).

The Tardieu scale measures the intensity of the muscular reaction to passive movement. The arc of motion should be measured by a goniometer. The angle of resistance is the measure relative to the position of minimum stretch for all joints. It is a good option to evaluate the gain after treatment (►**Table 2**).

Gait can be used to evaluate the improvement of spasticity, either in clinical observation or in the gait laboratory using dynamic electromyography (EMG).[5]

Other tests are also used, such as upper limb skill tests and dynamometry hold,[6] measurement of functional independence, Barthel index (quantitative method that evaluates independence in daily activities), quantitative muscle strength and myometrial tests,[7] and the Lyon Université scale, which evaluates automatisms.[8] Initially, spasticity treatment should focus on the causal factor, be it tumor,

Table 1 Modified Ashworth Scale and Penn Scale

Modified Ashworth Scale		Penn Scale
Degree	**Description**	**Description**
0	Normal muscular tonus	Absence of spasms
1	Increase in tone at the beginning or end of the arc of motion	Only spasms precipitated by stimuli
1+	Increased tonus in less than half of the arc of motion, manifested by abrupt tension and followed by minimal resistance	
2	Increased tonus in more than half of the arc of motion, but the affected part is easily mobilized	Spontaneous, strong and irregular spasms, less than one per hour
3	Considerable increase in muscle tone with difficult passive movement	Spontaneous spasms, one or more per hour
4	Rigid parts in flexion or extension	Spontaneous spasms, more than ten per hour

Table 2 Tardieu Scale

Modified Tardieu Scale	
Degree	**Description**
0	No resistance in the course of passive movement
1	A slight resistance along the course of the passive movement, without precision of the specific angle
2	Clear stiffness at a specific angle, interrupting the stretch, followed by relaxation.
3	Fatigable Clin that lasts less than 10 seconds and appears at a specific angle, while the evaluator is maintaining pressure.
4	Non-fatigable Clin that lasts for more than 10 seconds and appears at a specific angle while the evaluator is maintaining pressure.

inflammation, multiple sclerosis, infectious disease, vascular disease, degenerative disease, hydrocephalus, etc. It is mandatory to prevent or eliminate factors that aggravate spasticity, such as pain, visceral dysfunctions, decubitus ulcers, urinary infections, constipation, heterotopic ossification, ingrown nail, psychological stress and sleep disorders.

Neurosurgical treatment of spasticity is diverse. Intrathecal infusion of myorelaxants, such as baclofen, tizanidine, midazolam, clonidine or morphine, is indicated in patients with preserved motor function and when oral medication is not tolerated or effective. Spinal cord stimulation is an option in mildest cases. Nerve neurotomies such as shutter, sciatic, posterior tibial, fibular or femoral — in the lower limbs — and musculocutaneous, radial or median in the upper limbs, are options for more localized spasticity.

Percutaneous radiofrequency rhizotomy is used in debilitated patients and in the treatment of spastic bladder. The longitudinal myelotomy (longitudinal section of the spinal cord gray matter) is reserved for paraplegics with total impairment of sexual and sphincter function. The lesion of the Lissauer tract and the posterior horn of the spinal cord, proposed by Sindou in 1969, is used in the treatment of spasticity and pain in the lower limbs.[9] Dentatotomy is efficient in the treatment of spasticity evidenced by several casuistics.[10] A selective dorsal rhizotomy (SDR) is a safe, economical and possible technique to be performed in most centers with neurosurgical support, especially pediatric. It is an excellent option in cases of ambulatory patients and quadrispastic children.

Patient Selection

Up to the present moment, there are no completely efficient measures to repair the damage to motor areas that control movement. We have several therapeutic measures for the treatment of spasticity, which include: drug therapy, physical therapy, occupational therapy, applications of botulinum toxin, orthopedic surgery, SDR, in addition to the surgical procedures already explained. The choice for the use of these therapies is extremely important for the patient, since victims of polytraumatism are usually young with long survival, and that children with CP have a mean survival of 20 years.[11]

Selective dorsal rhizotomy is a definitive surgery in which the cauda equina is exposed through osteoplastic laminotomy followed by L2-S1 roots identification.

The results of dorsal rhizotomy have been known since the initial experiments of Sherington (1894) in decerebrated cats. In 1889, Abbe and Bennett described the result of nerve root section with pain control.[1,13] In 1913, Foerster achieved improvement in spasticity after dorsal rhizotomy was performed.[14] Despite good results, dorsal rhizotomy was abandoned for about half a century, due to the comorbidities related to the procedure. Only in 1960s, Gros et al performed partial rhizotomies EMG to help identify dysfunctional nerves.[15] Fasano et al described the criteria for evaluating abnormal motor responses after electrical nerve stimulation.[16] The traditional surgery proposed by Peacock et al consists of a laminotomy from L1 to L5 with a laminectomy of S1-S2.[17] In many services, the level of the approach is varied, including lumbar topographies or medullary cone (MC), aiming to maintain a balance between the preservation of strength and the elimination of spasticity.[3]

The use of electromyography (EMG) to define which dorsal roots were injured also became a reason for discussion due to the variability of the motor response,[18] of the standardization of the technique used in each center,[19] the use of drugs used in anesthetic induction that may interfere with the results of stimulation,[20] and the variability of segmental innervation of the musculature of the lower limbs.[21] One study performed a histological analysis of the sectioned roots of children with CP submitted to SDR, and found that the altered roots in the EMG presented axonal degeneration or demyelination. The roots that appeared normal in the EMG presented minimal histological alterations limited to myelin sheath or demyelination without axonal degeneration, showing that this is a significant method to find the roots that should be sectioned.[22]

Spastic patients present contractions sustained at a stimulation of 50 Hz, but did not present the same contralateral pattern.[21] We have observed in daily practice that a stimulation of 5 Hz is enough to differentiate the motor and sensitive roots . Intraoperative EMG is essential in the identification of the hyperactive roots, contributing to a balance between the reduction of spasticity, bladder control and the preservation of sensitivity.

Studies have shown that SDR is accompanied by significant improvement in several parameters, for example, improvement in motor function,[23–25] significant spasticity reduction,[26] strength gain,[27] increase in movement amplitude,[28,29] and qualitative[30] and quantitative.[31,32] improvements in the upper limbs motor function. Some services use strict criteria to indicate SDR, including the Reimer index, which, when $> 50\%$, can postpone SDR for a period of 6 to 12 months.[3] However, early dorsal rhizotomy would prevent a posterior approach in soft tissues and articular joints.[33]

In the end of the 1980s, the main concern with intraoperative complications was the risk of bronchospasm and

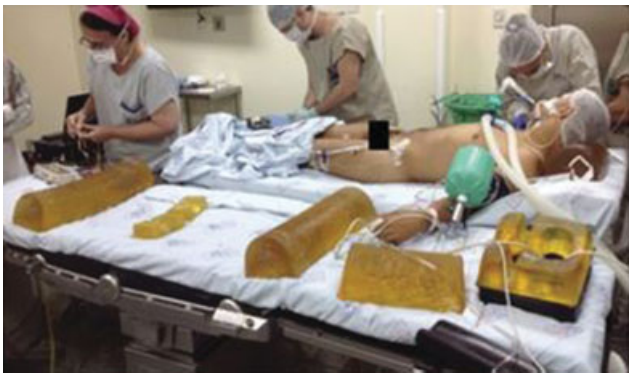


Fig. 1 Patient intubated on a side stretcher at the surgical table. Appropriate cushions are positioned to avoid decubitus ulcers after the patient is positioned in ventral decubitus.

aspiration pneumonia; However, with the development of new anesthetic techniques and new drugs, the risks were reduced.[34]

Children with CP who evolve with spastic diplegia or tetraplegia, associated with an important spastic component in the lower limbs and minimal impairment in the upper limbs, are the main beneficiaries of this technique. Selective dorsal rhizotomy is not indicated for children under 2 years old because the CP cannot be safely diagnosed in this age group. Dystonia is not an absolute contraindication for surgery, but if there are lesions in basal nuclei with dystonic predominance, other procedures present better results, such as pallidotomy or deep cerebral stimulation. History of multiple orthopedic surgeries counterclaims the procedure due to fixed deformities and muscle weakness.[24]

The main objective of SDR is the reduction of two levels in the Ashworth scale in the deprecated muscular target of the lower limbs. In 50% of the cases, there is also improvement in the upper limbs.[35]

For a good postsurgical outcome, the patient should be duly selected. The clinical examination will define which segments are most affected by the disease and which would be the focus of the rhizotomy. A multidisciplinary team that includes physiatrist, orthopedist, neuropediatrician, psychologist and physical therapist is essential. Posture, sphicnter control, amplitude of the articular movements, whether there are bone or muscular deformities, presence of dystonia, dyskinesias, presence of spasms, gait observation, cognition and comorbidities should be evaluated.

Technique Description

The technique created by Park et al[36] in 1991 differs from the others by removing the lamina of one or two vertebrae, while traditional techniques use laminectomy from five to seven vertebrae.

The patient is sedated and intubated in dorsal decubitus on the lateral stretcher at the surgical table (►**Fig. 1**). Medications that do not alter the EMG activity, such as long-lasting neuromuscular blockers, should be avoided.

After orotracheal intubation, electrodes are introduced bilaterally in the long, large lateral, tibial anterior and medial gastrocnemius muscles (►**Fig. 2**).

Subsequently, the patient is transferred carefully to the ventral decubitus position to maintain soft structures at strategic points of the body to avoid decubitus ulcers. In this position, electrodes are introduced in the perichannel region and the wires are fixed with adhesive in the patient's lower limb (►**Fig. 3**).

We use continuous EMG and a trigger with 14 channels to stimulate the following L1-L2, L2-L3, L3-L4, L5-L5, L5-S1, S1-S2 and on-the-side segments. The interpretation of the EMG result is done by the neurophysiologist. Intraoperative EMG provides valuable information to the neurosurgeon that helps differentiate the sensory root of the motor, in addition, the mapping of the sphincter fibers is a safety factor for not adding deficits to the patient.[37] It is also necessary to have the utmost care with the sacral fibers of S2 to S4 to protect the bladder and sexual function.[38] The patient is kept in a slight position of Trendelenburg to reduce CSF losses. Radioscopy or ultrasonography (in case of children < 10 years old) is used to find the vertebral level to be approached (previously chosen through magnetic resonance imaging [MRI]) to find the MC end, and the incision is made after marking this level (►**Fig. 4**). Since laminectomy should be limited to this segment, it is important that the MC is found.

After making a horizontal incision, with the opening of the subcutaneous cell tissue, we dissected the dorsal musculature away from the thorny process until the slides of the L1 vertebra were exposed, in this example (►**Fig. 5**). After

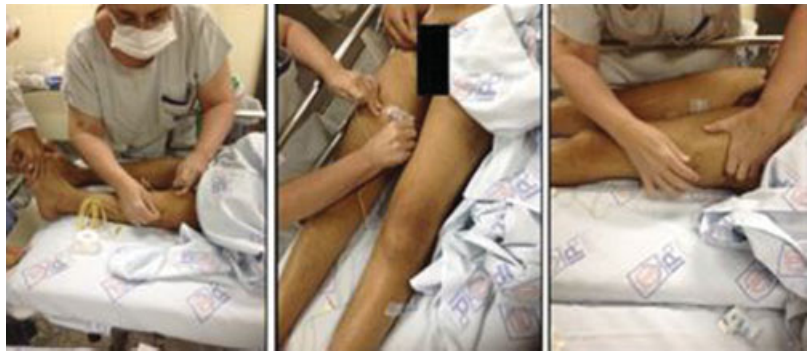


Fig. 2 Positioning of the EMG electrodes in the muscles of the lower limbs.

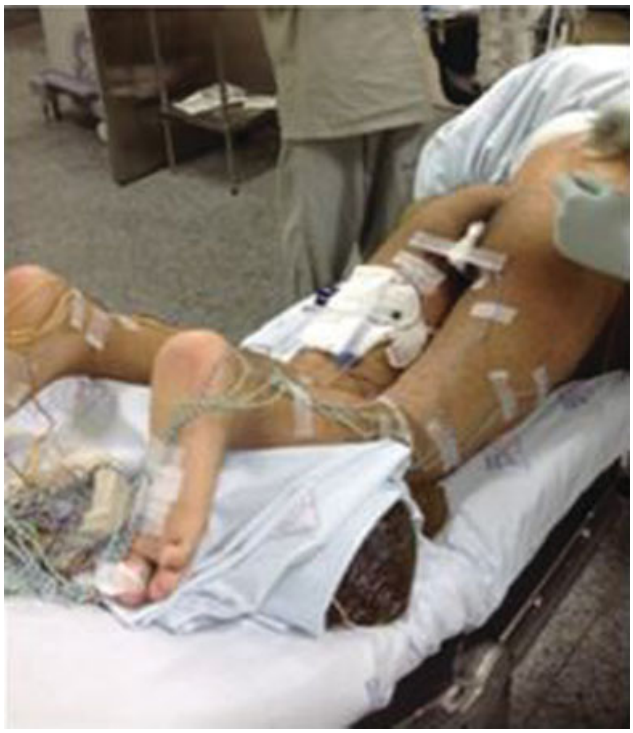


Fig. 3 Patient in ventral decubitus with electrodes positioned on the lower limbs and in the perichannel region.

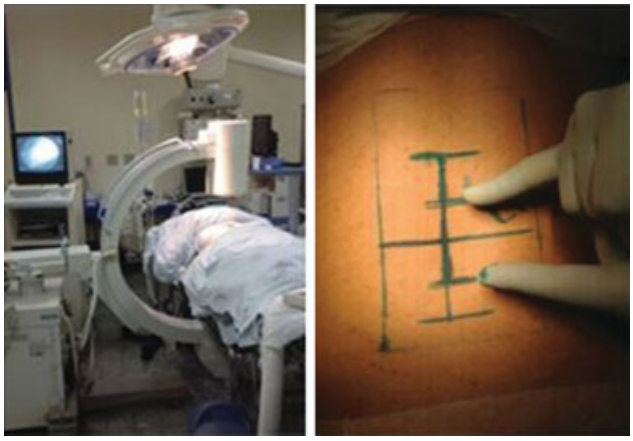


Fig. 4 Left: patient positioned in ventral decubitus at the moment radioscopy is performed to find the level of the spine that will be approached. Right: marking on the skin with the size of the incision.

exposure of the interlaminar space, the yellow ligament is removed with visualization of the dural sac. A linear incision is made to expose the medulla and visualize the MC and the cauda equina.

From this moment, saline solutions should be avoided because they alter the responses of the EMG. The edges of the dura mater are anchored with Vicryl or nylon 4.0 to keep the channel open. The first foramen of the anterior and posterior roots, lateral to the MC, is sought. The root is found, it is divided into four parts to initiate the stimulation to pulses of 0.1 thousandth of a second to a frequency of 0.5 Hz and then 50 Hz, and then identify if we are stimulating motor or sensory fibers. In spasticity, sensory fibers are hyperactive;

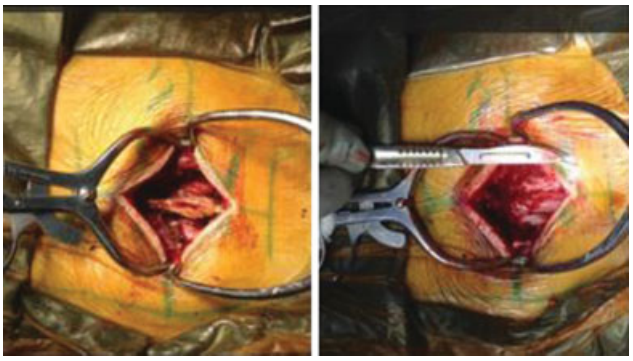


Fig. 5 Left: dorsal musculature distanced with visualization of the supraspinatus ligament and spinous process of L1. Right: after laminotomy, exposure of the dural sac to the level of the medullary cone.

In these cases, the most altered part for neurolysis is chosen, preserving those that are in better condition. By not choosing to cut the entire sensory root, it avoids the pain of deafferentation. In the Fig. 6a, we visualize the medullary dura mater at the open L1 level, exposing the MC and the cauda equina. We find the L1 sensory root and use a latex repair to separate the motor from the sensory part (►**Fig. 6b**). Half of the fibers in the L1 dorsal root are cut without stimulation (►**Fig. 6c**). In sequence, we stimulated L2 roots with EMG, isolating the sensory part and separating it into four parts. Again, we stimulate each segment to evaluate the degree of hyperactivity and recorded the electrical patterns of the related muscles. The most injured segments are sectioned.

The root that has already been cut is separated from the others with a tape or vascular shoelace, so as not to risk approaching them again (►**Fig. 6d**). After finding another root and separating again with repair (►**Fig. 6d**), we do a new stimulation and repeat the whole process (►**Figs. 6e** and **6f**) until you approach the whole L2 S2 segment or, depending on the case, those in which the patient has more functional impairment.

The stimulation of nerve roots intraoperatively assesses the functional integrity of the nerve, since it is visually impossible for the surgeon to make this differentiation. As each root is stimulated, a motor response in the musculature of the corresponding segment is perceived, and the information of the action potential is received in the software that analyzes and records the stimuli corresponding to each root. In ►**Fig. 7**, we observe a graphic example of stimulation. The motor latency was 7 seconds and the sensory was 9 seconds. It shows that the L3 root is being stimulated and that the action potential has a late peak to the Yellow Line, which marks the division between motor and sensory, confirming it to be a sensory root. In the left column (in blue) the stimulations are separated into the four parts of the root. It is noted that parts 2 and 3 are more hyperactive. Therefore, these parts can be sectioned, preserving parts 1 and 4.

The advantages of this technique consist in the reduction of spinal deformity, especially in children, if compared with the extensive laminectomy in the traditional technique, improvement of spasticity in the hip, due to the section in the first lumbar dorsal root, reduced surgical access with lower muscular manipulation, and, consequently, less postoperative pain

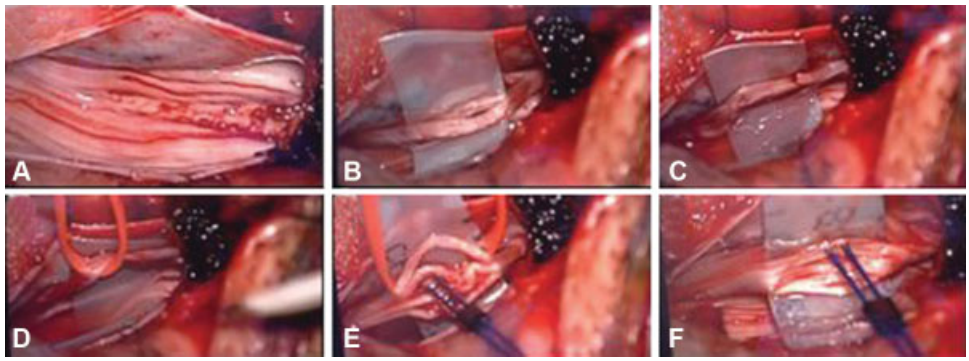


Fig. 6 Intraoperative images showing the open dura mater with visualization of the medullary cone and roots being stimulated during electromyography with bipolar configuration.

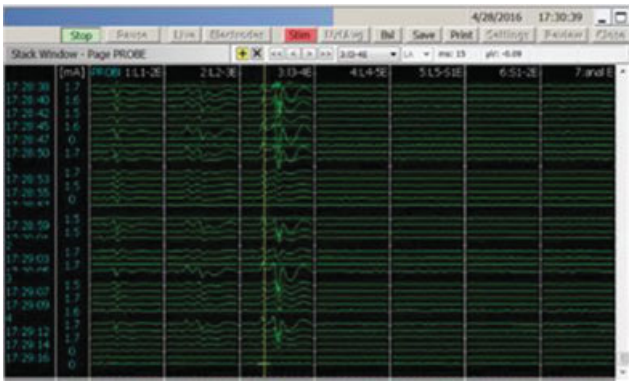


Fig. 7 Stimulation of the L3 segment. We visualize that the wave pulse is to the right of the yellow line and denotes the separation between a motor or sensory impulse. The left side (blue) shows the division of the four parts, evidencing that parts 2 and 3 of the L3 root are hyperactive and should be sectioned.

and early resumption of rehabilitation activities. However, the risks are shared with other procedures such as paraplegia, paralytic bladder, sexual impotence and sensitivity deficit.

A study that included 95 patients treated with SDR in childhood, and accompanied them for periods varying from 20 to 28 years, showed that 91% of the patients submitted to surgery reported that the surgical treatment positively impacted the quality of life. In 42% of the patients, there was improvement in ambulation, 88% would recommend the procedure for other patients and there were no late complications for these patients.[39]

Daunter et al selected patients with CP who underwent SDR in infancy (before 10 years old) and compared them with an unoperated control group. They concluded that the SDR group presented less pain, fatigue and functional decline compared with the nonsurgical group.[40]

The SDR technique by single-segment laminoplasty provides a less invasive approach, and the incidence of scoliosis after this approach is comparable with the natural history of children accompanied as outpatients.[41]

Conclusion

Selective dorsal rhizotomy is efficient in the treatment of severe spasticity. It is a surgery with low morbidity, and electrophysiological stimulation has shown to be efficient in the choice of root segments that should be safely sectioned. However, for a successful treatment, the patient should be rigorously selected. In addition to the functional improvement of the spastic patients, there is an expressive improvement in the quality of life of the caregivers.

Conflicts of Interests

The authors declare that there are no conflicts of interests.

References

1 Rumeau-Rouquette C, Grandjean H, Cans C, du Mazaubrun C, Verrier A. Prevalence and time trends of disabilities in school-age children. Int J Epidemiol 1997;26(01):137–145
2 Kuban KCK, Leviton A. Cerebral palsy. N Engl J Med 1994;330(03): 188–195
3 Farmer JP, Sabbagh AJ. Selective dorsal rhizotomies in the treatment of spasticity related to cerebral palsy. Childs Nerv Syst 2007; 23(09):991–1002
4 Abolhasani H, Ansari NN, Naghdi S, Mansouri K, Ghotbi N, Hasson S. Comparing the validity of the Modified Modified Ashworth Scale (MMAS) and the Modified Tardieu Scale (MTS) in the assessment of wrist flexor spasticity in patients with stroke: protocol for a neurophysiological study. BMJ Open 2012;2(06):1136–1144
5 Lianza S, Koda LC. Avaliação da capacidade. In: Lianza S (editor). Medicina de reabiliatação. 3a ed. Guanabara Koogan: Rio de Janeiro; 2001
6 Pierson SH. Outcome measures in spasticity management. Muscle Nerve Suppl 1997;6:S36–S60
7 Penta M, Thonnard JL, Tesio L. ABILHAND: a Rasch-built measure of manual ability. Arch Phys Med Rehabil 1998;79(09):1038–1042
8 Millet MF. Neurochirurgie dans le paraplegic spastiques. Resultats a moyen treme de la radicellotomie posterieure selective. In: Simon L (editor). Actualites en reeducation fonctionnelle et readaptation. Paris1981:76–85
9 Sindou MP. History of the neurosurgical treatment for spasticity. Oper Tech Neurosurg 2004;7(03):96–99
10 Teixeira MJ, Fonoff ET. Surgical treatment of spasticity. Rev Med (São Paulo) 2004;83(1–2):17–27
11 Evans PM, Evans SJW, Alberman E. Cerebral palsy: why we must plan for survival. Arch Dis Child 1990;65(12):1329–1333
12 Abbe R. A Contribution to the Surgery of the Spine. J Neurosurg 1964;21(01):820–823 (reprint from The Medical Record)
13 Bennett WH. Acute spasmodic pain in the left lower extremity was completely relieved by sub-dural division of the posterior roots of certain spinal nerves, all other treatment having proved useless. Med Chir Trans 1889;72:329–348, 3

14 Foerster O. On the indications and results of the excision of posterior spinal nerve roots inmen. Surg Gynecol Obstet 1913; 16:463–474
15 Gros C, Ouaknine G, Vlahovitch B, Frèrebeau P. [Selective posterior radicotomy in the neurosurgical treatment of pyramidal hypertension]. Neurochirurgie 1967;13(04):505–518
16 Fasano VA, Barolat-Romana G, Ivaldi A, Sguazzi A. [Functional posterior radiculotomy, in the treatment of cerebral spasticity. peroperative electric stimulation of posterior roots and its use in the choice of the roots to be sectioned]. Neurochirurgie 1976;22 (01):23–34
17 Peacock WJ, Arens LJ. Selective posterior rhizotomy for the relief of spasticity in cerebral palsy. S Afr Med J 1982;62(04):119–124
18 Warf BÇ, Nelson KR. The electromyographic responses to dorsal rootlet stimulation during partial dorsal rhizotomy are inconsistent. Pediatr Neurosurg 1996;25(01):13–19
19 Steinbok P, Kestle JR. Variation between centers in electrophysiologic techniques used in lumbosacral selective dorsal rhizotomy for spastic cerebral palsy. Pediatr Neurosurg 1996;25(05):233–239
20 Chabal C, Jacobson L, Little J. Effects of intrathecal fentanyl and lidocaine on somatosensory-evoked potentials, the H-reflex, and clinical responses. Anesth Analg 1988;67(06):509–513
21 Phillips LH II, Park TS. Electrophysiologic mapping of the segmental anatomy of the muscles of the lower extremity. Muscle Nerve 1991;14(12):1213–1218
22 Fukuhara T, Nakatsu D, Namba Y, Yamadori I. Histological evidence of intraoperative monitoring efficacy in selective dorsal rhizotomy. Childs Nerv Syst 2011;27(09):1453–1458
23 McLaughlin J, Bjornson K, Temkin N, et al. Selective dorsal rhizotomy: meta-analysis of three randomized controlled trials. Dev Med Child Neurol 2002;44(01):17–25
24 Engsberg JR, Ross SA, Collins DR, Park TS. Effect of selective dorsal rhizotomy in the treatment of children with cerebral palsy. J Neurosurg 2006;105(1, Suppl):8–15
25 Mittal S, Farmer JP, Al-Atassi B, et al. Long-term functional outcome after selective posterior rhizotomy. J Neurosurg 2002; 97(02):315–325
26 Abbott R, Johann-Murphy M, Shiminski-Maher T, et al. Selective dorsal rhizotomy: outcome and complications in treating spastic cerebral palsy. Neurosurgery 1993;33(05):851–857, discussion 857
27 Gul SM, Steinbok P, McLeod K. Long-term outcome after selective posterior rhizotomy in children with spastic cerebral palsy. Pediatr Neurosurg 1999;31(02):84–95
28 Steinbok P, Reiner AM, Beauchamp R, Armstrong RW, Cochrane DD, Kestle J. A randomized clinical trial to compare selective posterior rhizotomy plus physiotherapy with physiotherapy alone in children with spastic diplegic cerebral palsy. Dev Med Child Neurol 1997;39(03):178–184
29 Wright FV, Sheil EM, Drake JM, Wedge JH, Naumann S. Evaluation of selective dorsal rhizotomy for the reduction of spasticity in cerebral palsy: a randomized controlled tria. Dev Med Child Neurol 1998;40(04):239–247
30 Albright AL, Barry MJ, Fasick MP, Janosky J. Effects of continuous intrathecal baclofen infusion and selective posterior rhizotomy on upper extremity spasticity. Pediatr Neurosurg 1995;23(02): 82–85
31 Beck AJ, Gaskill SJ, Marlin AE. Improvement in upper extremity function and trunk control after selective posterior rhizotomy. Am J Occup Ther 1993;47(08):704–707
32 Buckon CE, Sienko Thomas S, Aiona MD, Piatt JH. Assessment of upper-extremity function in children with spastic diplegia before and after selective dorsal rhizotomy. Dev Med Child Neurol 1996; 38(11):967–975
33 Marbini A, Ferrari A, Cioni G, Bellanova MF, Fusco C, Gemignani F. Immunohistochemical study of muscle biopsy in children with cerebral palsy. Brain Dev 2002;24(02):63–66
34 Van de Wiele BM, Staudt LA, Rubinstien EH, Nuwer M, Peacock WJ. Perioperative complications in children undergoing selective posterior rhizotomy: a review of 105 cases. Paediatr Anaesth 1996;6(06):479–486
35 Vall JAÇ. Lima ALO, Martins AO. O impacto da rizotomia dorsal seletiva na qualidade de vida de crianças espásticas portadoras de paralisia cerebral. Arq Bras Neurocir. 2008;27(01):7–11
36 Park TS, Johnston JM. Surgical techniques of selective dorsal rhizotomy for spastic cerebral palsy. Technical note. Neurosurg Focus 2006;21(02):e7
37 Shalash AS, Ghany WAA. Intraoperative Electrophysiological Monitoring During Selective Dorsal Rhizotomy in Children with Spastic Cerebral Palsy. Egypt J Neurol Psychiat Neurosurg 2010;47 (01):505–510
38 Huang JÇ, Deletis V, Vodusek DB, Abbott R. Preservation of pudendal afferents in sacral rhizotomies. Neurosurgery 1997; 41(02):411–415
39 Park TS, Liu JL, Edwards C, Walter DM, Dobbs MB. Functional Outcomes of Childhood Selective Dorsal Rhizotomy 20 to 28 Years Later. Cureus 2017;9(05):e1256
40 Daunter AK, Kratz AL, Hurvitz EA. Long-term impact of childhood selective dorsal rhizotomy on pain, fatigue, and function: a case-control study. Dev Med Child Neurol 2017;59(10):1089–1095
41 Funk JF, Haberl H. Monosegmental laminoplasty for selective dorsal rhizotomy–operative technique and influence on the development of scoliosis in ambulatory children with cerebral palsy. Childs Nerv Syst 2016;32(05):819–825

Traumatic Dissection of Arterial Cervical Vessels: Report of Two Cases and Literature Review

Dissecção arterial traumática de vasos craniocervicais: Relato de casos e revisão da literatura

Guilherme Finger[1] Tobias Ludwig do Nascimento[1] Julia Carolina Lusa Tessaro[2] Eduarda Tanus Stefani[2] Maria Eduarda Conte Gripa[2] Eduardo Ekman Tisbierek[2] Luiz Carlos Porcello Marrone[3] Carla Bittencourt Rynkowski[4]

[1] Department of Neurosurgery, Hospital Cristo Redentor, Porto Alegre, RS, Brazil
[2] Universidade Luterana do Brasil, Canoas RS, Brazil
[3] Department of Neurology, Universidade Luterana do Brasil, Canoas RS, Brazil
[4] Department of Intensive Care Unit, Hospital Cristo Redentor, Porto Alegre, RS, Brazil

Address for correspondence Guilherme Finger, MD MsC, Rua Domingos Rubbo 020, Porto Alegre, RS, 91040-000, Brazil (e-mail: guilhermefingermd@gmail.com).

Arq Bras Neurocir 2021;40(3):e245–e252.

Abstract

Even though traumatic dissection of cervical arterial vessels is the major cause of stroke among adults, it is still an underdiagnosed disease in neurosurgical emergencies, since most patients do not have or present subtle clinical signs in the acute phase. The authors report two interesting cases of cervical artery dissection with different traumatic mechanisms and present a broad literature review about this subject.

Keywords

- internal carotid dissection
- vertebral artery dissection
- cerebrovascular trauma

Resumo

Embora a dissecção traumática de vasos cervicais seja um das principais causas de isquemia cerebral em adultos, ainda é um patologia subdiagnosticada nas emergências, uma vez que os pacientes são assintomáticos ou oligossintomáticos na fase aguda. Os autores descrevem dois casos interessantes de dissecção de artérias cervicais por diferentes mecanismos traumáticos, seguidos de ampla revisão da literatura sobre o tema.

Palavras-chave

- dissecçao artéria carótida
- dissecçao vertebral
- trauma cerebrovascular

Introduction

Arterial dissection corresponds to a detachment between the layers of the artery wall creating a false blood path. This phenomenon either impairs the perfusion of tissues downstream or causes bleeding.

According to its etiology, it can be classified as spontaneous, iatrogenic or traumatic. The mortality of traumatic cases range from 20 to 40%, depending on the association with other traumas. Furthermore, it is usually an underdiagnosed etiology of stroke, whose neurologic sequelae, in this scenario, affects between 40 and 80% of the patients.[1]

received
May 4, 2020
accepted
August 4, 2020
published online
November 26, 2020

DOI https://doi.org/10.1055/s-0040-1718422.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Traumatic dissection requires specific considerations that will be addressed in this article associated with the reports of two cases.

Case Report

Case 1

A 52-year-old male patient sought hospital care reporting pain in the left anterior cervical region. The pain started abruptly, after rotational movement of the neck to hit a ball with the head during a soccer match, and persisted with intensity 4/10 on the following days. Two days after the event, he woke up with complete right hemiparesis associated with motor aphasia and mild dysarthria. The patient underwent cranial tomography without contrast, which did not show hemorrhages nor hematomas, but revealed loss of cortico-subcortical differentiation in the vascular territory of the upper trunk of left middle cerebral artery. The patient was not submitted to the thrombolysis criteria due to having an ictus delta longer than 4 ½ hours. During hospitalization and etiological investigation of the ischemic event, signs compatible with dissection of the left carotid artery were identified on angiotomography (►**Fig. 1**). The patient received treatment with antiplatelet therapy associated with strict blood pressure control and motor physiotherapy. During follow-up, a significant paresis improvement in the right lower limb and aphasia was shown, despite monoparesis in the right upper limb, that persisted during 6 months of follow-up after the event, with a strength grade 3.

Case 2

Female patient, 39 years old, victim of car accident, received medical attention at the scene and was transported to the polytrauma reference hospital. On hospital arrival, at the emergency room, the patient was alert, oriented in space and time, Glasgow coma scale was 15/15, there was no motor deficits and cranial nerves were intact. During abdominal examination, she reported abdominal pain, whose investigation showed a small

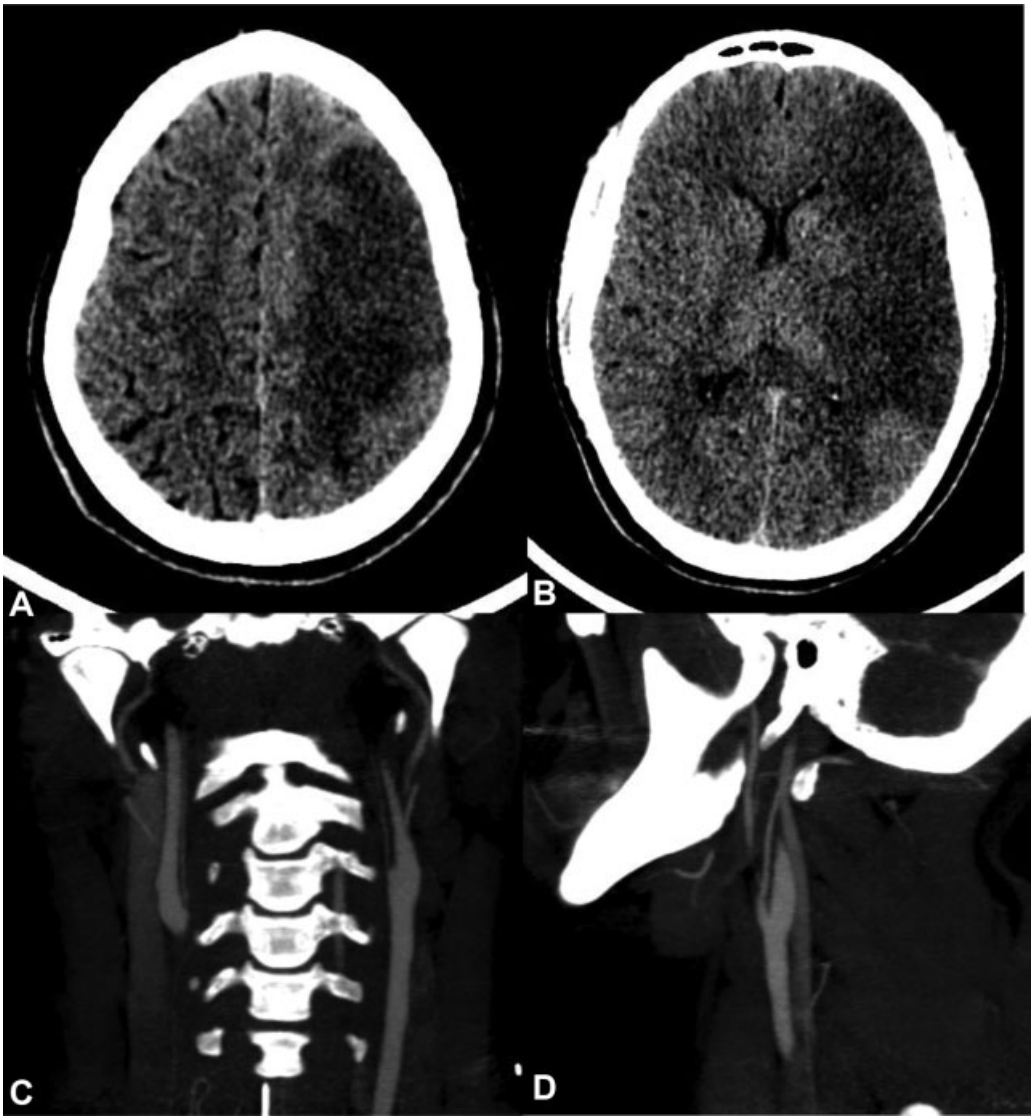


Fig. 1 Traumatic dissection of the left internal carotid with ischemia on the vascular territory of the left middle cerebral artery. Non-contrasted CT scan (**A e B**), hypodensity in the territory of the left middle cerebral artery. Angiotomography of cervical arteries showing gradual narrowing and blood flow obstruction in the left internal carotid artery (**D**). Angiotomography showing right internal carotid dissection

amount of free fluid in the pelvis and pneumoperitoneum. Exploratory laparotomy was performed and a laceration in the jejunum was identified at 20 cm from the Treitz angle, qualified for primary correction. The patient had a good evolution in the immediate postoperative period. On the 2nd postoperative day (and after the trauma), the patient developed hypoesthesia and monoparesis in the left upper limb, without hyporeflexia or alterations restricted to a dermatome and myotome (thus excluding injury to the second radicular motor neuron or brachial plexus). In the subsequent hours, the neurological condition worsened, evolving with complete left hemiplegia. The CT investigation evidenced sparse areas of hypodensity in the territory of the right middle and right anterior cerebral arteries. Further investigation with angiotomography pointed the dissection of the right internal carotid artery in its cervical portion (►**Fig. 2**). The patient received antiplatelet therapy, with slight neurological improvement, and was discharged from the hospital with complete and disproportionate left hemiparesis, with force 1 on the distal left upper limb and grade 2 proximal, and force 2 on the left lower limb.

Discussion

Arterial Anatomy

The arteries that irrigate the brain originate from the brachiocephalic branch (common right carotid artery), from the aortic arch (common left carotid artery) and from the right and left subclavian arteries (right and left vertebral artery, respectively). The common carotid artery divides itself at the carotid bulb level (topography of the 4th cervical vertebra) in internal carotid artery (ICA) and external carotid artery (ECA). Based on the classification published by Bouthillier, the ICA is divided in 7 segments, from C1 to C7 (►**Fig. 3**).[2] The cervical segment from the ICA is located medially to the internal jugular vein and anteriorly to the vagal nerve, ascending in the neck toward the petrous portion of the temporal bone.

The vertebral artery (VA) is classified in 4 segments. The first segment (V1) starts in the origin of the VA and goes up to the vertebral foramen of the sixth cervical vertebra. The V2 segment ascends throughout the cervical foramen to the second cervical vertebra. From the exit of this vertebra foramen ahead it is considered the V3 segment, in which there is an external curvature followed by an internal curvature that stays along the superior border of the Atlas and ascends from the foramen magnum to the intracranial space. From this point on, it is considered the V4 segment (►**Fig. 4**).

Fig. 2 Angiotomography showing dissection of the right carotid artery without arterial flow above the dissection

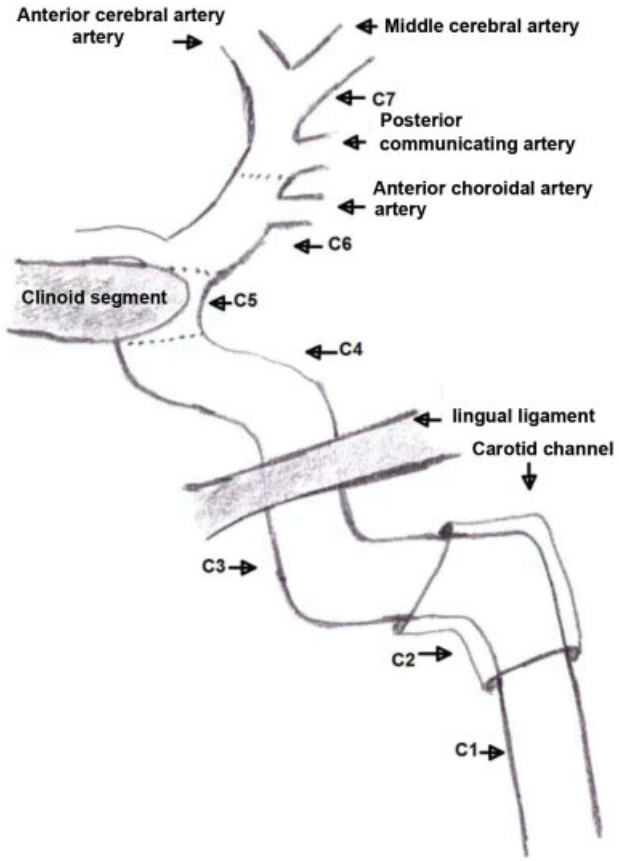


Fig. 3 **Internal Carotid Artery**. C1–cervical segment: ascends from the carotid bifurcation into the entrance of the temporal bone. C2–petrous segment, divided in two subsegments inside the carotid channel – ascending and horizontal parts. C3–lacerum segment, from the carotid channel to the lingual ligament. C4–cavernous segment from the lingual ligament through the cavernous sinus (posterior ascending, horizontal and anterior ascending parts). C5–clinoid segment, a wedge shaped segment between the proximal and distal dural ring. C6–ophtalmic segment, originates in the distal dural ring extending up to the origin of the posterior communicating artery. C7–communicaitng segment, from the emergence of the posterior communicating artery until carotid bifurcation.

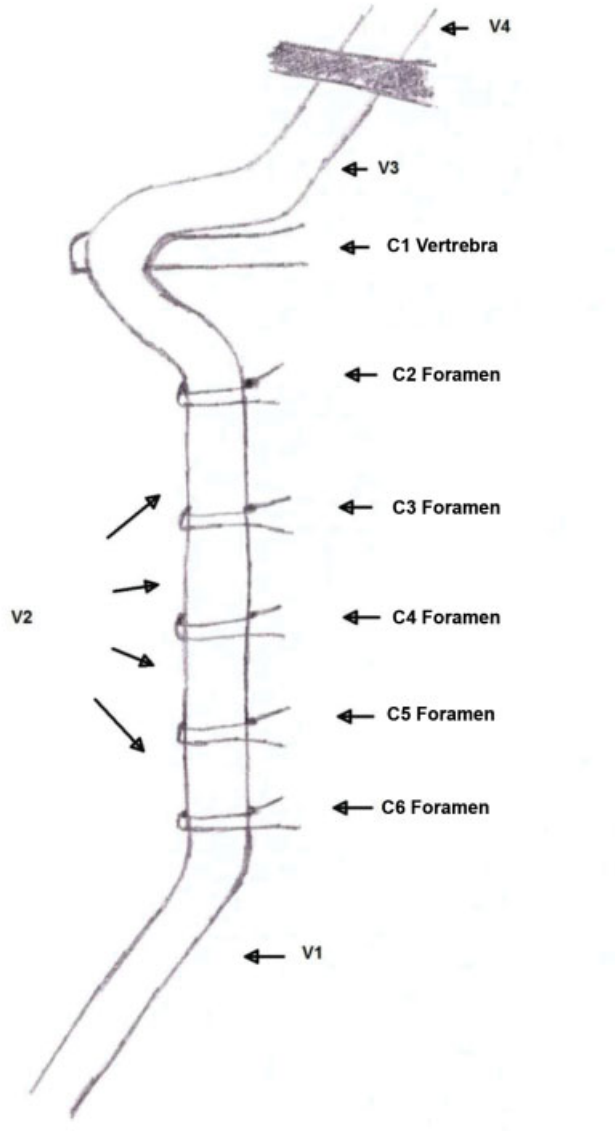


Fig. 4 Vertebral Artery

Epidemiology

Arterial dissection of extra- and intracranial vessels is the main cause of stroke in young adults.[3] Yet, they present different patterns of incidence; traumatic carotid dissection has its peak in the 6th decade of life, while vertebral dissection presents a more homogeneous distribution between the 3rd, 4th and 6th decades of life.[4]

Dissection of the extradural portion of the craniocervical arteries is more common than intradural, since it is a mobile segment with no rigid structures of protection. Analyzing extradural branches, the ICA is more affected than the VA, in a proportion of 3:1.[5] When considered intradural lesions, the VA is more affected than the ICA.

Considering patients victims of craniocervical trauma, without stratifying the cinematics, the incidence of carotid artery or VA dissection varies from 1.7 to 4.9%. Also, the incidence of combined traumatic lesion of the carotid artery with the vertebral is 6.5%. The segment C1 of the ICA is the most common site of the dissection, with an estimated incidence of 2.5 to 3.0/100,000 people. On the other hand, the extradural VA dissection has an estimated incidence of 1.0 to 1.5 cases/100.000 people, independent of the trauma mechanism.[4,6–8]

Analyzing only craniocervical blunt trauma victims, the incidence of carotid lesions varies from 0.1 to 2.6%; and, only among polytrauma patients, the incidence reaches 2.7%. On the other hand, the incidence of vascular lesions in victims of penetrating trauma varies from 3 to 40%.

However, the true incidence of carotid dissection due to trauma may be greater, since the diagnosis is established usually when symptoms set in, which can be immediately after the trauma or during its segment (due to ischemia, progressive dissection, thromboembolic symptoms or bleeding).[9,10]

Etiology

Dissections can occur in penetrating or blunt craniocervical trauma. Carotid dissection of blunt trauma is predominantly associated with severe kinematics and direct trauma to the cervical region – being its main cause automobile collisions. Traumas that result in skullbase fractures (especially in the petrous segment of the carotid canal) also represent a high risk for carotid dissection.[8]

In 1974, Crissey et al described four mechanisms that can lead to C1 injury: 1–direct trauma through anterolateral direction of the neck, 2–cervical hyperextension associated with rotation, 3–blunt intraoral trauma and 4–fractures of the skull base bones involving the carotid canal. In addition, mechanisms of distraction/flexion, distraction/extension or lateral flexion forces on the cervical spine can result in carotid or vertebral dissection.[9]

On the other hand, vertebral dissection in blunt trauma is not necessarily associated with the severity of the trauma. It can occur in trivial traumas, such as spinal manipulation maneuvers or even Valsalva maneuvers. The VA dissection in car crashes of severe kinematics is usually associated with a fracture or dislocation of the cervical spine. The VA is more susceptible to dissection by blunt trauma in V1 and V3, which are segments of greater mobility. The V2 segment is more susceptible to foraminal bone lesions or cervical dislocations.[7]

Penetrating craniocervical injuries can be caused by stab wounds, explosives or projectiles. The kinematics of these cases can cause direct lesions in the tissues they pass through, destroying structures along their path. More severe kinematic injuries, such as high-speed projectiles of civil and military war, cause direct and indirect injuries, which are disruptions of adjacent tissues by shock waves. These injuries can affect the blood vessels, leading to ischemia (intimal dissections with obstruction of the vessels) or bleeding with arteriovenous fistulas and traumatic pseudoaneurysms (when they affect the adventitial layer).

Although the external factors are crucial conditions, some underlying pathologies may predispose to traumatic dissection of cervical vessels. Among them are Marfan syndrome, Ehler-Danlos syndrome type IV, autosomal dominant

polycystic kidney disease, type I imperfecta osteogenesis, α1-antitrypsin deficiency and fibromuscular dysplasia.

Pathogenesis

The arterial wall consists of three layers (endothelium/intima, middle muscle layer and adventitia). Dissection is characterized as rupture and separation of these three layers, hence occurring either between the endothelium and the middle muscle layer (subintima dissection), or between the middle muscle layer and the adventitia (subadventitial dissection). Factors such as size of the endothelium lesion, associated hemodynamic forces and vascular resistance, determine whether the dissection will result in stenosis or aneurysmatic dilatation of the artery. Subintima dissection tend to cause stenosis, while subadventitia dissections tend to cause pseudoaneurysms.

The ICA dissection normally occurs in the first two centimeters after the carotid bulb, ending usually proximal to its entrance in the temporal bone. The VA is more susceptible at the entrance point in the transverse foramen of C6, because the artery is relatively fixed at the bony orifice of the foramen while the segment C5/C6 has elevated mobility. Besides, the greater mobility the vertebral artery has in rotation at the atlantoaxial junction or flexion/extension at the atlanto-occipital junction makes this region particularly susceptible to dissection by minor trauma.

The traumatic extradural dissections of the ICA and VA usually presents with thromboembolic events with subintima lesions, resulting in stenosis, occlusions and thromboembolism. The intradural dissections tend to cause subadventitia lesions, resulting in vessel rupture (with bleeding) or formation of a pseudoaneurysm (with immediate or late bleeding).

Clinical Manifestations

Neurological changes can occur over the first 24 hours after the trauma and only 10% of patients have clinical manifestations when arriving at the hospital.[4,7] Clinical warning signs include cervical hematoma, cerebral infarction identified at computed tomography (CT), type II or III Le Fort fracture, Glasgow coma scale (ECG) < 6 points and skull base fractures. In penetrating skull trauma, lesions close to the pterion, or crossing the midline, lead to intracranial vascular injury in up to 40% of cases.[10]

When present, clinical manifestations of dissection range from headache and cervical pain to severe neurological compromise. Because of different vascular territory supply, neurological manifestations of carotid lesions are distinct from the vertebral lesions. Despite this, extradural segments show common signs and symptoms such as cervical pain, hemorrhage externalized by the upper airway or expanding cervical hematoma.

A classic triad of traumatic carotid dissection is characterized by pain (cervical region, face and head), Horner's syndrome and ischemic cerebral symptoms or ipsilateral retina ischemia (secondary to the ophthalmic artery embolization). The three components are found concurrently in less than a third of patients with C1 dissection.

The usual clinical manifestation of V1 dissection includes cervical and occipital pain, of high intensity, with symptoms of cerebellar ischemia (such as vertigo, dysdiadochokinesia and ipsilateral dysmetria).

Intracranial vessels dissections tend to bleed immediately after rupture of the vessel, or later, due to bleeding from pseudoaneurysms. The characteristic clinical picture of ICA dissection and rupture of its intracranial portion is a carotid-cavernous fistula when the rupture is found in the cavernous segment (C4). This lesion comes along with a cavernous syndrome: paresis of the extrinsic ocular musculature, eyeball protrusion, chemosis, eye pain, but preservation of visual acuity (►**Fig. 5**).

Diagnostic Imaging

Diagnosis of craniocervical vessels dissection is confirmed with imaging tests that allow visualization of the vessels as well as their blood flow. For this matter, CT, magnetic resonance imaging (MRI) and arteriography are the exams that can provide the diagnosis, with different degrees of sensitivity and specificity. When there is a reduction in the lumen of the vessel $> 50\%$, the use of cerebral ultrasound with Doppler is another method that can be used.[11]

It is a challenge to make the diagnosis in asymptomatic patients and determine which patient should be submitted to a vascular investigation. Some criteria have been described to increase the investigative positive predictive value. Vascular lesions can be found in 44 to 90% of the patients with the following findings: blunt trauma of severe cinematic, diffuse axonal injury, ECG ≤ 8, face fractures Le Fort II or III or fractures of the skull base (especially from the temporal bone). In these cases, an image study must be performed.

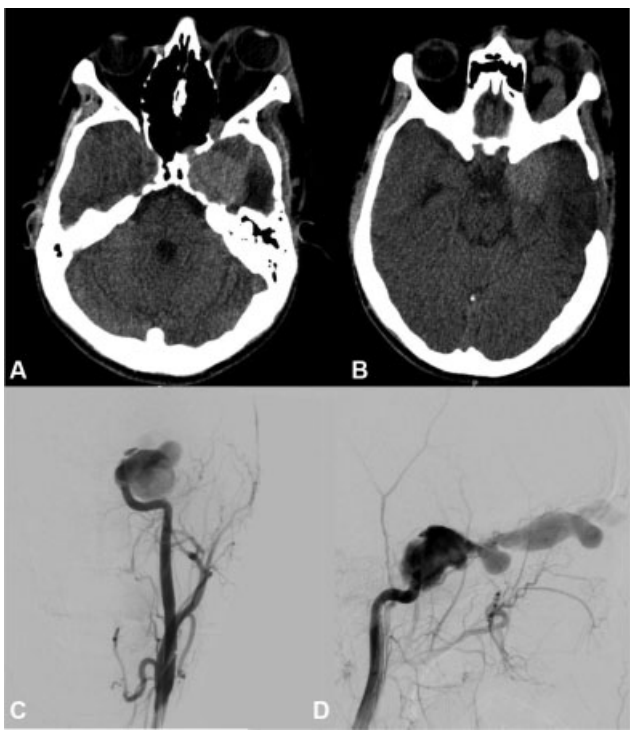


Fig. 5 Patient with traumatic carotidcavernous fistula

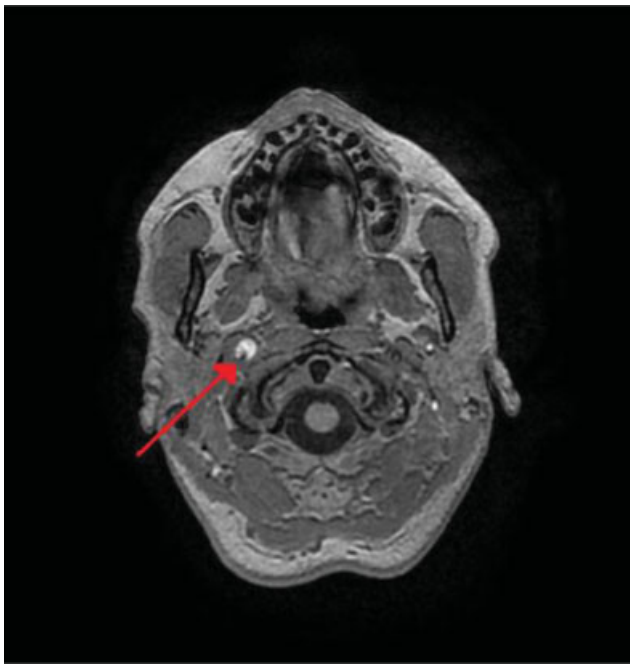


Fig. 6 Angioresonance showing right internal carotid dissection.

Computed Tomography

Although the gold-standard exam for diagnosis of dissection may be arteriography, computed angiotomography is, possibly, a more appropriate test for screening severe polytrauma patients. This examination allows the visualization of the cerebral parenchyma in search of signs of infarction, in addition to the visualization of the patency of the cervical vessels and brain vascularization. The limitation of the angiotomography is the exposure to radiation (mainly for children, adolescents and pregnant women). Furthermore, the hypodense image in the region of the cervical vessels, which corresponds to intramural hematomas, can also be seen in atheromatous plaques, making it difficult to distinguish and establish the right diagnosis.[12]

Magnetic Resonance Imaging

Craniocervical MRI and angiotomography combined present a sensibility of 99%. These methods are especially useful in pregnant women, young patients or patients with renal failure, since they do not use ionizing radiation or iodinated contrast agent.[12]

The evaluation of the arterial dissection in the MRI consists of acquisition phases[1]: diffusion images – diffusion weighted imaging (DWI) and fluid attenuation inversion recovery (FLAIR) to assess the occurrence of cerebral infarction secondary to dissection[2]; T1 and T2 images to assess the presence of intramural hematoma[3]; angioresonance (angioRM) to assess the vessel lumen. The classic finding of dissection in MRI is an eccentric periluminal halo, indicative of intramural hematoma. The intramural bleeding and its expansion can be easily identified in sequences with the fat saturation technique (►**Fig. 6**).[13]

Time between dissection onset and images in MRI or angiotomography is a potential limitation for this method, because the sensibility is greater in the first 2 days after the dissection. Hence, the evolutive pattern of presentation must be considered. In the acute phase, the hematoma consists primarily of deoxyhemoglobin and has an isointense presentation when compared with the underlying muscle tissue. Subacute hematomas contain intra and extracellular methaemoglobin and therefore present hypersignal in both T1 and T2. This pattern persists for months, when the hyperdensity gradually becomes isointense. Ruptures of the intima may also be visualized in MRI, especially in T2.

Arteriography

Arteriography is the gold standard method for diagnosis of craniocervical arterial dissection. Besides the sensitivity of 97 to 100%, it allows endovascular therapy when indicated.[13]

The most common finding in arteriography is the irregular size of the vessel with its gradual thinning from the breaking point of the wall. Other arteriographic finding of carotid dissection is the "double-lumen" sign[13] (►**Fig. 7**).

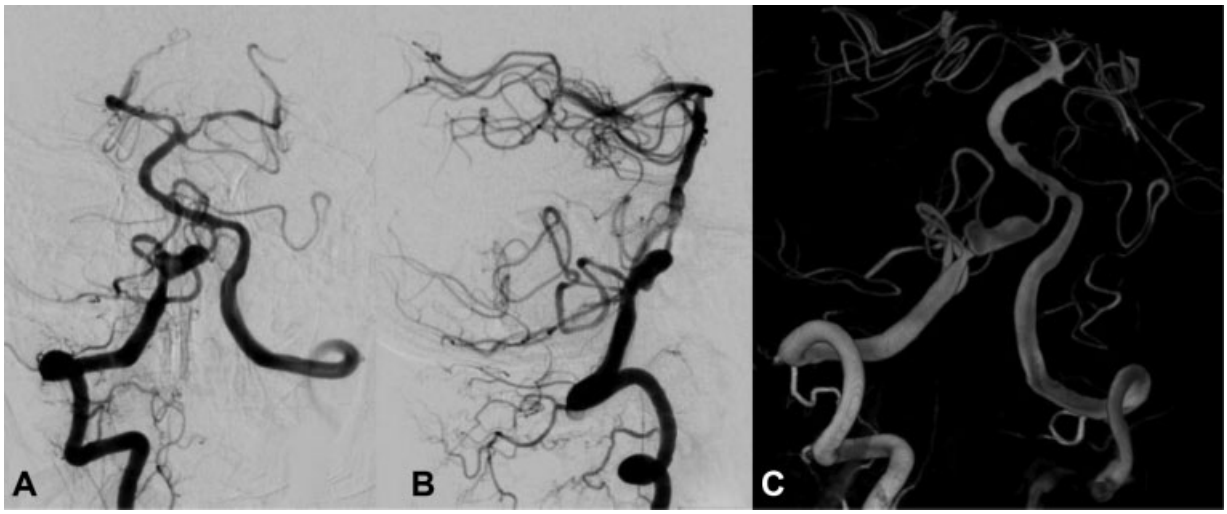


Fig. 7 Dissecting traumatic aneurysm on the right vertebral artery with luminal narrowing distal to the aneurysm

Although it is considered the gold standard, arteriography is unable to assess the thickness of the vessel wall, because it shows only its lumen. In cases of subadventialial dissections, there may be no significant lumen stenosis, thus providing a false-negative result.

It is worth mentioning that arteriography is an invasive exam with risks related to the insertion of the catheter (vascular perfusion, hematomas or pseudoaneurysms in the femoral artery), to the contrast administration and also risk of cerebral ischemia.

Ultrasound

The sensitivity of ultrasound to detect carotid and vertebral dissection varies from 70 to 90%, with the exception that it will only be evident on Doppler when the stenosis reduces the vessel light by at least 50% and there is high resistance to distal flow. The direct signs are the visualization of the intramural hematoma itself, a double lumen in the inner layer of the vessel, a double lumen with a thrombus in the center, the pencil tip sign (abrupt termination of the flow due to the thrombus), the guitar rope sign (when the light narrowing is $> 75\%$), and the rat tail sign (progressive reduction of the vessel lumen).

On the other hand, the indirect signs are the increase in the pulsatility index (the intramural hematoma compromises the flow at the dissection site) and a difference $> 50\%$ in the flow speed when compared with the normal side.[11]

Another contribution of ultrasound is with transcranial doppler (TCD) for tracking internal carotid dissection in cases of traumatic brain injury (TBI). Because the clinical manifestation may be difficult to establish the diagnosis, asymmetry $> 25\%$ in the speed flow, as well as reduction of pulsatility index (< 0.8), suggests dissection of the ipsilateral internal carotid artery. This finding in the routine TCD of the TBI can serve as an alert for suspected dissection, and a more accurate assessment of the craniocervical vessels is indicated.

Prognosis

Mortality due to traumatic carotid and VA dissection, without treatment before clinical manifestations, is $\sim 25\%$. About ¼ of vertebral injury survivors evolve with neurological sequelae, reaching 40% in cases of carotid injuries.[14] However, retrospective studies suggest a 6% incidence of cerebral ischemia in traumatic dissections if treated in the asymptomatic phase.[4]

Treatment

Conservative treatment of traumatic lesions in the cervical region is usually adopted, with endovascular or surgical therapy reserved for exceptional cases. Surgical or endovascular treatment is reserved for cases with refractory luminal irregularities, worsening of the neurological condition despite drug treatment or expanding pseudoaneurysm. About 16.3% of patients fail drug therapy and require surgical or endovascular intervention.

Conservative Treatment

The treatment of carotid or vertebral dissection involves antithrombotic therapy with either anticoagulation or antiplatelet therapy, whose determination of which therapy is more efficient is still controversial.[15] In either choice, drug treatment should be started promptly, especially for the prevention of future thromboembolic events, and maintained for a long period. Besides, drug treatment is recommended even in asymptomatic patients or with small dissections.

When anticoagulation is chosen, the initial choice is by parenteral route, with unfractionated heparin. After starting the therapeutic dose, the maintenance dose is adjusted according to the activated partial thromboplastin time (APTT), which must be between 50 and 70 seconds. Then oral anticoagulation is started, which must be continued for 3 to 6 months with the goal of maintaining the international normalized ratio of prothrombin time (RNI) between 2.0 and 3.0.

If antiplatelet therapy is chosen, it can be performed with acetylsalicylic acid 100mg/day and Clopidogrel Bisulfate 75 mg/day.[16]

Both platelet antiaggregation and anticoagulation are equivalent in terms of effectiveness in reducing neurological sequelae, without increasing the risk of bleeding.[17]

It is noteworthy that, although many patients with cervical vessels dissection present signs and symptoms of neurological impairment and brain infarction present on cranial CT, intravenous thrombolysis is not indicated. This last therapy is contraindicated due to the high risk of bleeding at the site of the lesion in the vessel wall.

Endovascular Treatment

Endovascular treatment indications in this scenario include cases of complete vessel transection with blood leakage to the neck, recurrent symptoms despite drug treatment, cerebral hypoperfusion (in situations of multiple vessel involvement or poor collateral circulation), patients with anticoagulation contraindication (previous intracranial hemorrhage) and patients with symptomatic or expanding pseudoaneurysms.

Previously, endovascular treatment consisted of the original vessel occlusion through embolization. Recently, reconstructive stent-assisted coil embolization and placement of a flow-diverted stent have been reported as effective therapeutic modalities. The stent-assisted pseudoaneurysm embolization technique in the original vessel is recommended for dissections with saccular portions, since coils can obliterate the weakest area of the aneurysmal sac and the stent can promote endothelial growth, preventing narrowing secondary to dissection. However, this technique requires the use of combined antiplatelet therapy, so it needs careful assessment.[14]

Surgical Treatment

Surgical procedures are preferentially reserved for complex lesions that are unable to be treated by endovascular technique. Arterial obliteration, in the vertebral artery, by surgical ligation is considered tolerable in the context of therapeutic failure of the other modalities. Extraintracranial vascular reconstruction for the carotid system by bypass may be indicated in specific cases.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Schicho A, Luerken L, Meier R, et al. Incidence of traumatic carotid and vertebral artery dissections: results of cervical vessel computed tomography angiogram as a mandatory scan component in severely injured patients. Ther Clin Risk Manag 2018; 14:173–178
2 Bouthillier A, van Loveren HR, Keller JT. Segments of the internal carotid artery: a new classification. Neurosurgery 1996;38(03): 425–432, discussion 432–433
3 Yesilot Barlas N, Putaala J, Waje-Andreassen U, et al. Etiology of first-ever ischaemic stroke in European young adults: the 15 cities young stroke study. Eur J Neurol 2013;20(11):1431–1439
4 Galyfos G, Filis K, Sigala F, Sianou A. Traumatic Carotid Artery Dissection: A Different Entity without Specific Guidelines. Vasc Spec Int 2016;32(01):1–5
5 Debette S, Grond-Ginsbach C, Bodenant MCervical Artery Dissection Ischemic Stroke Patients (CADISP) Group. , et al; . Differential features of carotid and vertebral artery dissections: the CADISP study. Neurology 2011;77(12):1174–1181
6 Sposato LA, Klein F. Enfermedad carotídea aterosclerótica extracraneal. Neurol Argentina2011
7 Nedeltchev K, Baumgartner R. Traumatic cervical artery dissection. Front Neurol Neurosci 2005;20:54–63
8 Foreman PM, Harrigan MR. Blunt Traumatic Extracranial Cerebrovascular Injury and Ischemic Stroke. Cerebrovasc Dis Extra 2017;7(01):72–83
9 Crissey MM, Bernstein EF. Delayed presentation of carotid intimal tear following blunt craniocervical trauma. Surgery 1974;75(04): 543–549
10 Mohan IV. Current optimal assessment and management of carotid and vertebral spontaneous and traumatic dissection. Angiology 2014;65(04):274–283
11 Bouzat P, Oddo M, Payen JF. Transcranial Doppler after traumatic brain injury: is there a role? Curr Opin Crit Care 2014;20(02):153–160
12 Sporns PB, Niederstadt T, Heindel W, et al. Imaging of Spontaneous and Traumatic Cervical Artery Dissection : Comparison of Typical CT Angiographic Features. Clin Neuroradiol 2019;29(02): 269–275
13 Shakir HJ, Davies JM, Shallwani H, Siddiqui AH, Levy EI. Carotid and Vertebral Dissection Imaging. Curr Pain Headache Rep 2016; 20(12):68
14 Urasyanandana K, Songsang D, Aurboonyawat T, Chankaew E, Withayasuk P, Churojana A. Treatment outcomes in cerebral artery dissection and literature review. Interv Neuroradiol 2018;24(03):254–262
15 Markus HS, Hayter E, Levi C, Feldman A, Venables G, Norris JCADISS trial investigators. Antiplatelet treatment compared with anticoagulation treatment for cervical artery dissection (CADISS): a randomised trial. Lancet Neurol 2015;14(04): 361–367. Doi: 10.1016/S1474-4422(15)70018-9
16 Lorga Filho AM, Azmus AD, Soeiro AM, et al. Diretrizes Brasileiras de antiagregantes plaquetários e anticoagulantes em Cardiologia. Arq Bras Cardiol 2013
17 Daou B, Hammer C, Mouchtouris N, et al. Anticoagulation vs antiplatelet treatment in patients with carotid and vertebral artery dissection: A study of 370 patients and literature review. Neurosurgery 2017;80(03):368–379

Brain Tumor Heterogeneity

Heterogeneidade dos tumores cerebrais

Telmo Augusto Barba Belsuzarri[1] Maick Willen Fernandes Neves[1] Otávio Augusto da Costa[2] Diego Alves Soares[2] Fernando Antônio de Melo Filho[1] Mariana Mazzuia Guimarães[1] Tiago Fernandes Gonçales[1] Wolnei Marques Zeviani[1] João Flávio Mattos Araújo[1]

[1] Department of Neurosurgery, Faculdade de Medicina, Pontifícia Universidade Católica de Campinas, Campinas, SP, Brazil
[2] Department of Neurosurgery, Faculdade de Medicina, Pontifícia Universidade Católica de Campinas, Campinas, São Paulo, Brazil

Address for correspondence Telmo Augusto Barba Belsuzarri, MD, Department of Neurosurgery, Faculdade de Medicina, Pontifícia Universidade Católica de Campinas, Avenida John Boyd Dunlop s/n, Campinas, SP, 13060904, Brazil (e-mail: telmobelsuzarri@hotmail.com).

Arq Bras Neurocir 2021;40(3):e253–e256.

Abstract

Tumor heterogeneity is the concept that different tumor cells provide distinct biomorphological lesions, gene expressions, proliferation, microenvironment and graduated capacity of metastatic lesions. Brain tumor heterogeneity has been recently discussed about the interesting interaction of chronic inflammation, microenvironment, epigenetics and glioma steam cells. Brain tumors remain a challenge with regards to medication and disease, due to the lack of treatment options and unsatisfactory results. These results might be the result of the brain tumor heterogeneity and its multiple resistance mechanisms to chemo and radiotherapy.

Keywords

- brain tumor
- tumor heterogeneity
- glioma stem cell
- genetics
- epigenetics
- microenvironment

Resumo

Heterogeneidade tumoral significa que diferentes células tumorais levam a lesões morfológicas e fenotípicas distintas, com diferentes morfologias celulares, expressão gênica, metabolismo, microambiente, proliferação e possibilidade de lesões metastáticas. A heterogeneidade dos tumores cerebrais malignos tem sido o foco essencial de pesquisas recentes devido às interações notáveis entre genética, epigenética, microambiente e células-tronco glioma, todas mediadas por inflamação crônica. Tumores cerebrais ainda são um desafio no que tange a medicação e doença, podendo, com a carência de opções terapêuticas aliada a resultados insatisfatórios, ocorrer devido à heterogeneidade do tumor e seus múltiplos mecanismos de resistência à quimio e radioterapia. Foi realizada uma revisão da literatura na base de dados PubMed usando os termos: *brain tumor*, *heterogeneity*, *epigenetic, microenvironment*, e *glioma stem cells*.

Palavras-chave

- tumor cerebral
- heterogeneidade tumoral
- células-tronco glioma
- genética
- epigenética
- microambiente

Introduction

Tumor heterogeneity means that different tumor cells lead to distinct morphological and phenotypic lesions, with different cell morphology, gene expression, metabolism, microenvironment, proliferation and possibility of metastatic lesions.

Malignant brain tumors have unsatisfactory results, despite advanced multimodal treatments with neurosurgery, oncology and chemotherapy. In adults, glioblastoma multiforme (GBM) is the most aggressive and most common malignant brain tumor, with a global survival of patients of between 4 to 6 months without treatment, and of 14 months with multimodal therapy.[1]

received
October 22, 2017
accepted
December 18, 2017
published online
March 13, 2018

DOI https://doi.org/10.1055/s-0038-1625962.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

In addition, brain tumors represent the leading cause of mortality in children, with medulloblastoma (MB) being the first cause.[2] Recently, transcriptional studies showed distinct molecular subgroups of MB, which differ among themselves in demographic data, transcriptomes, genetics, and prognosis. These studies not only established genetic subtypes, but also paved the way for the pathogenesis of MB and the possibility of cerebellar stem cells precursors.[3,4]

The lack of adequate treatments for brain tumors can occur due to tumor heterogeneity, which is controlled by at least two mechanisms that can be integrated through clonal evolution and hierarchies, and by the hypothesis of carcinogenic stem cells.[5]

In the present study, we will analyze the possible integration of the genomics, epigenomics, stem cell, chronic inflammation and microenvironment hypotheses of these brain tumors.

Clonal Evolution and Stem Cell Model

The clonal evolution model indicates that all cancerous cells can proliferate, change, and regenerate due to random mutations, creating clonal subpopulations within the tumor.[5]

On the other hand, the stem cell hypothesis proposes that cancers are hierarchically organized, with cells with the same properties of stem cells at the apex of this organization.[5]

The two models can be integrative, and recent studies have defended the existence of cancerous stem cells (CTCs) and have shown, in the laboratory, that these cells have greater tumorigenic potential, and are potentially more resistant to radiation and chemotherapy.[6,7]

Glioma Stem Cells

The GBM has several aspects, such as polymorphism and cellular heterogeneity, which makes it an essential lesion for the research. Glioblastoma multiforme CTCs (CTGs) have similar characteristics to normal neural progenitors, such as self-renewal capacity, long-term proliferation, and neurospheres formation. However, few studies describe its ability for multiple nervous system cells (neurons, astrocytes and oligodendrocytes).[6]

The molecular signs that control tumor formation and maintenance are slightly similar to normal progenitors, but differ in frequency, aberrant markers, and chromosomes. Glioblastoma multiforme CTC has already been shown with surface marker of the CD133 stem cells; However, other surface markers are emerging, such as A2B5, CD15, and CD171. There is evidence that not all CTGs present the classic marker CD133, but the genotypic profile of the brain tumor differs among the patients and the surface markers may also vary. In addition, the inflammation process during the course of the disease is multiple, and CTG plays a key role in the maintenance and promotion of microenvironments and niches.[6]

Microenvironment and Glioma Stem Cell Niches

Vascular Niche

The CTGs are in specific anatomical-functional sites with direct contact between specific cell types and extracellular matrix, as well as with cytokines and important factors for renewal and proliferation. Interestingly, healthy neural cells, as well as the CTGs, are also regulated by adhesion and by the vascular niche. In addition, they promote angiogenesis through proangiogenic growth factors, such as vascular endothelial growth factor (FCEV), endothelial migration and tube formation. Tumors with CD133+ have more necrosis, hemorrhages and are highly vascularized when compared with tumors with CD133-.[8,9]

Similarly, the complexity between CTGs and endothelial cells is far from trivial. Recent studies have shown that between 20 and 90% of endothelial cells within the tumor present the same mutations present in GBMs, such as the epidermal growth factor receptor (RFCE) and the alteration in chromosomes.[7,9]

Moreover, it was demonstrated that the CTGs cause a differentiation in the pericites, thus maintaining the function of the vessel and the development of the tumor. They also express several biological markers of pericites, such as the actin smooth muscle α, NG2, CD248 and CD146, and are also endothelial cells recruiters via SDF-1/CXCR4. In general, we see the integration of CTGs with the vascular niche in a dual-hand pathway.[8,9]

Hypoxia Signaling

Gliomas promote a recruitment of vessels, mediated by tumor, and also neovascularization. However, these vessels are disorganized, and the oxygen supply is limited in specific areas, with irregular blood flow and hypoxic oxygen stress level, $< 5\%$. These hypoxic regions often express MGMT, and are linked to tumor resistance and poor prognosis, since the cells produce more CD133.[10,11]

In normal homeostasis, the cells hydroxylate the hypoxia-inducible factor (HIF), responsible for promoting genes and activating and modulating responses that involve cell survival, motility, metabolism and angiogenesis.[10,11]

The HIF-1α is expressed in several tissues; however, the HIF-2α is not restricted only to the CTGs: it is overexpressed by them in gliomas, and is practically not expressed in cells that are not CTGs. Moreover, its overexpression is crucial for the reprogramming of cancer, by increasing the CD133 cells, and by positive regulation of OCT4, Nanog and C-MYC mRNA.[12,13] There are also other hypoxia inducing genes, which are more expressed when in hypoxia state: GLUT1, SerpinB9 and FCEV.[12,13]

Sathornsumetee et al showed, in a study with 60 recurrent malignant gliomas, that carbonic anhydrase 9 (AC9) and HIF-2α, expressed in acidotic and hypoxic niches, were associated with a poor prognosis and a survival rate of < 1 year with the use of bevacizumab.[14]

Glioma Stem Cells Pathway

Notch proteins (1, 2, 3, 4) are essential during the development of the central nervous system, as they promote renewal and contribute to stem cell survival, and are also crucial for adult neuronal plasticity. Pathologically, notch signaling modulates the progression of the brain tumor and the differentiation of stem cells. In addition, the γ-secrease cascade releases the Notch intracellular domain, and its inhibition is an improved

response to temozolomide, decreasing the radioresistance, cell growth, and the differentiation of CTGs.[15–17]

Tyrosine Kinase Receptor Signaling

Tyrosine kinase receptors (TKRs) are pathways promoted by several cytokines and growth factors, such as epidermal growth factor and fibroblasts growth factor. One of these paths is the PI3K/Akt/mTOR, found in GBMs and overexpressed by CTGs. This pathway is activated by the FCEV, which increases tumor growth and transduces several stem cell markers, such as CD133, which have increased Akt pathway and are directly correlated with the degree of the tumor.[5]

Hedgehog

The Sonic hedgehog protein is crucial for the embryological formation and differentiation of the structures of the dorsal brain; In adults, it regulates neural stem cells. In GBM, this protein is overactivated, and is related to the expression of genes and stem cell markers, such as CD133, promoting growth and contributing to tumor survival. In rats, the inhibition of the hedgehog pathway leads to apoptosis induction, reduction of self-renewal, and also to a better response of temozolomide.[18,19]

Glioma Stem Cell Transcription Factors

Several signaling pathways lead to extracellular signals to the regulating factors of CTGs transcription, such as OCT4, Sox2, C-Myc and Olig2.

OTC4 and Sox2 factors interact in the regulation and differentiation of embryonic stem cells, as well as in the increase of the CTGs, and in the promotion of the tumorigenic activity.[20] c-Myc leads to cell reprogramming in the fibroblast to induce a pluripotency. In addition, it is correlated with the degree of the tumor, and is further expressed in CTGs, which can reach $\sim$ 50% of the CD133 positive cells.[21] The Olig^2 is a transcription factor restricted to the central nervous system, specifically to the oligodendrocyte and multipotent progenitors. It is overexpressed in diffuse astrocytomas, oligodendrogliomas and oligoastrocytomas.[22,23] In fresh human GBMs, it is positive in 85% of the gliomas cells that are positive for Ki67, and in $\sim$ 98% of All CTGS CD133.

Olig^2 can also control CTG proliferation in the different forms of adhesion and cell cycle.[23]

Epigenetic Regulation of Glioma Stem Cells

Epigenetic is the occurrence of a hereditary DNA change, which regulates gene expression, without changing the actual DNA sequence. Recently, DNA methylation in high-grade gliomas is one of the most significant progressions, with the identification of mutations of the enzyme isocitrate dehydrogenase 1 (IDH-1).[5] Isocitrate dehydrogenases are multiple mutations that lead to the specific change of the Krebs cycle enzymes. Isocitrate dehydrogenase mutant enzymes generate an oncometabolite known as D-2-hydroxylglutarate (D-2-HG), instead of the α-ketoglutarate (α-CG), in the citric acid cycle. This protein promotes gliomagenesis through the activation of HIF-1 nuclear translocation, which leads to an increase in cell proliferation and angiogenesis, as well as to the hypermethylation of histones, which restructure the cellular epigenetic state.[23]

In addition, the histones methylation process can control proteins transcription. It opens the chromatin by means of methylation of H3K4 to promote its transcription. The closure occurs by the H3K27, thereby interrupting the process. Histone methyltransferase is stimulated in hypoxic CTGs, supporting the HIF-2 expression pathway and the tumorigenic pathway.[24]

Another epigenetic factor is the microRNAs (miRNAs), which are noncodifier regulatory RNAs, with an essential role in neural development/biological process, and in the tumorigenesis of the GBM, composed approximately by 22 noncodifier nucleotides with regulator gene expression ability downwards and translation inhibition. Therefore, they have an essential role in CTG pluripotency, reprogramming, and pathway. MircroRNA-124, miRNA-146a and miRNA-34a contribute to gliomagenesis, while miRNA-125b and miRNA-9 regulate the process of resistance to chemotherapy and radiotherapy.[25,26]

Chronic Inflammation Process

As already discussed, the development of brain cancer is an interaction of multiple processes, from genetic alterations to inflammation. Several genetic mutations have already been related to cerebral tumorigenesis, such as: tumor protein p53 (PT-53), homologous to tensine phosphatase (FTEN), neurofibromatosis type 1 (NF-1), RFCE, retinoblastoma (RB) and regulatory subunit 1 of phosphoinositide-3-kinase (SR1FI3Q). Most of these genes code proteins related to tumor suppression. Their mutations may lead to alterations in the metabolic circuits, such as: tyrosine kinase receptor (RTC)/RAS (rat sarcoma)/FI3Q, via p53, via RB, and via of the IDH-1 or IDH-2.23

Brain cancer development occurs with the integration between genetics, epigenetic and inflammation. In cancer, inflammation has two pathways: the intrinsic pathway, which is the integration between genetic events that lead to the chronic inflammatory microenvironment, and the extrinsic pathway, which leads to a constant inflammation and facilitates the development of cancer. Due to its persistent inflammation, immunosuppressive and inhibitory cytokines are secreted, and the cells that infiltrate the tumor secrete inflammation mediators instead of a cytotoxic response. Therefore, the microglyphs and macrophages associated with tumors (MATs) secrete cytokines and growth factors that create a propitious microenvironment for tumor growth and invasion.[23]

In addition, cyclooxygenase (COX), in particular COX2, has an essential role in chronic inflammation due to the increase of prostaglandins, prostacyclin and thromboxane. Cyclooxygenase -2 is increased in the premalignant lesions, and is overexpressed in malignant tumors, with the existence of a correlation between its levels and the tumor aggressiveness.[24]

Similarly, changes in the signal transductor protein and transcription activator (TSAT) can be a crucial point in cancer immune deregulation. Transcription activator proteins are cytoplasmic transcription factors that mediate the signaling of tyrosine kinase/growth factors and cytoplasmic enzymes.

The TSAT-3 is overactivated in several brain tumors, and increases the inflammatory process by means of IL-6 and IL-10, also inducing immunosuppression, and decreasing neutrophils activity and natural exterminating cells.[23,24]

IL-10,Similarly, inflammatory cytokines activate and release free NF-κB, which translocates into core genes and transcribes genes that code antiapoptotic proteins and proinflammatory cytokines, chemokines, adhesion molecules, proteases and DNA repair proteins, such as MGMT.[24] Temozolomide and other chemotherapies add an alkyl group to the tumoral DN to stop the cell cycle and provoke tumor death. On the other hand, MGMT has the function of repairing the DNA and removing the alkyl groups, which results in resistance to temozolomide.[23]

Thus, chronic inflammation causes oxidative stress, with the release of reactive oxygen and nitrogen specimens, which deregulate the repair of wrong pairings (RPE) of DNA, the base excision repair (REB), the nucleotide excision repair (REN), and the cell cycle and homologous recombination (RH). This oxidative stress creates a vicious circle for genetic instability and epigenetic silencing, called microsatellite instability (MSI).[23,24]

Conclusion

Brain tumors are one of the most aggressive lesions in existence, although they are one of the less understood. Future perspectives point to the interruption of the cell cycle in the stem cell pathways, for the differentiation of phenotypes/genotypes and the hierarchy of stem cells in the brain tumor. Finally, the chronic inflammation can be a bridge between the genetic and epigenetic disorder, creating a complex tumor microenvironment and, because of this, more studies are necessary to provide better forms of treatment to our patients.

Conflicts of Interest
We declare that the authors have not received payments or allowances from any institution, we have no ties with any company that could relate to the work developed, and we do not hold any patent that may be involved with the scientific production of this work.

References

1 Stupp R, Mason WP, van den Bent MJ, et al; European Organisation for Research and Treatment of Cancer Brain Tumor and Radiotherapy Groups; National Cancer Institute of Canada Clinical Trials Group. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352(10):987–996
2 Manoranjan B, Venugopal C, McFarlane N, et al. Medulloblastoma stem cells: modeling tumor heterogeneity. Cancer Lett 2013;338 (01):23–31
3 Kool M, Korshunov A, Remke M, et al. Molecular subgroups of medulloblastoma: an international meta-analysis of transcriptome, genetic aberrations, and clinical data of WNT, SHH, Group 3, and Group 4 medulloblastomas. Acta Neuropathol 2012;123(04):473–484
4 Taylor MD, Northcott PA, Korshunov A, et al. Molecular subgroups of medulloblastoma: the current consensus. Acta Neuropathol 2012;123(04):465–472
5 Schonberg DL, Lubelski D, Miller TE, Rich JN. Brain tumor stem cells: Molecular characteristics and their impact on therapy. Mol Aspects Med 2014;39:82–101
6 Bao S, Wu Q, Sathornsumetee S, et al. Stem cell-like glioma cells promote tumor angiogenesis through vascular endothelial growth factor. Cancer Res 2006;66(16):7843–7848
7 Bao S, Wu Q, McLendon RE, et al. Glioma stem cells promote radioresistance by preferential activation of the DNA damage response. Nature 2006;444(7120):756–760
8 Singh SK, Hawkins C, Clarke ID, et al. Identification of human brain tumour initiating cells. Nature 2004;432(7015):396–401
9 Ricci-Vitiani L, Pallini R, Biffoni M, et al. Tumour vascularization via endothelial differentiation of glioblastoma stem-like cells. Nature 2010;468(7325):824–828
10 Harris AL. Hypoxia–a key regulatory factor in tumour growth. Nat Rev Cancer 2002;2(01):38–47
11 Keith B, Simon MC. Hypoxia-inducible factors, stem cells, and cancer. Cell 2007;129(03):465–472
12 Li Z, Bao S, Wu Q, et al. Hypoxia-inducible factors regulate tumorigenic capacity of glioma stem cells. Cancer Cell 2009;15 (06):501–513
13 Li Z, Wang H, Eyler CE, Hjelmeland AB, Rich JN. Turning cancer stem cells inside out: an exploration of glioma stem cell signaling pathways. J Biol Chem 2009;284(25):16705–16709
14 Sathornsumetee S, Cao Y, Marcello JE, et al. Tumor angiogenic and hypoxic profiles predict radiographic response and survival in malignant astrocytoma patients treated with bevacizumab and irinotecan. J Clin Oncol 2008;26(02):271–278
15 Fan X, Khaki L, Zhu TS, et al. NOTCH pathway blockade depletes CD133-positive glioblastoma cells and inhibits growth of tumor neurospheres and xenografts. Stem Cells 2010;28(01):5–16
16 Wang J, Wakeman TP, Lathia JD, et al. Notch promotes radioresistance of glioma stem cells. Stem Cells 2010;28(01):17–28
17 Wang R, Chadalavada K, Wilshire J, et al. Glioblastoma stem-like cells give rise to tumour endothelium. Nature 2010;468(7325):829–833
18 Cayuso J, Ulloa F, Cox B, Briscoe J, Martí E. The Sonic hedgehog pathway independently controls the patterning, proliferation and survival of neuroepithelial cells by regulating Gli activity. Development 2006;133(03):517–528
19 Clement V, Sanchez P, de Tribolet N, Radovanovic I, Ruiz i Altaba A. HEDGEHOG-GLI1 signaling regulates human glioma growth, cancer stem cell self-renewal, and tumorigenicity. Curr Biol 2007;17 (02):165–172
20 Ikushima H, Todo T, Ino Y, et al. Glioma-initiating cells retain their tumorigenicity through integration of the Sox axis and Oct4 protein. J Biol Chem 2011;286(48):41434–41441
21 Wang J, Wang H, Li Z, et al. c-Myc is required for maintenance of glioma cancer stem cells. PLoS One 2008;3(11):e3769
22 Ligon KL, Huillard E, Mehta S, et al. Olig2-regulated lineage-restricted pathway controls replication competence in neural stem cells and malignant glioma. Neuron 2007;53(04):503–517
23 Mostofa AG, Punganuru SR, Madala HR, Al-Obaide M, Srivenugopal KS. The Process and Regulatory Components of Inflammation in Brain Oncogenesis. Biomolecules 2017;7(02):E34
24 Gallo M, Ho J, Coutinho FJ, et al. A tumorigenic MLL-homeobox network in human glioblastoma stem cells. Cancer Res 2013;73 (01):417–427
25 Zhang Y, Dutta A, Abounader R. The role of microRNAs in glioma initiation and progression. Front Biosci 2012;17:700–712
26 de la Iglesia N, Puram SV, Bonni A. STAT3 regulation of glioblastoma pathogenesis. Curr Mol Med 2009;9(05):580–590

Rare Case of Young Patient with Intraventricular Angiomatous Meningioma

Caso raro de paciente jovem com meningioma angiomatoso intraventricular

Gabriel Carvalho Heemann[1] Rafael Silva Paglioli[2] Ricardo Chmelnitsky Wainberg[3]

[1] Medicine Student, Pontifícia Universidade Católica do Rio Grande do Sul (PUC-RS), Porto Alegre, RS, Brazil
[2] Resident doctor, Neurosurgery Service, Hospital São Lucas, PUC-RS, Porto Alegre, RS, Brazil
[3] Preceptor doctor, Neurosurgery Service, Hospital São Lucas, PUC-RS, Porto Alegre, RS, Brazil

Address for correspondence Gabriel Carvalho Heemann, Medicine Student, Pontifical Catholic University of Rio Grande do Sul (PUC-Rs), Porto Alegre, RS, Brazil (e-mail: gabriel.heemann@gmail.com).

Arq Bras Neurocir 2021;40(3):e257–e262.

Abstract

Pediatric meningiomas are rare and account for only 2.2% of the central nervous system (CNS) tumors. In this age group, they are more frequently located in atypical sites, such as, mainly, the ventricular system, with a frequency of 8.8 to 13.6%. Adding this to the fact that the angiomatous subtype constitutes only 2.1% of all meningiomas, the rarity of the case reported here is corroborated. We report a 17-year-old female patient diagnosed with intraventricular angiomatous meningioma; she underwent surgical resection of the tumor in the body and frontal horn of the right lateral ventricle, and there were no neurological sequelae. With a follow-up of 26 months, there was no recurrence and the patient had clinical stability. Intraventricular tumors usually have slow growth and reach a considerable size until they cause symptoms and then are diagnosed. In addition, the deep location of the tumor and its proximity to eloquent areas make these tumors a neurosurgical challenge. The angiomatous subtype, due to the presence of hypervascularization (consisting of $>$ 50% of vascular components), may, in some cases, hinder surgical resection as well as be erroneously diagnosed. However, surgical treatment aimed at total resection of the lesion remains the conduct of choice in the case reported here, especially in patients in the first two decades of life, in which the use of radiation is avoided. Specifically when it comes to the surgery, we chose a transcalosal approach that allows a good transoperative visualization of the lesion when located in the body and frontal horn of the lateral ventricle.

Keywords

- meningioma
- intraventricular neoplasms
- pediatrics
- lateral ventricles

Resumo

Meningiomas pediátricos são raros, representando apenas 2,2% dos tumores do sistema nervoso central (SNC). Em tal faixa etária, localizam-se com maior frequência em sítios atípicos, como, principalmente, o sistema ventricular – com frequência de 8,8

received
February 20, 2017
accepted
May 31, 2017
published online
June 23, 2017

DOI https://doi.org/10.1055/s-0037-1604037.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

a 13,6%. Em vista disso, e de que o subtipo angiomatoso constitui apenas 2,1% de todos meningiomas, corrobora-se a raridade do caso aqui relatado: paciente feminina de 17 anos diagnosticada com meningioma angiomatoso intraventricular. Foi submetida à ressecção cirúrgica de tumor em corpo e corno frontal do ventrículo lateral direito, não havendo sequela neurológica. Com acompanhamento de 26 meses, não apresentou recidiva e demonstra estabilidade clínica. Tumores intraventriculares geralmente possuem crescimento lento e atingem tamanho considerável até ocasionarem sintomas e serem, então, diagnosticados. Somado a isso, a localização profunda do tumor e a proximidade com áreas eloquentes tornam tais tumores um evidente desafio neurocirúrgico. O subtipo angiomatoso, por apresentar hipervascularização (é constituído por > 50% de componentes vasculares), pode tanto dificultar, em alguns casos, a ressecção cirúrgica quanto ser erroneamente diagnosticado. Porém, o tratamento cirúrgico visando à ressecção da lesão mantém-se como a conduta de escolha no caso aqui relatado, especialmente em pacientes nas duas primeiras décadas de vida, nos quais se evita o uso de radiação. Especificamente em relação à cirurgia, optou-se por uma abordagem transcalosa que possibilita uma boa visualização transoperatória da lesão quando localizada em corpo e corno frontal do ventrículo lateral.

Palavras-chave
- meningioma
- neoplasia intraventricular
- pediatria
- ventrículos laterais

Introduction

Meningiomas have a progressively higher incidence with increasing age, with a mean age of presentation of 65 years old. Thus, they constitute the most frequently reported tumors of the central nervous system (CNS) in adulthood.[1] Children and adolescents cases are rare, representing 2.2 to 2.6% of CNS tumors.[1,2] In this age group, they are more frequently located in unusual sites, such as in the ventricular system.[3]

Such intraventricular meningiomas have the particularities of being slow-growing and reaching a considerable size until they become symptomatic.[4] In addition, the deep localization and the relationship with the underlying eloquent areas make tumor resection a neurosurgical challenge.[5,6] In view of this, and that the angiomatous subtype – defined for presenting > 50% of the vascular components at the microscopic analysis – constitutes only 2.1% of all meningiomas, it is credited to the case reported herein.[7] We are conscious of the fact that this is possibly the first report of a patient in the first 2 decades of life with angiomatous meningioma in the intraventricular site.

In this report, we aim to expose our neurosurgical experience in a case with rare variants and to conduct a review of the literature on the main aspects that we deem necessary to support our conduct.

Case Description

A 17-year-old female patient, previously healthy, presented orbital headache for 3 months, followed by blurred and double vision. On physical examination, convergent strabismus by right lateral rectus muscle paresis was found. In the other cranial pairs, sensitivity, strength and reflexes were preserved and there were no meningeal signs. It was then performed an investigation with cranial magnetic resonance imaging (MRI), which evidenced an expansive lesion in the frontal horn of the right ventricle, directly ahead of the foramen of Monro, with dimensions of 2.0 × 1.3 × 1.8 cm (AP x L x H) in the larger diameter sections. The lesion presented moderate hyperintensity with small hypointense foci in the T2 weighted images. On T1, it was isointense, and after the contrast showed intense and homogeneous impregnation, except for the same hypointense T2-weighted spots. There were no signs of dilatation of the supratentorial ventricular system (►**Fig. 1 A-D**). Such radiological features suggested the diagnosis of intraventricular

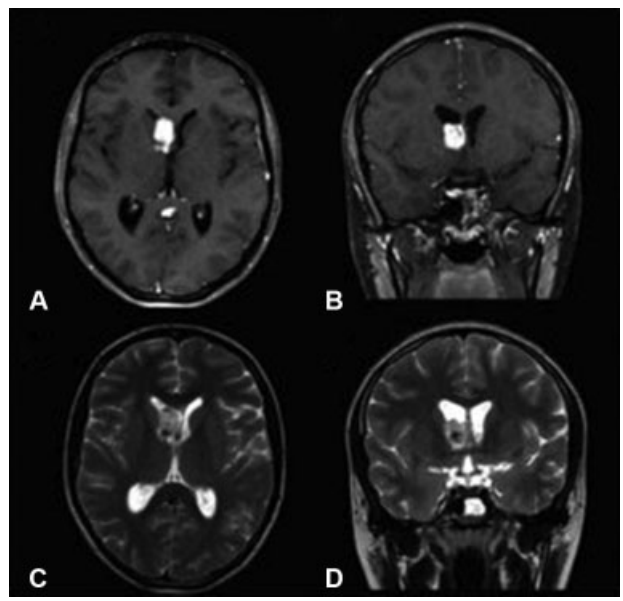


Fig. 1 Preoperative magnetic resonance imaging: A and B – T1 with gadolinium, axial (a) and coronal (b). Lesion with intense uptake at the level of the right frontal horn, close to the foramen of Monro. C and D – T2 axial (C) and coronal (D). Hyperintense lesion, with a focus of hypointense calcification (also visualized in A).

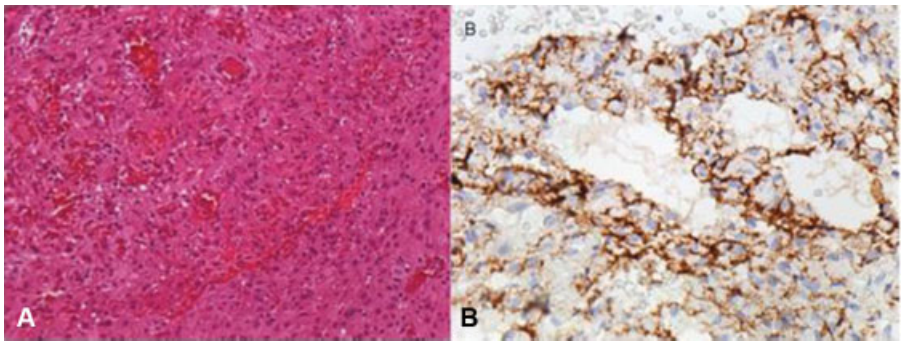


Fig. 2 (A) Hematoxylin and eosin staining, 200 x magnification: Image evidencing histopathological features of meningioma and significant vascular component. (**B**) Immunohistochemistry, Magnification - Analysis of 400 times: tumor cells presenting positive for epithelial membrane antigen.

meningioma, with calcification areas. It was considered an occasional finding, since the topography was not compatible with the presentation symptoms.

Surgical treatment was indicated, and this was performed at the same hospitalization, due to the risk of acute hydrocephaly. The approach was performed by the transcalous approach, with the following steps: dorsal decubitus and head in neutral position; bicoronary incision; right frontal paramedian craniotomy, with lateral extension of 5.5 cm from the midline and 5.5 cm from the coronary suture to the front; opening of the dura mater in "Ç" format based on the midline; under microscopy, dissection of the interhemispheric fissure and removal of the frontal lobe with positioning of the fixed spatula in Leyla support on the medial surface; identification of the rotating of the cingulate and pericalous arteries; 1.2 cm calosotomy starting from the transition between the knee and the corpus callosus body; identified the vegetating greyish lesion inside the right frontal horn, which presented softened consistency, aspirable after coagulation, and vascularized; resection of the lesion through coagulation and aspiration and by fragments, providing small residue adhered to the ependyma of the thalamocauded droppings. Postoperative without intercurrences and absence of new deficits, remaining diplopia and strabismus. The histopathologic analysis and the immunohistochemical profile demonstrated extensive vascularization and low mitotic index (Ki67 $< 2\%$). In addition, the results verified are: epithelial membrane antigen (EMA), positive; cytokeratin (CK), negative; progesterone receptor, negative; and glial fibrilar acid protein (GFAP), positive (►**Fig. 2 A-B**). Thus, the diagnosis of angiomatous meningioma (World Health Organization [WHO] grade I) is confirmed. The postoperative MRI showed small residual focus along the striated thalamus (►**Figs. 3 A-D** and **4 A-D**). After 6 months, the patient underwent strabismus correction with an ophthalmologist at another institution. Currently, with $\sim$ 26 months of follow-up, she is asymptomatic and without evidence of recurrence of the residual lesion.

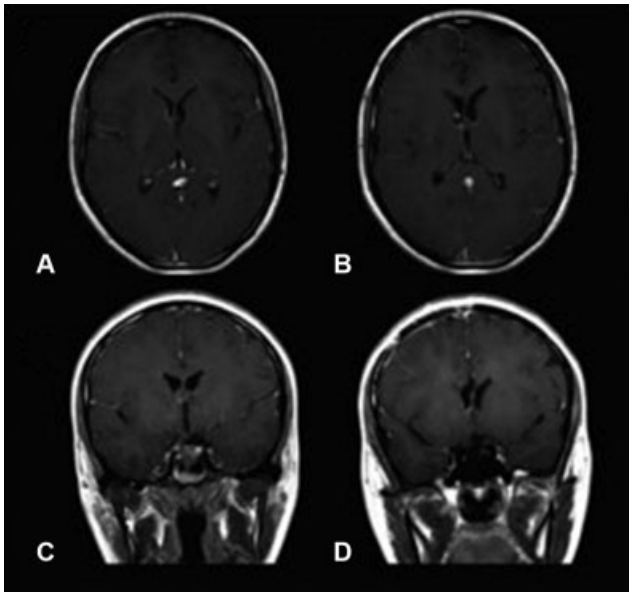


Fig. 3 Postoperative magnetic resonance imaging: T1 with gadolinium, axial planes (A and B) and Coronals (C and D). Small residual focus near the foramen of Monro, adhered to the striate thalamus vein (identified in the transoperatory).

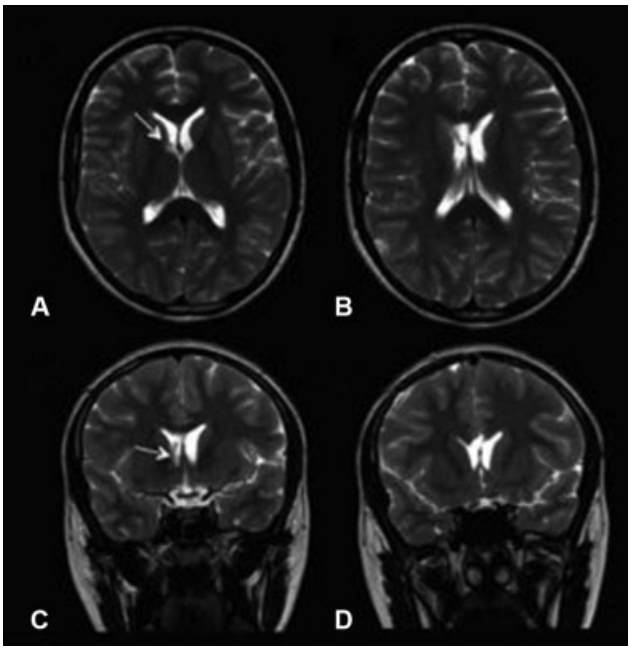


Fig. 4 Postoperative magnetic resonance imaging: T2 axial (A and B) and coronal (C and D). Small residual focus at the level of the foramen of Monro (arrows).

Discussion

Meningiomas are tumors that predominate in the 5th and 6th decades of life, having an average age of presentation of 65 years old.[1] In general, they represent 36.4% of the primary CNS tumors and ~ between 24 and 30% in adults.[1,8] On the other hand, in the pediatric population, the prevalence of CNS tumors varies between 0.4 and 4.6%.[2,3,9–13] Gender equivalence also contrasts with what occurs in the adult population, which has a ratio between female and male gender of 2:1.[1,14] It is believed that this difference is due, especially in the prepubertal period, to the absence of the effect of hormones in the corticosteroid receptors of the cells of the meningioma.[10,15–17]

In the first two decades of life, there is a higher incidence of grade II (atypical) and grade III (anaplasic) meningiomas, according to the WHO: 9.9 and 8.9%, respectivly.[2,18] They are characterized by being genetically and phenotypically more aggressive, with a high frequency of cerebral invasion.[9,14] Among the most frequent grade I meningiomas, the angiomatous subtype occurs in 2.8% of the cases,[2] and in 2.1% of all meningiomas at any age.[19] This subtype is defined when the vascular component exceeds 50% of the total tumor area.[7,19] However, differential diagnosis is necessary with hemangioblastoma and hemangiopericytoma, with essential immunohistochemical and morphology roles in the diagnostic confirmation: MIB-1/Ki67 low index and positivity for progesterone receptor, EMA, vimetin, cytokeratin and desmoplatelet.[7,19–23]

Since these tumors are uncommon, the characteristics of angiomatous meningiomas are considered in few studies.[7,19,24,25] They may present moderate to severe cerebral edema with a frequency of 74 to 88.9%,[7,19] due to hypervascularization, increased capillary permeability and vascular endothelial growth factor (VEGF) secretion.[19] In magnetic resonance imaging, they may present more signs of flow voids, rarely present necrosis, and they tend to have homogeneous enhancement to paramagnetic contrast.[19,23]

Meningiomas in pediatric patients present in atypical sites more frequently than in adults: in the lateral ventricles, in the skull base, and in the posterior fossa.[2,3,10,15,26] The intraventricular localization occurs in 11%, compared with between 0.3 and 3% in all ages and between 0.5 and 4.5% in adults.[2,10,27]

Intraventricular meningiomas (IVMs) are in the lateral ventricles (more common on the left side) in 76% of the cases; 16% in the 3rd ventricle; and 7%, in the 4th ventricule.[5,27] There are studies suggesting that lateral ventricles are the favorite site of pediatric IVMs.[26,28] These originate from the choroid plexus, growing on the corodic screen.[4] The vascularization of the tumor depends on its location in the ventricle, and, in general, the main nutrient vessels depart from the choroidal arteries and are of small caliber.[27]

Clinically, pediatric IVMs are usually asymptomatic, until they reach large dimensions in the lateral ventricles, where the risk of hydrocephaly is lower. On the other hand, when located in the 3rd or 4th ventricle, the obstruction of the cerebrospinal fluid (CSF) flow may result in manifestations in early stages of the tumoral growth.[5,27,29,30] Therefore, symptoms – headache, nausea, vomiting, and visual disturbances[5,27,31]–are more frequently related to tumor compression and to an insidious increase in intracranial pressure. Indolent cognitive deficits compromising memory and attention can also occur.[32,33] Typical symptoms of acute intracranial pressure increase are uncommom.[29] The clinic thus correlates with the location of the tumor within the ventricle, the size of the tumor and the direction of its growth.[27] Finally, we emphasize that the clinical presentation of the patient reported – convergent strabismus by paresis of the right lateral rectus muscle – showed no correlation with the tumor, which still had a relatively small size and its location did not justify the signs and symptoms.

Intraventricular meningiomas usually present the classic radiological appearance of other meningiomas: well-defined globular form, but without dural tail. They are usually isoitense to hypoitensive in T1-weighted images, hyperintense in T2-weighted image and undergo strong contrast enhancement.[16,27] In particular, in the pediatric population, other more frequent intraventricular tumors may difficult the differential diagnosis: chorioid plexus tumors, ependymoma, primitive neuroectoplasmic tumor, teratoma and astrocytoma.[30,34] Chorioid plexus tumors usually affect children < 10 years old, and, at MRI, they have a multilobulated mass with intense contrast enhancement and fronds appearance. Ependymomas represent approximately one-third of CNS tumors in children < 3 years old and are characterized by necrosis, hemorrhage, cyst formation, and for presenting, in MRI, hypointense in T1 and hyperintense and heterogeneous in T2.[35]

The surgical approach of a benign IVM is a neurosurgical challenge, in view of its deep location and its proximity to eloquent areas and vessels of the ventricles walls.[5,34] The extension of the initial resection is an independent prognostic factor, with significant association with recurrence and malignization.[2] The patient reported here did not present recurrence in the 26 months of follow-up, which is a result consistent with the literature. In a 2012 review, with 201 cases of several series, there were only 8 recurrences.[27] However, in a meta-analysis with 677 cases of meningiomas in the first 2 decades, the numbers are more meaningful. There were 141 recurrences, with an average presentation of 3.6 years and with mortality for this event in 46 cases.[2] Recurrence in this age group occurs basically in cases of atypical and anaplastic meningiomas, or after partial resection.[36] Mortality and postsurgical morbidity in postpubertal patients, as is the case of the patient reported here, are approaching the ones observed in meningioma cases in adults.[2] The use of adjuvant radiotherapy should be avoided in young patients, and it may be possible to opt for serial evaluation and reoperation in case of recurrence.[2,3,8–11,14,18,37]

In the literature, there are several surgical approaches for IVM resection: temporoparietal approach, transfrontal, medial posterior temporal gyrus, posterior inferior temporal gyrus, parieto-occipital, and transcalous.[5,34] The choice is individualized and based on the location of the tumor within the ventricle, the tumor size and its vascular network, to always preserve the adjacent cerebral tissue, performing small

corticoectomies and retracting as little as possible.[5,6,27,30,33,34] The rationality behind the choice of the gem approach is determined by the option that allows the best access to the largest axis of the lesion, to minimize transcortical transgression, by the spectrum of neurological deficits Pre-operative, proximity with the aforementioned eloquent structures, besides the anatomical knowledge of the cortical and white substance.[29] In the reported case, we chose the transcallosal approach to be the one that allows the best access to the frontal horn and lateral ventricle body. This approach avoids cortical injury; However, certain care is needed with the possible presence of tributary cortical veins of the superior sagittal sinus, which can be anticipated in the preoperative examinations, and with the corpus callosus, which should be distinguished from the gyrus rotation by the color change.[5] The posterior transcallosal approach has disconnection syndrome as one of its possible complications; however, the experience in our neurosurgery service demonstrates that the risk is minimal, since we have performed surgeries with the resection of the two thirds Posterior calosotomy of the corpus callosus with very low rate of this postoperative syndrome.[5,30,33,38] Despite the degree of difficulty, IVM surgery has shown low rates of morbidity and mortality in the last decades, and most postoperative complications – visual deficits and apraxias – are temporary.[27,29,34] These low rates are consistent with the case reported here, which did not present postoperative complications or transoperative sequelae.

Conclusion

Intraventricular angiomatous meningioma is a rare entity, even more in patients in the first 2 decades of life. The clinic is unspecific in most cases, making it necessary to assess MRI for diagnosis and definition of the surgical approach, and the histopathological analysis is what defines the diagnosis of the angiomatous subgroup. Surgical resection is the treatment of choice. However, the objective of total resection should not be above the objective of preserving the functions and the quality of life of the patient.

Conflicts of Interests

The authors declare that there are no conflicts of interests.

References

1 Ostrom QT, Gittleman H, Fulop J, et al. CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2008-2012. Neuro-oncol 2015;17(Suppl 4): iv1–iv62

2 Kotecha RS, Pascoe EM, Rushing EJ, et al. Meningiomas in children and adolescents: a meta-analysis of individual patient data. Lancet Oncol 2011;12(13):1229–1239

3 Menon G, Nair S, Sudhir J, Rao BR, Mathew A, Bahuleyan B. Childhood and adolescent meningiomas: a report of 38 cases and review of literature. Acta Neurochir (Wien) 2009;151(03): 239–244, discussion 244

4 Bhatoe HS, Singh P, Dutta V. Intraventricular meningiomas: a clinicopathological study and review. Neurosurg Focus 2006;20 (03):E9

5 Nanda A, Bir SÇ, Maiti T, Konar S. Intraventricular Meningioma: Technical Nuances in Surgical Management. World Neurosurg 2016;88:526–537

6 Lyngdoh BT, Giri PJ, Behari S, Banerji D, Chhabra DK, Jain VK. Intraventricular meningiomas: a surgical challenge. J Clin Neurosci 2007;14(05):442–448

7 Hasselblatt M, Nolte KW, Paulus W. Angiomatous meningioma: a clinicopathologic study of 38 cases. Am J Surg Pathol 2004;28(03): 390–393

8 Kwee LE, van Veelen-Vincent ML, Michiels EM, Kros JM, Dammers R. The importance of microsurgery in childhood meningioma: a case report. Childs Nerv Syst 2015;31(01):161–165

9 Liu Y, Li F, Zhu S, Liu M, Wu C. Clinical features and treatment of meningiomas in children: report of 12 cases and literature review. Pediatr Neurosurg 2008;44(02):112–117

10 Ravindranath K, Vasudevan MÇ, Pande A, Symss N. Management of pediatric intracranial meningiomas: an analysis of 31 cases and review of literature. Childs Nerv Syst 2013;29(04):573–582

11 Santos MV, Furlanetti L, Valera ET, Brassesco MS, Tone LG, de Oliveira RS. Pediatric meningiomas: a single-center experience with 15 consecutive cases and review of the literature. Childs Nerv Syst 2012;28(11):1887–1896

12 Cushing HL, Eisenhardt L. Meningiomas: their classification, regional behavior, life history and surgical end results. Charles C Thomas Springfield, III; 1938

13 Mehta N, Bhagwati S, Parulekar G. Meningiomas in children: A study of 18 cases. J Pediatr Neurosci 2009;4(02):61–65

14 Arivazhagan A, Devi BI, Kolluri SV, Abraham RG, Sampath S, Chandramouli BA. Pediatric intracranial meningiomas–do they differ from their counterparts in adults? Pediatr Neurosurg 2008; 44(01):43–48

15 Jaiswal S, Vij M, Mehrotra A, Jaiswal AK, Srivastava AK, Behari S. A clinicopathological and neuroradiological study of paediatric meningioma from a single centre. J Clin Neurosci 2011;18(08): 1084–1089

16 Whittle IR, Smith C, Navoo P, Collie D. Meningiomas. Lancet 2004; 363(9420):1535–1543

17 Donnell MS, Meyer GA, Donegan WL. Estrogen-receptor protein in intracranial meningiomas. J Neurosurg 1979;50(04):499–502

18 Kotecha RS, Junckerstorff RÇ, Lee S, Cole CH, Gottardo NG. Pediatric meningioma: current approaches and future direction. J Neurooncol 2011;104(01):1–10

19 Liu Z, Wang C, Wang H, Wang Y, Li JY, Liu Y. Clinical characteristics and treatment of angiomatous meningiomas: a report of 27 cases. Int J Clin Exp Pathol 2013;6(04):695–702

20 Rao S, Rajkumar A, Kuruvilla S. Angiomatous meningioma: a diagnostic dilemma. Indian J Pathol Microbiol 2008;51(01):53–55

21 Bansal D, Diwaker P, Gogoi P, Nazir W, Tandon A. Intraparenchymal Angiomatous Meningioma: A Diagnostic Dilemma. J Clin Diagn Res 2015;9(10):ED07–ED08

22 Rathod GB, Vyas K, Shinde P, Goswami SS, Tandan RK. Angiomatous meningioma in 49 years old male A rare case report. Int J Curr Microbiol Appl Sci 2014;3(11):256–260

23 Meng Y, Chaohu W, Yi L, Jun P, Songtao Q. Preoperative radiologic characters to predict hemangiopericytoma from angiomatous meningioma. Clin Neurol Neurosurg 2015;138:78–82

24 Hwang J, Kong D-S, Seol HJ, Nam D-H, Lee J-I, Choi JW. Clinical and Radiological Characteristics of Angiomatous Meningiomas. Brain Tumor Res Treat 2016;4(02):94–99

25 Ben Nsir A, Chabaane M, Krifa H, Jeme H, Hattab N. Intracranial angiomatous meningiomas: A 15-year, multicenter study. Clin Neurol Neurosurg 2016;149:111–117

26 Rushing EJ, Olsen C, Mena H, et al. Central nervous system meningiomas in the first two decades of life: a clinicopathological analysis of 87 patients. J Neurosurg 2005;103(6, Suppl):489–495

27 Ødegaard KM, Helseth E, Meling TR. Intraventricular meningiomas: a consecutive series of 22 patients and literature review. Neurosurg Rev 2013;36(01):57–64, discussion 64

28 Deen HG Jr, Scheithauer BW, Ebersold MJ. Clinical and pathological study of meningiomas of the first two decades of life. J Neurosurg 1982;56(03):317–322
29 Fusco DJ, Spetzler RF. Surgical considerations for intraventricular meningiomas. World Neurosurg 2015;83(04):460–461
30 Liu M, Wei Y, Liu Y, Zhu S, Li X. Intraventricular meninigiomas: a report of 25 cases. Neurosurg Rev 2006;29(01):36–40
31 Rochat P, Johannesen HH, Gjerris F. Long-term follow up of children with meningiomas in Denmark: 1935 to 1984. J Neuro Surg 2004;100(2, Suppl Pediatrics)179–182
32 Kashiwazaki D, Takaiwa A, Nagai S, et al. Reversal of cognitive dysfunction by total removal of a large lateral ventricle meningioma: a case report with neuropsychological assessments. Case Rep Neurol 2014;6(01):44–49
33 Nakamura M, Roser F, Bundschuh O, Vorkapic P, Samii M. Intraventricular meningiomas: a review of 16 cases with reference to the literature. Surg Neurol 2003;59(06):491–503, discussion 503–504
34 Grujicic D, Cavallo LM, Somma T, et al. Intraventricular Meningiomas: A Series of 42 Patients at a Single Institution and Literature Review. World Neurosurg 2017;97:178–188
35 Agarwal A, Kanekar S. Intraventricular Tumors. Semin Ultrasound CT MR 2016;37(02):150–158
36 Caroli E, Russillo M, Ferrante L. Intracranial meningiomas in children: report of 27 new cases and critical analysis of 440 cases reported in the literature. J Child Neurol 2006;21(01): 31–36
37 Okechi H, Albright AL. Intraventricular meningioma: case report and literature review. Pediatr Neurosurg 2012;48(01):30–34
38 Paglioli E, Martins WA, Azambuja N, et al. Selective posterior callosotomy for drop attacks: A new approach sparing prefrontal connectivity. Neurology 2016;87(19):1968–1974

Use of Vacuum-suction in Depressed Skull Fractures – Case Report and Technical Nuances of Nonoperative Treatment

Uso da vácuo-sucção nas fraturas em afundamento – Relato de caso e aspectos técnicos do tratamento não-operatório

Rodrigo Moreira Faleiro[1] Sérgio Cavalheiro[2,3] João Tiago Alves Belo[1]
Vítor Vieira de Souza Moraes[1] Aieska Kellen Dantas dos Santos[1] Ellano de Brito Pontes[1]
Rodrigo de Oliveira Teixeira[4] Aretha Miranda Silva[3] Nathalia Lacerda Eller Costa[3]

[1] Department of Neurosurgery, Hospital Felício Rocho e Hospital de Pronto-Socorro João XXIII , Belo Horizonte, MG, Brazil
[2] Department of Neurosurgery, Universidade Federal de São Paulo, São Paulo, SP, Brazil
[3] Department of Neurosurgery, Faculdade Ciências Médicas de Minas Gerais, Belo Horizonte, MG, Brazil
[4] Department of Nuclear Engineering, Instituto Militar de Engenharia, Rio de Janeiro, RJ, Brazil

Address for correspondence Vítor Vieira de Souza Moraes, MD, Departamento de Neurocirurgia, Hospital Felício Rocho, Avenida Contorno, 9530–Barro Preto, Belo Horizonte, MG, 30110-934, Brazil (e-mail: vieirafcmmg@gmail.com).

Arq Bras Neurocir 2021;40(3):e263–e267.

Abstract

Up to 20% of victims from skull fractures are represented by the pediatric population, and 50% of these lesions are depressed skull fractures. The treatment is multimodal in nature, ranging from conservative treatment to open surgical repair. The last one is associated, although in a small proportion, to complications, such as infections, hematomas and even death, besides the risks of the anesthetic procedure itself. The authors of the present article present a case report of the successful treatment of a depressed skull fracture in a newborn patient, using the vacuum-suction technique. The use of vacuum-suction may be beneficial for the pediatric patients, as it is a quick, non-invasive procedure, without the need for general anesthesia.

Keywords

- neurosurgery
- pediatric neurosurgery
- skull fractures
- depressed skull fractures
- vacuum-suction

Resumo

Até 20% das vítimas de fraturas de crânio são representadas pela população pediátrica, e 50% dessas lesões são fraturas em afundamento. O tratamento é multimodal, que vai desde o conservador até a correção cirúrgica aberta da falha óssea. O último é associado, embora em uma pequena proporção, a complicações como infecções, hematomas e até mesmo óbito, além dos riscos inerentes ao procedimento anestésico por si só. Os autores do presente artigo apresentam um relato de caso do tratamento bem sucedido de uma fratura em afundamento em um paciente recém-nascido, com o uso da técnica de vácuo-sucção. O uso da técnica de vácuo-sucção pode ser benéfico para os pacientes pediátricos pelo fato de ser um procedimento rápido, não invasivo e sem necessidade do uso de anestesia geral.

Palavras chave

- neurocirurgia
- neurocirurgia pediátrica
- fratura craniana
- fratura em afundamento
- vácuo sucção

received
April 22, 2020
accepted
August 5, 2020
published online
October 16, 2020

DOI https://doi.org/10.1055/s-0040-1718423.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Depressed skull fractures are an entity often associated with high kinetic energy trauma, leading to misalignment of the skull bone fragments from their original position.[1,2] Up to 20% of the patients with skull fractures are represented by the pediatric population, and it is noteworthy that in half of these cases, the type of injury is characterized by a depressed fracture. In this age group, especially in young children, this entity is associated with obstetric trauma, falls and physical injury.[3]

The treatment of depressed skull fractures is multimodal in nature, ranging from conservative treatment, with clinical observation and expectation of spontaneous fracture reduction, to surgical procedures to correct the bone defect.[3–6]The authors present a case report of the correction of a depressed skull fracture in a pediatric patient, using the physical principles of vacuum suction, described through the vectors applied over the skull, and its benefits.

Case Report

A newborn patient suffered a head injury during labor. She didn't evolve with any neurological complications, but was immediately submitted to a cranial computed tomography (CT) scan, after a skull defect was detected on physical examination (►**Fig. 1**). She was diagnosed with a depressed skull fracture, being referred to a neurological surgeon after hospital discharge. The CT scan (►**Fig. 2**) shows a depressed right frontal bone fracture, with no underlying brain injuries. Interventional treatment was indicated to avoid future complications, such as seizures, and for cosmetic reasons. Nonsurgical treatment was chosen, considering its possible complications, especially in young children. Elevation of the depressed skull fracture was made using a vacuum extractor (pediatric oxygen mask, connected to a vacuum source). The procedure was conducted under sedation and lasted ~ 15 minutes. No complications occurred in the postprocedural period. Postoperative CT scan shows adequate resolution of depressed skull fracture (►**Fig. 3**). Note: the patient's parents agreed with the publication of the images submitted in the present article, for scientific purposes only, without any form of identification through the subject's name or hospital records.

Fig. 1 Depressed skull fracture – physical Exam.

Discussion – Treatment Modalities

Depressed skull fractures, by definition, are caused by relatively high kinetic energy traumas, capable of promoting displacement of bone fragments toward the interior of the skull.[1,3–5]In this specific lesion, the largest area of bone depression may be located at or adjacent to the fracture interface and the intact cranial surface, when multiple fragments are displaced perpendicular to the cranial surface.[1,3,7] Ping pong fracture is a special type of depressed fracture, commonly found in neonates and young children, who are victims of low kinetic brain injury.[8,9] In such cases, a skull bone depression occurs, without necessarily demonstrating a fracture line in radiological studies, similar to a greenstick fracture. It occurs mainly due to the smaller thickness and density, and greater resilience of bone tissue in this population, and is rarely associated with intracranial lesions.[10]

In 25% of the cases, patients do not have any focal deficits or other neurological complications, such as an altered level of consciousness or seizures. Another 25% may have only a brief loss of consciousness. However, in a large number of cases, surgical treatment is indicated, for several purposes: relief of pressure on the underlying brain parenchyma, at the fracture location (with subsequent increase in cortical blood flow), reduction of the risk of future epilepsy, correction of cosmetic deformities and prevention of infection (in open fractures).[3,11,12]

The standard treatment for depressed skull fractures is the surgical elevation of bone fragments back to their normal position. The procedure is indicated when the area of bone depression is larger than the full thickness of the affected bone. In simple depressed fractures, without injury to the dura and underlying parenchyma, surgical treatment is brief, based on exposure of the bone defect and deformity correction. In cases where there are dural lesions and injury to the brain parenchyma, as well as gross contamination (in open fractures), it is imperative to perform more aggressive treatment, with debridement of devitalized tissues, hemostasis and hermetic closure of the dura mater.[3,13,14]

Discussion – Physical Aspects

It is important to describe the physical aspects that are responsible for the success of the vacuum-suction procedure in the treatment of depressed skull fractures. First, to understand the concept of vacuum, created within the dome of the object, applied over the skull, it is necessary to understand the concept of pressure.

Pressure is known to be a physical quantity that measures how much force is being exerted per unit area. The unit of

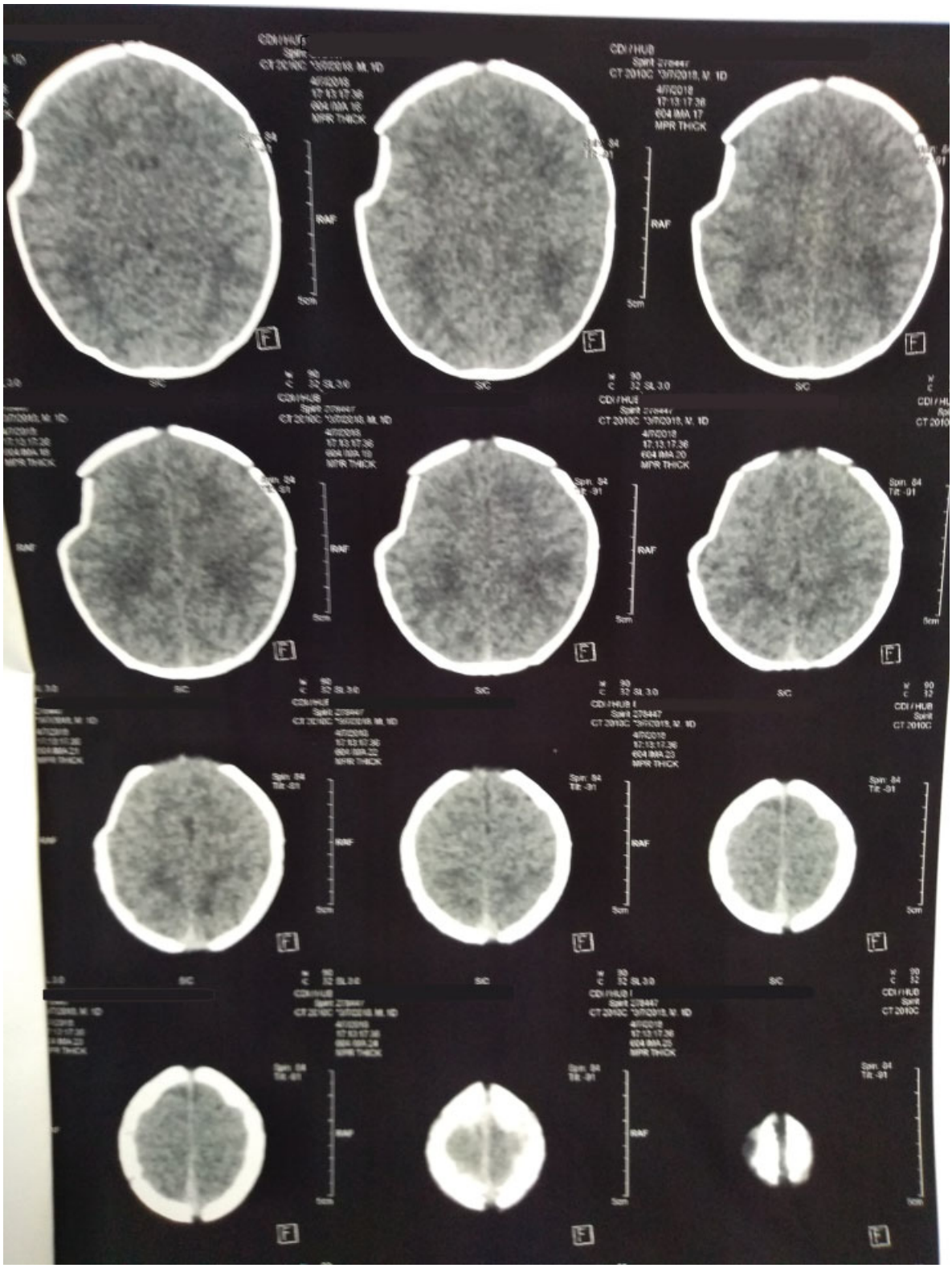


Fig. 2 Computed tomography scan of the head – preprocedure.

measure used in the international system is newton/meter^2 (N/m^2), which is related to atmospheric pressure. The value of 1 atm represents the action of the weight of the atmospheric air layer (force weight) per unit surface area of the earth at sea level (atmospheric pressure reference). The ratio between these two units is 1 atm = 100,000 N/m^2. Considering the gravitational acceleration of the Earth close to 9.8 m/s^2, for each 1 m^2 of area (the average human body has an area of 1.90 m^2 for men and 1.6 m^2 for women), the human being is subjected to an atmospheric pressure equivalent to the weight created by a mass of 10 tons.[15] The reason our body is not overwhelmed by the action of the earth's atmosphere is

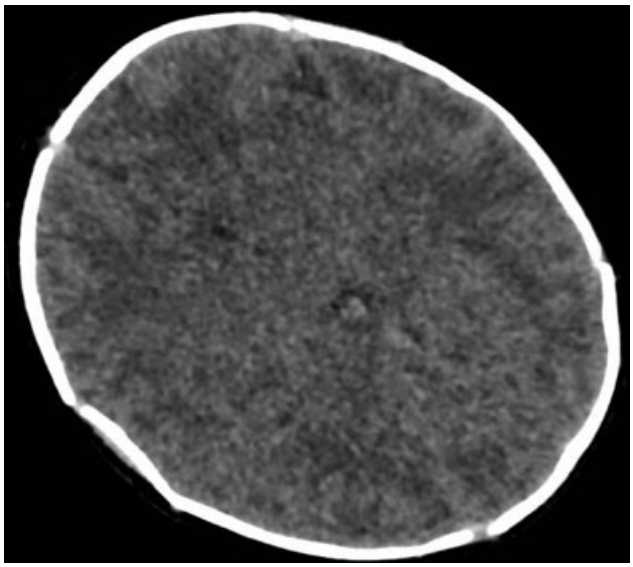


Fig. 3 Computed tomography scan of the head – postprocedure.

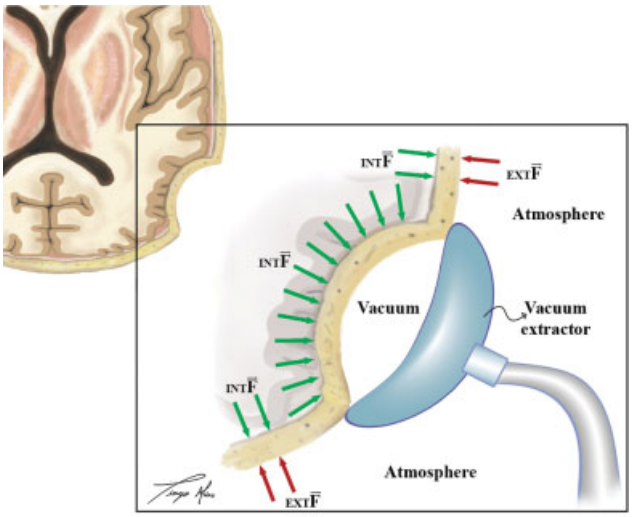


Fig. 5 Vacuum suction effect on force vectors.

that we have an internal body pressure that balances with the external pressure of the atmosphere, as with an open container completely filled with air. Therefore, the internal pressure of the object, and the external pressure of the atmosphere, exert on its walls equivalent force vectors, from inside to outside, and from outside to inside (same area, same pressure, therefore, same forces) (►**Fig. 4**). If we remove the internal pressure from the container, we will establish the vacuum (►**Fig. 5**). In the absence of pressure in its interior, external forces, caused by the still existing atmospheric pressure, will overwhelm the stability of the object itself, making it easy to be crushed, like a plastic bottle or a metal can.

The presence of force vectors caused by the atmospheric pressure are extremely powerful and, inside the skull, they can overlap the resistance of its vault, in the absence or in a great reduction of external force vectors, a phenomenon established by the reduction of the pressure on the vacuum suction device (vacuum setting or pressure reduction). As shown in the ►**Fig. 5**, the internal pressure around the lesion is the same, and the magnitude of the forces acting on each unit of area will be equal at all points of contact. This is the rationale that justifies why the vacuum suction therapy is more homogeneous than a conventional manual surgical intervention.[15]

Analyzing ►**Fig. 4**, one can notice the action of three force vectors on the skullcap, in symmetrical and central positions to the lesion. It is noted that, by decomposing the lateral symmetrical forces, the components that are in the direction of the central force are responsible for reconstituting the cranial box back to its shape, prior to the deformation. Each component of the lateral internal forces in this direction (Fy) has, in the least deformed part, a magnitude smaller than that of the central force, corroborating the presumption that the vacuum suction is a smoother and more homogeneous procedure than the conventional ones.

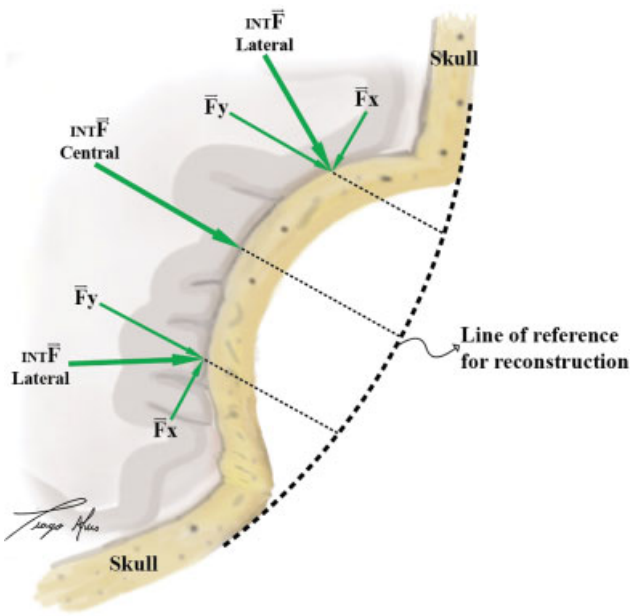


Fig. 4 Force vectors on the skull.

Discussion – Surgical versus Nonsurgical Treatment

Although morbidity and mortality associated with surgical treatment is small, all patients undergoing this treatment modality are at risk, ranging from local complications (infections, hematomas) to death. Other disadvantages are the prolongation of hospitalization, in all its medical, social and economic aspects, and the anesthetic risks associated with surgical treatment.[1,13] These details become even more important in addressing the pediatric population, because of their greater vulnerability to the possible complications associated to the procedure. On account of the above, the possibility of conservative and noninvasive treatments has become an increasingly frequent reality.[16]

In newborns, the fact that there is continuous brain growth during development, positively contributes to skull remodeling and, over the years, there is a tendency to attenuation of the depressed area. As ping-pong fractures are more frequent in this population, they may not require surgery during their treatment.[4,17,18]

Several less invasive modalities of treatment have been proposed over the years, in a continuous process of updating and inventing new techniques. One is the correction of the bone depression with the use of vacuum suction. The technique was first described in the literature in 1985.[1,12,19] This procedure has the advantages of its efficiency, practicality and safety. Moreover, it avoids complications associated with the anesthetic procedure and those inherent to a craniotomy or trepanation during invasive approaches.[8,13] The proposed technique uses the principle of local negative pressure establishment, with traction of the affected bone segment to its previous position, and its main object of treatment is focused on ping pong fractures. Although directed predominantly to the pediatric population (especially < 2 years old), some authors have already been successful in treating older individuals. The greatest extreme ever reported in the literature was the treatment of a depressed fracture of a 17-year-old girl.[8,13]

The procedure is performed briefly and without the need for general anesthesia. Using appropriate equipment to create a negative pressure gradient, it is attached to the patient's scalp surface, on the topography of the bone defect, and is performed for only a few seconds, with light traction over it, until adequate clinical results are evident (reduction of bone and soft tissue retraction). The use of obstetric vacuum extractors and milk suction pumps for this purpose has been reported in the literature.[13,20]

The complications associated with the procedure reported in the literature are minimal, and are restricted to local complications, such as bruises and subgaleal edema, which resolve spontaneously.[3] However, attention should be paid to the possibility of more serious lesions, such as intracranial hematomas, that may develop after traction of the bone board and adjacent structures. Radiological control (head CT scan) after the procedure may help in the detection of incipient complications. It is also of great importance that the attending physician pay attention to the accurate diagnosis of the type of fracture and the possibility of associated intracranial injuries. The presence of complications such as dural laceration, subdural and epidural hematomas, and open depressed fractures still deserve standard surgical treatment, to achieve better outcomes for the patient.[13,14]

Conclusion

The use of vacuum suction for the treatment of depressed skull fractures has proven to be an important tool for the neurosurgeon, especially when it comes to the pediatric population. The low rate of associated complications, the absence of the need to subject the patient to surgical stress and all its deleterious effects, and the reduction of procedure-related costs, confirm the excellence of this treatment method, as long as it is well indicated. The possibility of creating specific protocols for the management of depressed fractures, including this nontraditional method of treatment, may be a convenient reality in the future.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Johnston JM, Park TS. Depressed skull fracture. J Neurosurg 2006; 105(06):515–516, author reply 516
2 Hossain MZ, Mondle MS, Hoque MM. Depressed skull fracture: Outcome of surgical treatment. TAJ 2008;21:140–146
3 Geisler FH, Rodriguez E, Manson PN. Traumatic Skull and Facial Fractures. In: ELLENBOGEN, Richard G., ABDULRAUF, Saleem I., SEKHAR, Laligam N. Principles of Neurological Surgery. 3. ed Philadelphia: Elsevier Saunders; 2012. Cap. 22. 3–783
4 Steinbok P, Flodmark O, Martens D, Germann ET. Management of simple depressed skull fractures in children. J Neurosurg 1987;66 (04):506–510
5 Zalatimo O, Ranasinghe M, Dias M, Iantosca M. Treatment of depressed skull fractures in neonates using percutaneous microscrew elevation. J Neurosurg Pediatr 2012;9(06):676–679
6 Tan KL. Elevation of congenital depressed fractures of the skull by the vacuum extractor. Acta Paediatr Scand 1974;63(04):562–564
7 Heary RF, Hunt CD, Krieger AJ, Schulder M, Vaid C. Nonsurgical treatment of compound depressed skull fractures. J Trauma 1993; 35(03):441–447
8 de Paul Djientcheu V, Njamnshi AK, Ongolo-Zogo P, Ako S, Essomba A, Sosso MA. Depressed skull fractures in children: Treatment using an obstetrical vacuum extractor. Pediatr Neurosurg 2006;42(05):273–276
9 Pollak L, Raziel A, Ariely S, Schiffer J. Revival of non-surgical management of neonatal depressed skull fractures. J Paediatr Child Health 1999;35(01):96–97
10 Alexander E Jr, Davis CH Jr. Intra-uterine fracture of the infant's skull. J Neurosurg 1969;30(04):446–454
11 Preston D, Jackson S, Gandhi S. Non-traumatic depressed skull fracture in a neonate or 'ping pong' fracture. Case Reports 2015; 181:1–4
12 Dharmaraj ST, Embleton ND, Jenkins A, Jones G. Depressed skull fracture in a newborn baby. Arch Dis Child Fetal Neonatal Ed 2009;94(02):F137
13 Kim YJ, Lee SK, Cho MK, Kim YJ. Elevation of depressed skull fracture with a cup of breast pump and a suction generator : a case report in technical aspects. J Korean Neurosurg Soc 2007;42(04): 346–348
14 Miller JD, Jennett WB. Complications of depressed skull fracture. Lancet 1968;2(7576):991–995
15 Fox RW, Mcdonald AT. Fluid Statics. In: FOX, Robert W, MCDONALD, Alan T. Introduction to Fluid Mechanics. 5. ed New Jersey: John Wiley & Sons; 1998. Cap. 3. 44–48
16 Curry DJ, Frim DM. Delayed repair of open depressed skull fracture. Pediatr Neurosurg 1999;31(06):294–297
17 Saunders BS, Lazoritz S, McArtor RD, Marshall P, Bason WM. Depressed skull fracture in the neonate. Report of three cases. J Neurosurg 1979;50(04):512–514
18 Loeser JD, Kilburn HL, Jolley T. Management of depressed skull fracture in the newborn. J Neurosurg 1976;44(01):62–64
19 Wu CM, Hung KL, Chen TH. [A case report of depressed skull fracture of the newborn treated with a vacuum extractor]. Taiwan Yi Xue Hui Za Zhi 1985;84(02):270–275
20 Hung KL, Liao HT, Huang JS. Rational management of simple depressed skull fractures in infants. J Neurosurg 2005;103(01): 69–72

Remarkable Clinical Improvement Following Microsurgical Resection of Left Lingual Gyrus Cerebral Cavernous Malformation: A Case Report

Samer S. Hoz[1] Zahraa F. Al-Sharshahi[1] Mustafa M. Altaweel[1] Saja A. Albanaa[2]

[1] Department of Neurosurgery, Neurosurgery Teaching Hospital, Baghdad, Iraq
[2] College of Medicine, Baghdad University, Baghdad, Iraq

Address for correspondence Zahraa Al-Sharshahi, MB, BCh, BAO (NUI, RCSI), LRCP & SI, Department of Neurosurgery, Neurosurgery Teaching Hospital, Baghdad, Iraq (e-mail: zahraaalsharshahi@rcsi.com).

Arq Bras Neurocir 2021;40(3):e268–e271.

Abstract

Introduction Cerebral cavernous malformations (CCMs) are collections of dilated and irregular capillaries in the brain. Cerebral cavernous malformations are predominantly supratentorial; occipital CCMs are rare. Surgical removal is indicated for CCMs with recurrent hemorrhage, refractory seizures, and expanding lesions.

Case Description We describe a case of a 15-year-old male who presented with repeated tonic-clonic seizures and right homonymous hemianopia of 3-week duration. Magnetic resonance imaging (MRI) showed a mass located on the left medial occipital lobe, specifically in the left lingual gyrus. The T2-weighted and T2-gradient echo images confirmed the diagnosis of a CCM. Total microscopic resection was achieved. There were no surgical complications. The visual deficit improved, and the patient was seizure-free on subsequent follow-up visits.

Conclusion Surgical resection of an occipital CCM resulted in a remarkable improvement in terms of seizures and visual field deficits.

Keywords
- cerebral cavernous malformations
- left lingual gyrus
- microsurgical resection

Introduction

Cerebral cavernous malformations (CCMs) represent up to 15% of cerebral vascular lesions.[1] Eighty percent of CCMs have supratentorial location with the frontal and temporal lobes being the most common.[2] Cerebral cavernous malformations commonly present during the 2nd through to the 5th decades of life.[3] Convulsions, neurological deficits and bleeding are the most common forms of presentation of CCMs.[4,5] Surgical removal is the treatment of choice for supratentorial CCMs, particularly in enlarging lesions, medically refractory seizures or lesions with recurrent hemorrhages.[6] The occipital lobe represents a rare site for CCMs and microsurgical resection is challenging especially for medial occipital lesions due to their proximity to the eloquent visual areas around the calcarine sulcus. In addition, the bridging veins may represent an obstacle during the occipital interhemispheric approach.[2] Reports on the outcomes of CCMs in this location are scarce. Here, we present a case report on a surgically-treated medial occipital CCM with complete resolution of both visual deficits and seizures.

Case Description

A 15-year-old, right-handed male presented with repeated seizures of 3-month duration and right homonymous hemianopia of 3-week duration. The seizures were generalized tonic-clonic, occurred at a frequency of three times per week. The patient was on dual anti-epileptic medications, namely carbamazepine and sodium valproate, at maximum doses. On

received
April 4, 2020
accepted
August 5, 2020
published online
October 16, 2020

DOI https://doi.org/10.1055/s-0040-1718427.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

examination, the patient was conscious, oriented, and had no weakness. Ophthalmological and visual field assessment revealed a right homonymous hemianopia with intact optic disc and ocular motility with no visual hallucination, alexia nor agraphia. Cranial CT scan showed a left medial occipital mass of mixed density (hypo- and hyperdense) without a surrounding brain edema. Magnetic resonance imaging (MRI) showed a mass located on the left medial occipital lobe, specifically in the left lingual gyrus (medial occipitotemporal gyrus). The T2-wighted and T2-gradient echo images showed a mixed intensity core (popcorn appearance), which represents hemorrhages at different stages. This lesion was surrounded by a hypointense rim that represented the characteristic hemosiderin ring around the CCM (old hemorrhage). The mass was nonenhancing and there was no surrounding edema (►**Fig. 1**). Electroencephalography (EEG) showed epileptiform discharges localized in the left occipital lobe. Total microsurgical resection of the CCM was achieved through the left occipital interhemispheric approach, in prone position. The surrounding cortex and adjacent bridging veins were preserved (►**Fig. 2**). A postoperative MRI confirmed the complete resection of the CCM (►**Fig. 3**). The pathology report revealed dilated, cystic spaces lined by endothelial cells filled with blood with thick fibrous walls and hemosiderin laden macrophages, a picture consistent with a CCM. The surgery was uneventful and the patient was discharged at 5 days postoperatively. At his 1-month follow-up visit, the patient reported a complete resolution of the visual deficits, and this was confirmed by ophthalmological examination and visual field assessment. The patient was continued on his dual anti-epileptic medications over the next 3 months; the medications were then tapered slowly over the course of 6 months, and were stopped completely at 9 months post-discharge. At the 22-month follow-up visit, the EEG was normal, and the patient was not taking any anti-epileptic medications and his postoperative seizure score (Engle score) was class one (seizure-free).

Discussion

Cerebral cavernous malformations are mulberry-like, benign lesions representing dilated vascular channels with no intervening brain parenchyma.[7] The incidence of CCMs in the general population is of 0.5%.[8] Cerebral cavernous malformations can be familial (20%) or sporadic (80%).[9] Familial CMMs are inherited in an autosomal dominant manner,

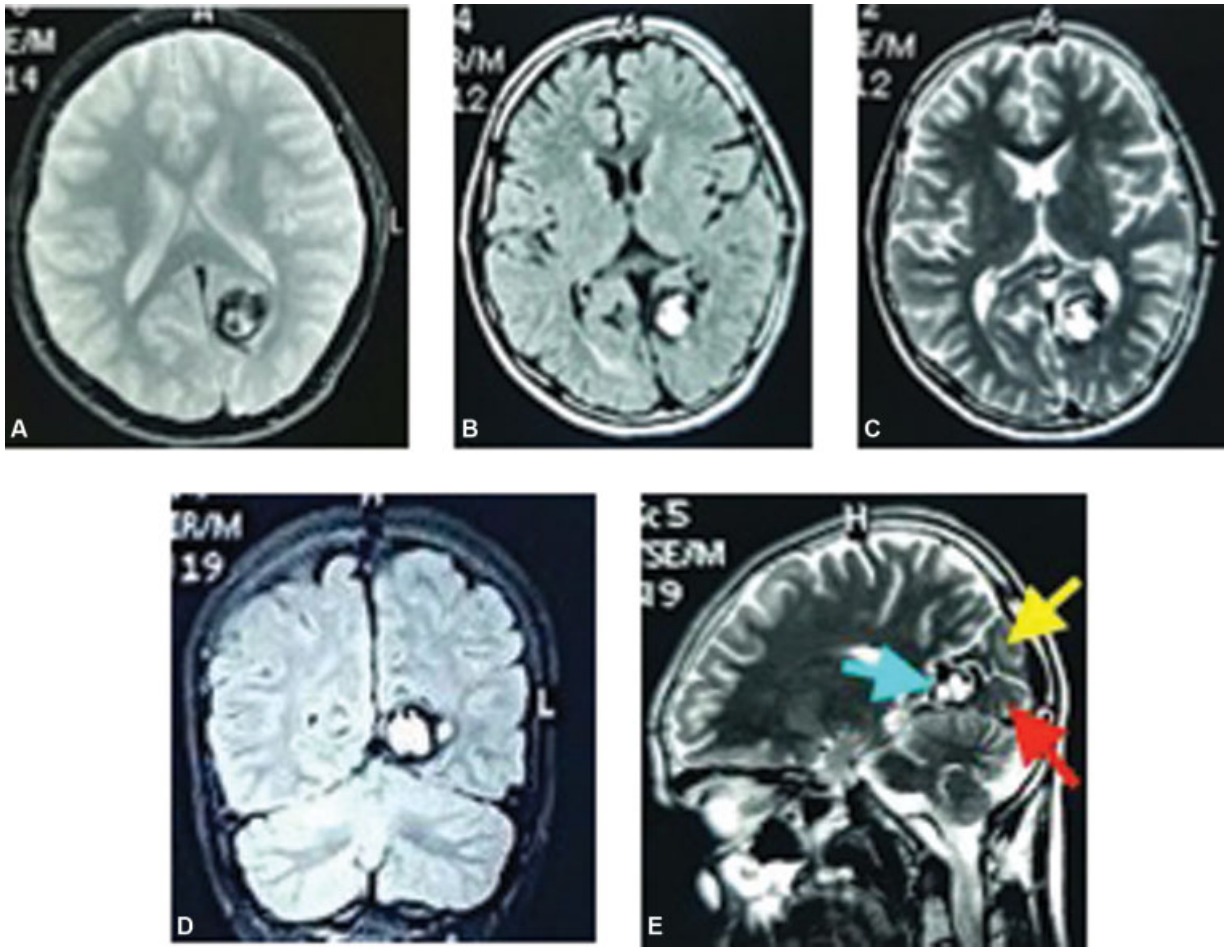


Fig. 1 Preoperative magnetic resonance imaging studies: A,B,C (T2-gradient Echo, FLAIR, and T2 images, respectively), showing a left medial occipital cavernoma with mixed intensity core (popcorn appearance) surrounded by a hypointense hemosiderin ring, with no surrounding edema. D: Coronal view showing the proximity of CCM to the medial surface. E: Sagittal view showing the exact location of the CCM at the left lingual gyrus; red arrow: lingual gyrus, yellow arrow: cuneus, blue arrow: the cavernoma.

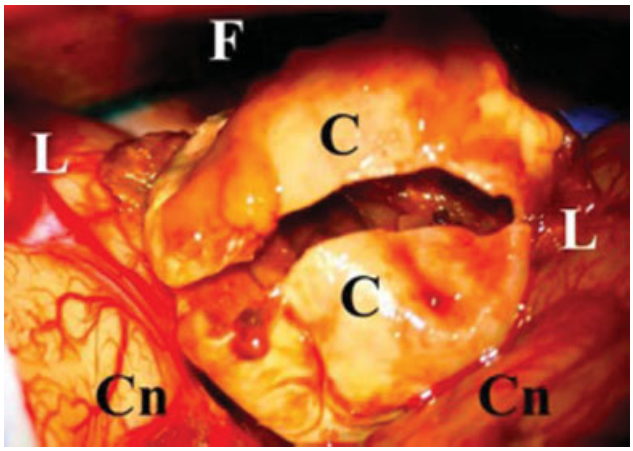


Fig. 2 An intraoperative image through the left occipital approach (prone position) showing the medial occipital cerebral cavernous malformation (CCM) in-situ, after initial dissection from the surrounding cortex. In this image, the CCM has a thick wall and is opened for internal decompression. C:CCM; Cn: Cuneus; F: Falx cerebri; L: Lingual gyrus.

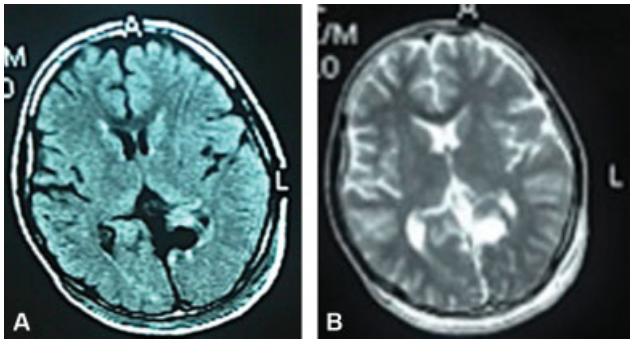


Fig. 3 Postoperative axial magnetic resonance imaging images; A: Flair, B: T 2. showing the total resection of the cerebral cavernous malformation, with intact surrounding cortex.

although with variable penetrance and presentation. Culprit genes include *CCM1* (*KRIT 1*), *CCM2* and *CCM3*. Loss-of-function mutations in these genes lead to derangements in cerebral endothelial cells signaling pathways.[10–12] Sporadic CMMs may arise de novo or secondary to radiation therapy, stereotactic radiosurgery, and brain biopsy.[13,14] Sporadic CMMs are often solitary and are more likely to be associated with developmental venous anomalies (DVAs).[9]

Cerebral cavernous malformations may present with seizures, focal neurological deficits or be detected as an incidental finding. The annual risk of hemorrhage is 3%.[15] The diagnosis of CCMs is confirmed by MRI. The use of catheter angiography is not recommended, as these lesions are devoid of blood flow and are hence "angiographically occult"[9,14]. However, 10% of CCMs may appear as "capillary brush," mimicking meningiomas.[9,14] Hemorrhagic cerebral metastases, especially those originating from melanomas and renal cell carcinomas, can also give a similar appearance to CCMs on MRI; however, these lesions are more likely to be junctional and heterogeneously enhancing; they also tend to have more surrounding cerebral edema.[9]

The management approach for CCMs is based on the risk of recurrent hemorrhage. In 2016, a systematic review that included 1,620 patients with CCMs reported a 15.8% (95% confidence interval [CI]: 13.7–17.9) risk of symptomatic intracranial hemorrhage (ICH).[16] Lesions associated with DVAs carry a higher risk of symptomatic ICH.[17] However, factors such as multiplicity, age, and gender had no independent prognostic significance.[16] Asymptomatic CCMs are managed conservatively with annual follow-ups.[10] Some experts may choose to do yearly MRIs; however, this approach does not alter management.[18] Rather, an immediate MRI is recommended upon the onset of acute symptoms, such as hemorrhage, seizure, or focal neurological deficit.[9] Surgical resection of asymptomatic CCMs is sometimes considered to be beneficial in light of psychological, occupational and economic factors.[9] Factors that influence surgical decision-making include the presence of refractory seizures, recurrent hemorrhages, or progressive neurological deficits, along with lesion-specific characteristics, including size and location.[9,19] Complications of untreated CCMs include ICH and focal neurological deficits[20]

In 2014, a systematic review and meta-analysis examined the effect of neurosurgical resection in a total of 3,400 patients who were followed-up for a median of 3.3 years.[21] The primary outcomes were non-fatal stroke, death, and a new-onset progressive focal neurological deficit.[21] The collective incidence of these outcomes after resection was 6.6 per 100 person-years (95%CI: 5.7–7.5).[21]

The CCM is a recognized etiology for refractory partial seizures.[22] Whether the removal of the hemosiderin ring should be performed in addition to the lesionectomy or not is a debatable issue.[23] However, the outcome of such procedures is, in general, satisfactory. Our case showed the effectiveness of complete CMM resection with its hemosiderin ring. Some studies have suggested that failure of lesionectomy is the only indication for invasive electrophysiological tests apart from the routine EEG.[23,24] Occipital CCMs, and particularly those located at the medial occipital zone, have intimate correlation with the visual apparatus. The remarkable aspect of our case is the complete resolution of visual symptoms and the achievement of seizure-free status; outcomes that are rarely reported after occipital cavernoma resection.[24]

Conclusion

Timely and meticulous microsurgical resection of occipital CCMs resulted in overt improvement in vision and satisfactory seizure-control.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Requena I, Arias M, López-Ibor L, et al. Cavernomas of the central nervous system: clinical and neuroimaging manifestations in 47 patients. J Neurol Neurosurg Psychiatry 1991;54(07):590–594
2 Cortés Vela JJ, Concepción Aramendía L, Ballenilla Marco F, Gallego León JI, González-Spínola San Gil J. Cerebral cavernous

malformations: spectrum of neuroradiological findings. Radiologia (Madr) 2012;54(05):401–409
3 Cohen DS, Zubay GP, Goodman RR. Seizure outcome after lesionectomy for cavernous malformations. J Neurosurg 1995;83(02): 237–242
4 Awad I, Jabbour P. Cerebral cavernous malformations and epilepsy. Neurosurg Focus 2006;21(01):e7
5 Awad IA, Robinson JR. Cavernous malformations and epilepsy, in Awad IA, Barrow DL (eds): Cavernous Malformations. Park Ridge, IL: American Association of Neurological Surgeons; 1993:49–64
6 Menzler K, Chen X, Thiel P, et al. Epileptogenicity of cavernomas depends on (archi-) cortical localization. Neurosurgery 2010;67 (04):918–924
7 Russel DS, Rubinstein LJ. 1989Tumours and hamartomas of the blood vessels. In: The pathology of tumours of the nervous system, 5th edn Edward Arnold, London727–790
8 Robinson JR, Awad IA, Little JR. Natural history of the cavernous angioma. J Neurosurg 1991;75(05):709–714
9 Del Curling O Jr, Kelly DL Jr, Elster AD, Craven TE. An analysis of the natural history of cavernous angiomas. J Neurosurg 1991;75(05): 702–708
10 Gomori JM, Grossman RI, Goldberg HI, Hackney DB, Zimmerman RA, Bilaniuk LT. Occult cerebral vascular malformations: high-field MR imaging. Radiology 1986;158(03):707–713
11 Ferroli P, Casazza M, Marras C, Mendola C, Franzini A, Broggi G. Cerebral cavernomas and seizures: a retrospective study on 163 patients who underwent pure lesionectomy. Neurol Sci 2006;26 (06):390–394
12 Kahane P, Munari C, Hoffmann D, et al. Approche chirurgicale multimodale des angiomes caverneux épileptogènes. Epilepsies 1994;6:113–130
13 Kivelev J, Koskela E, Setälä K, Niemelä M, Hernesniemi J. Long-term visual outcome after microsurgical removal of occipital lobe cavernomas. J Neurosurg 2012;117(02):295–301
14 Akers A, Al-Shahi Salman R, A Awad I, et al. Synopsis of Guidelines for the Clinical Management of Cerebral Cavernous Malformations: Consensus Recommendations Based on Systematic Literature Review by the Angioma Alliance Scientific Advisory Board Clinical Experts Panel. Neurosurgery 2017;80(05): 665–680
15 Zafar A, Quadri SA, Farooqui M, et al. Familial Cerebral Cavernous Malformations. Stroke 2019;50(05):1294–1301
16 Kim J. Introduction to cerebral cavernous malformation: a brief review. BMB Rep 2016;49(05):255–262
17 Choquet H, Pawlikowska L, Lawton MT, Kim H. Genetics of cerebral cavernous malformations: current status and future prospects. J Neurosurg Sci 2015;59(03):211–220
18 Winkler EA, Rutledge C, Ward M, et al. Radiation-induced Cavernous Malformation as a Late Sequelae of Stereotactic Radiosurgery for Epilepsy. Cureus 2018;10(03):e2308–e2308
19 Fritschi JA, Reulen HJ, Spetzler RF, Zabramski JM. Cavernous malformations of the brain stem. A review of 139 cases. Acta Neurochir (Wien) 1994;130(1-4):35–46
20 Horne MA, Flemming KD, Su ICCerebral Cavernous Malformations Individual Patient Data Meta-analysis Collaborators, et al . Clinical course of untreated cerebral cavernous malformations: a meta-analysis of individual patient data. Lancet Neurol 2016;15(02): 166–173
21 Poorthuis MH, Klijn CJ, Algra A, Rinkel GJ, Al-Shahi Salman R. Treatment of cerebral cavernous malformations: a systematic review and meta-regression analysis. J Neurol Neurosurg Psychiatry 2014;85(12):1319–1323
22 Kamezawa T, Hamada J, Niiro M, Kai Y, Ishimaru K, Kuratsu J. Clinical implications of associated venous drainage in patients with cavernous malformation. J Neurosurg 2005;102(01):24–28
23 Mouchtouris N, Chalouhi N, Chitale A, et al. Management of cerebral cavernous malformations: from diagnosis to treatment. ScientificWorldJournal 2015;2015:808314
24 Chohan MO, Marchiò S, Morrison LA, et al. Emerging Pharmacologic Targets in Cerebral Cavernous Malformation and Potential Strategies to Alter the Natural History of a Difficult Disease: A Review. JAMA Neurol 2019;76(04):492–500

Progressive Cerebral Arteriopathy – Moyamoya Disease: A Report of Two Cases with Different Clinical Presentation

Arteriopatia progressiva cerebral – Doença de moyamoya: Relato de dois casos com apresentações clínicas distintas

Marx Lima de Barros-Araújo[1] Tibério Silva Borges dos Santos[1] Irapuá Ferreira Ricarte[2] Guilherme Victor Sousa Medeiros[3] Joemir Jabson da Conceição Brito[3] Stephany Vargas Guindani[3] Larissa Clementino Leite de Sá Carvalho[4]

[1] University Hospital, Universidade Federal do Piauí, Teresina, PI, Brazil
[2] Institute of Neurosciences, Teresina, PI, Brazil
[3] Federal University of Piauí, Teresina, PI, Brazil
[4] Diferencial Integral Faculty, Teresina, PI, Brazil

Address for correspondence Marx Lima de Barros-Araújo, MD, Department of Neurology, University Hospital, Universidade Federal do Piauí, Teresina, PI, Brazil (e-mail: marx.neuro@gmail.com).

Arq Bras Neurocir 2021;40(3):e272–e276.

Abstract

Moyamoya disease is a chronic and unusual cerebrovascular disorder characterized by progressive stenosis and occlusion of the distal portions of internal carotid arteries and its main branches within the circle of Willis. Posterior circulation (vertebral and basilar arteries) may also be affected; however, this presentation is uncommon. As well as stenosis of the terminal portion of intracranial arteries, it is seen the development of a network of collateral vessels abnormally dilated at the base of the brain with an aspect of a "puff of smoke," whose term in Japanese is described as "moyamoya." The present study aims to report two consecutive cases of patients who presented to our service with different clinical manifestations. Further investigation with digital subtraction angiography showed a moyamoya pattern.

Keywords
- cerebral arteriopathy
- progressive vasculopathy
- moyamoya

Resumo

A doença de moyamoya (DMM) é uma desordem cerebrovascular crônica de rara incidência, caracterizada pela estenose progressiva das porções terminais das artérias carótidas internas, associada à proliferação de vasos colaterais anormalmente dilatados na base do crânio, cujo aspecto se assemelha a uma "fumaça," definido pelo termo em japonês "moyamoya." A circulação posterior (artérias vertebrais e artéria basilar) também pode ser acometida, porém de forma menos frequente. A apresentação clínica é variada. O presente estudo objetiva relatar dois casos de pacientes que apresentaram diagnóstico angiográfico compatível com a DMM e manifestações clínicas distintas.

Palavras-chave
- arteriopatia cerebral
- vasculopatia progressiva
- moyamoya

received
February 10, 2017
accepted
March 27, 2017
published online
April 28, 2017

DOI https://doi.org/10.1055/s-0037-1602378.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

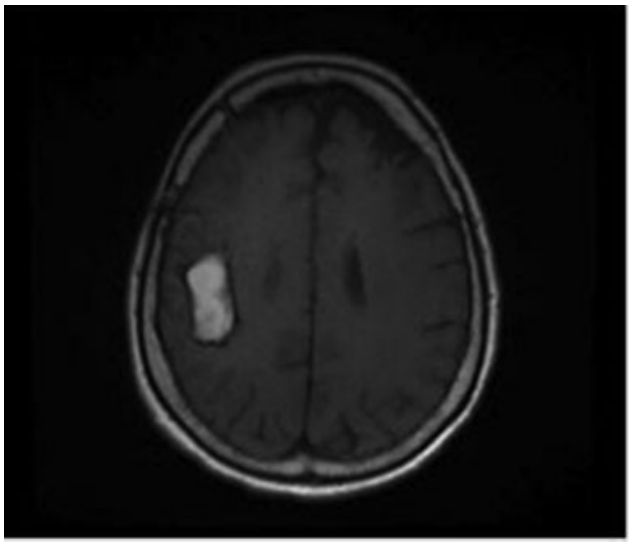


Fig. 1 MRI of the encephalon – FLAIR sequence, axial cut – showing right frontoparietal intraparenchymal hematoma.

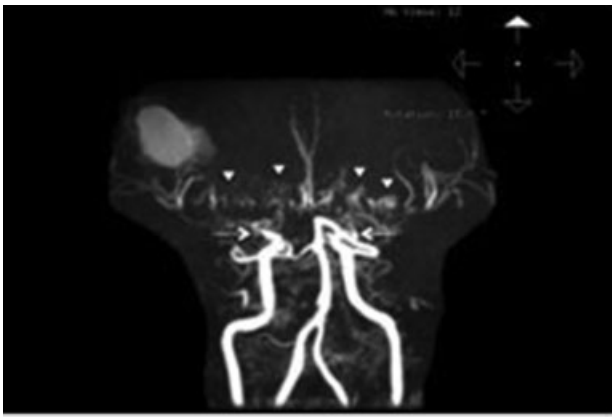


Fig. 2 Cerebral angioMRI image – arterial phase, 3D TOF – showing significant reduction of caliber in the terminal portions of the internal carotid arteries (arrows), with dilated collateral vessels at the base of the skull (arrowheads).

Introduction

Moyamoya disease (MMD) is a cerebrovascular disorder of rare incidence, characterized by stenosis and progressive occlusion of the terminal portions of the internal carotid arteries and their main branches in the circle of Willis.[1,2] The posterior circulation (vertebral arteries and basilar artery) can also be affected, but this occurs with less frequency.[3] In addition to progressive stenosis, it is observed in this pathology the development of a network of abnormally dilated collateral vessels at the base of the skull, which can take on an aspect of smoke, named in Japanese as "Moyamoya."[1,4] The clinical manifestation is variable, and the patient may be asymptomatic or they may have, among other symptoms, headaches, seizures, focal neurological deficit and even severe cases with ischemia or cerebral hemorrhage.[5–7] The present study aims to report two cases of patients, consecutively treated in our service, who presented angiographic diagnosis compatible with MMD and distinct clinical manifestations.

Case Report

Case 1–Female patient, 71 years old, hypertensive, presented with acute hemiplegia on the left side and lowering level of consciousness. Magnetic resonance imaging (MRI) of the cerebrum showed a right intraparenchymal frontoparietal hematoma (►**Fig. 1**). Cerebral angioMRI showed occlusion of the terminal portions of the carotid arteries (►**Fig. 2**).

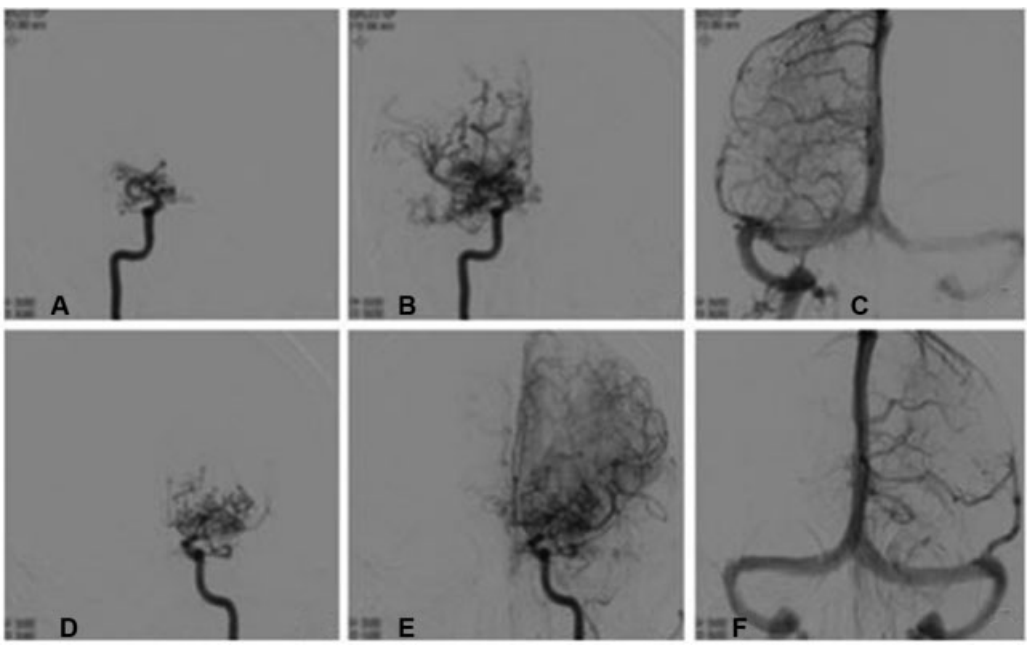


Fig. 3 Digital angiography image by subtraction – anteroposterior incidence – showing severe stenosis of the supraclinoid segment of the internal carotid arteries and their terminal branches (anterior and middle cerebral arteries), with collateral vessels dilated at the base of the skull ("Moyamoya vases"). The right internal carotid artery; D-F, left internal carotid artery. The venous phase is normal (C and F).

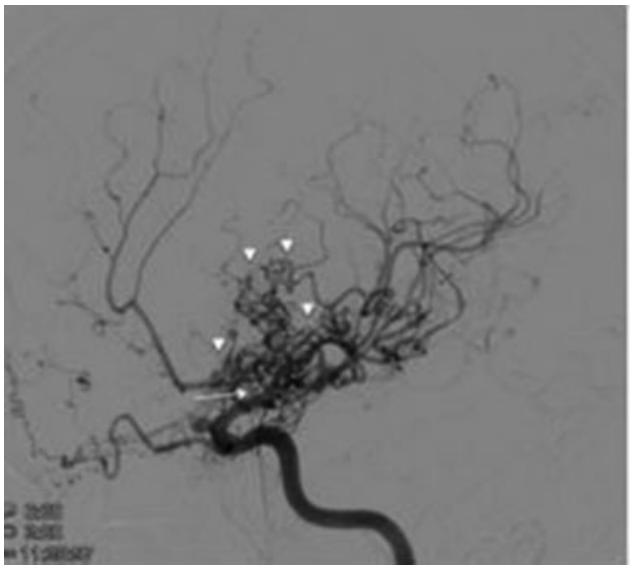


Fig. 4 Digital angiography image by subtraction – profile incidence – showing severe stenosis of the terminal portion of the left internal carotid artery and its branches (white arrow), with dilated collateral vessels at the base of the skull ("Moyamoya vases" – arrow heads).

Complementary investigation was then performed with digital angiography by subtraction, which showed severe internal bilateral stenosis of the supraclinoid carotid arteries, with the presence of dilated collateral vessels at the base of the skull (►**Figs. 3** and **4**). Additional exams showed the presence of a falcemic trait (hemoglobin dosage: S ¼ 36%).

Case 2–Female patient, 40 years old, with no previous history of comorbidities, arrived at our service with chronic

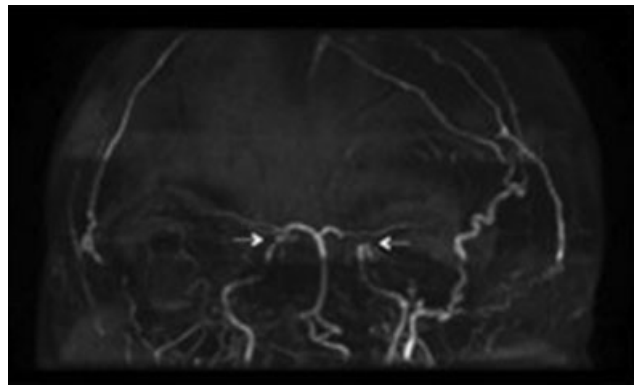


Fig. 5 Cerebral angioMRI image – arterial phase, 3D TOF – showing blood flow interruption in the intracranial segments of the internal carotid arteries (arrows).

headache refractory to various types of treatment. Neurological examination was normal. Cerebral angioMRI showed occlusion of the supraclinoid carotid arteries and vertebral arteries in their intracranial segments (►**Fig. 5**). Digital angiography was performed and evidenced subocclusive stenosis of the main intracranial arteries, with the encephalic circulation predominantly nourished by anastomosis between the left vertebral artery (intraforaminal segment – V2) with the anterior spinal artery. This, in turn, vascularized the basilar artery, the posterior cerebral arteries and the vessels of the anterior circulation through the posterior communicating arteries (►**Figs. 6** and **7**). A pial vascularization was observed through the marginal tentorial artery (also known as the Bernasconi and Cassinari artery), originated in

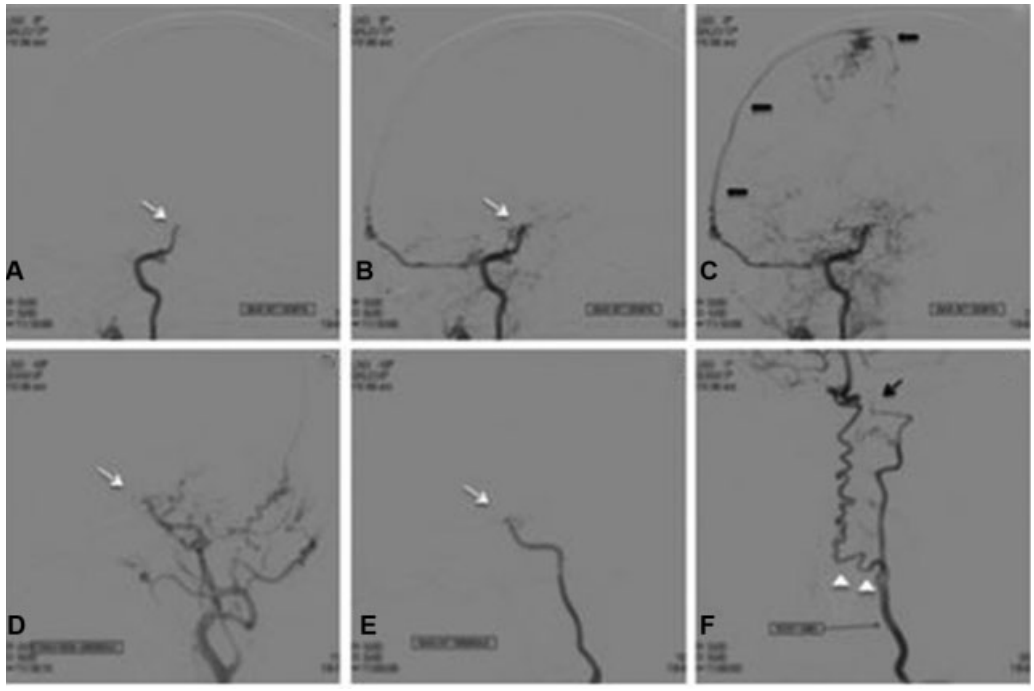


Fig. 6 Digital angiography image by subtraction showing: A, B, D, E, subocclusive stenosis of the supraclinoid segment of the internal carotid arteries (white arrows); transdural anastomosis with pial vascularization originated in the intracavernous segment of the right internal carotid artery (black arrows); F, anastomosis between the intraforaminal segment (V2) of the left vertebral artery and the anterior spinal artery (arrowheads), which meets the increased caliber. Occlusion of the intracranial segment of the vertebral artery (black arrow) is observed.

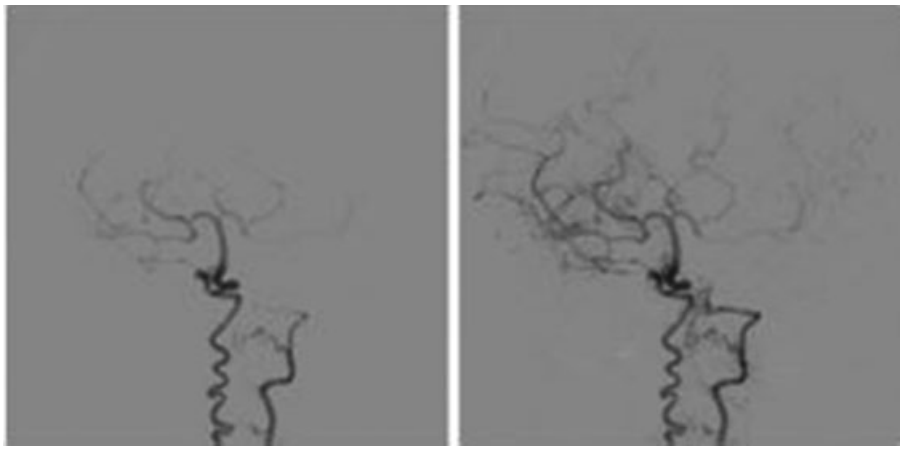


Fig. 7 Digital angiography image by subtraction with injection in the left vertebral artery – anteroposterior incidence – showing vascularization of the basilar artery and its branches through anastomosis with the anterior spinal artery.

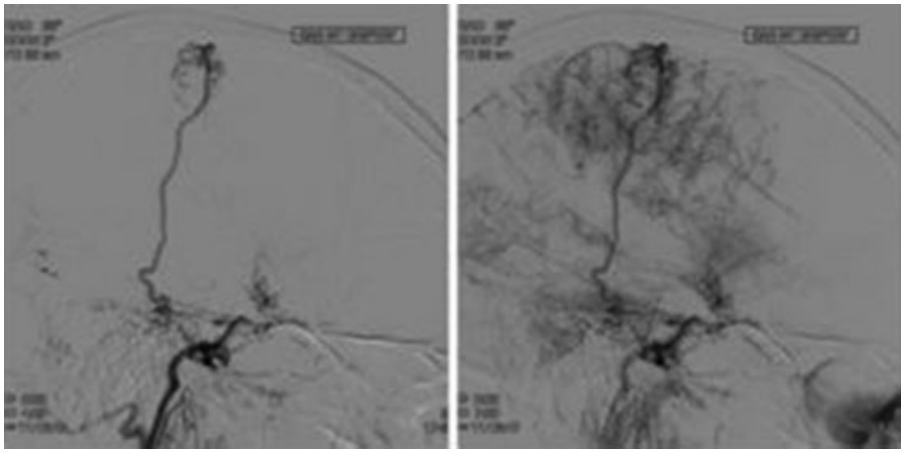


Fig. 8 Digital angiography image by subtraction – profile incidence – showing pial vascularization through the marginal tentorial artery (Bernasconi and Cassinari artery) originated in the intracavernous segment of the right internal carotid artery.

the intracavernous segment of the right internal carotid artery (►**Fig. 8**).

Discussion

Moyamoya disease is a rare pathology, with a reported incidence of 0.086 cases per 100,000 individuals.[8,9] Originally thought to affect predominantly people of Asian origin, it is now observed to afflict people from various ethnic backgrounds around the world. The incidence among females is two times higher than in males.[10,11] It is characterized by the progressive occlusion of the terminal portions of the carotid arteries and their main branches in the circle of Willis (anterior and middle cerebral arteries), with the compensatory development of a network of collateral vessels at the base of the skull (called "Moyamoya vases"). It usually affects the two cerebral hemispheres and has two peaks of presentation: the first, around the age of 5 years old, and the second, after 40 years old. The posterior circulation is affected in a less frequent way.[3] Most children with this pathology manifest symptoms resulting from cerebral ischemia, while adults present, more frequently, with intracranial hemorrhage.[3,9,12] In our study, we report the cases of two adult patients who presented to our service with distinct clinical manifestations: one of them, with severe and focal neurological deficit due to hemorrhage; the other, with progressive headaches and normal neurological examination. Extensive diagnostic investigation with neuroimaging exams and laboratory tests was performed, including thyroidopathy research, sickle cell anemia and atherosclerotic disease.

Conclusion

Moyamoya disease is a pathology of rare incidence and difficult diagnosis, with multiple forms of clinical presentation. Its diagnosis should be suspected in the clinical context of patients with neurological alteration and progressive occlusion of the carotid arteries and their intracranial terminal branches.

Conflicts of Interests

The authors declare that there are no conflicts of interests.

References

1 Suzuki J, Takaku A. Cerebrovascular "moyamoya" disease. Disease showing abnormal net-like vessels in base of brain. Arch Neurol 1969;20(03):288–299

2 Natori Y, Ikezaki K, Matsushima T, Fukui M. 'Angiographic moyamoya' its definition, classification, and therapy. Clin Neurol Neurosurg 1997;99(Suppl 2):S168–S172
3 Scott RM, Smith ER. Moyamoya disease and moyamoya syndrome. N Engl J Med 2009;360(12):1226–1237
4 Fukui M. Guidelines for the diagnosis and treatment of spontaneous occlusion of the circle of willis ('moyamoya' disease). Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan. Clin Neurol Neurosurg 1997;99(Suppl 2):S238–S240
5 Fukui M, Kono S, Sueishi K, Ikezaki K. Moyamoya disease. Neuropathology 2000;20(Suppl):S61–S64
6 Zheng W, Wanibuchi M, Onda T, et al. A case of moyamoya disease presenting with chorea. Childs Nerv Syst 2006;22(03): 274–278
7 Seol HJ, Wang KÇ, Kim SK, Hwang YS, Kim KJ, Cho BK. Headache in pediatric moyamoya disease: review of 204 consecutive cases. J Neurosurg 2005;103(5, Suppl)439–442
8 Uchino K, Johnston SÇ, Becker KJ, Tirschwell DL. Moyamoya disease in Washington State and California. Neurology 2005;65 (06):956–958
9 Gudepu RK, Qureshi MA, Qureshi IA, Rao L. Case Report: A case report of Moyamoya disease in a 36 year old African American woman. F1000 Res 2014;3:297
10 Caldarelli M, Di Rocco C, Gaglini P. Surgical treatment of moyamoya disease in pediatric age. J Neurosurg Sci 2001;45(02):83–91
11 Suzuki J, Kodama N. Moyamoya disease–a review. Stroke 1983;14 (01):104–109
12 Kuroda S, Houkin K. Moyamoya disease: current concepts and future perspectives. Lancet Neurol 2008;7(11):1056–1066

Sarcoidosis Mimicking Skull Base Meningioma

Sarcoidose mimetizando meningioma na base do crânio

Jennyfer Paulla Galdino Chaves[1] Carlos Alberto Mattozo[1] Adriano Keijiro Maeda[1] Luciane Filla[2] Aline Kelly de Cezaro Piva[2] Thiago Suzuki[2] Larissa Luvison Gomes da Silva[3] Alexandre Novicki Francisco[1]

[1] Department of Neurosurgery, Hospital Cajuru, Curitiba, PR, Brazil
[2] Department of Neurology, Hospital Cajuru, Curitiba, PR, Brazil
[3] Department of Pathology, Hospital Cajuru, Curitiba, PR, Brazil

Address for correspondence Jennyfer Paulla Galdino Chaves, MD, Departamento de Neurocirurgia, Hospital Cajuru, Curitiba, PR, Brazil (e-mail: jennyfergaldino@hotmail.com).

Arq Bras Neurocir 2021;40(3):e277–e279.

Abstract

Sarcoidosis is a systemic disease characterized by granulomatous inflammation. Pulmonary and lymphatic granulomatous involvement are common. We present a rare case report of involvement of the central nervous system affecting the ocular region and mimicking optic nerve sheath meningioma. We report the case of a 79-year-old female patient with progressive visual impairment with an evolution of 4 years. A magnetic resonance imaging scan of the cranium with gadolinium and intense homogeneous contrast enhancement revealed an expansive lesion in the right optic nerve, at the height of the optic canal. The patient was submitted to the neurosurgical approach with lesion biopsy, which showed sarcoidosis of the central nervous system. Due to the rarity of central nervous system involvement, the diagnosis of this pathology may unfortunately be postponed. The present article aims to elucidate this pathology as a differential diagnosis of retro-orbital tumors.

Keywords
- sarcoidosis
- ocular sarcoidosis

Resumo

Sarcoidose é uma doença sistêmica caracterizada por inflamação granulomatosa em que o envolvimento pulmonar e linfático é comum. Apresentamos um relato de caso raro de envolvimento do sistema nervoso central com acometimento ocular mimetizando meningioma da bainha do nervo óptico. Relatamos o caso de uma paciente de 79 anos, do sexo feminino, com diminuição visual progressiva com evolução de 4 anos. A ressonância magnética do crânio com gadolínio, mediante intenso realce homogêneo pelo meio de contraste, evidenciou uma lesão expansiva no nervo óptico direito, na altura do canal óptico. A paciente foi submetida a abordagem neurocirúrgica com biópsia de lesão, que evidenciou sarcoidose do sistema nervoso central. Devido à raridade do acometimento do sistema nervoso central, o diagnóstico dessa patologia pode ser, infelizmente, postergado. O presente artigo tem como objetivo elucidar a patologia como diagnóstico diferencial dos tumores retro-orbitários.

Palavras-Chave
- sarcoidose
- sarcoidose ocular

received
November 13, 2017
accepted
February 22, 2017
published online
April 24, 2018

DOI https://doi.org/10.1055/s-0038-1646933.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

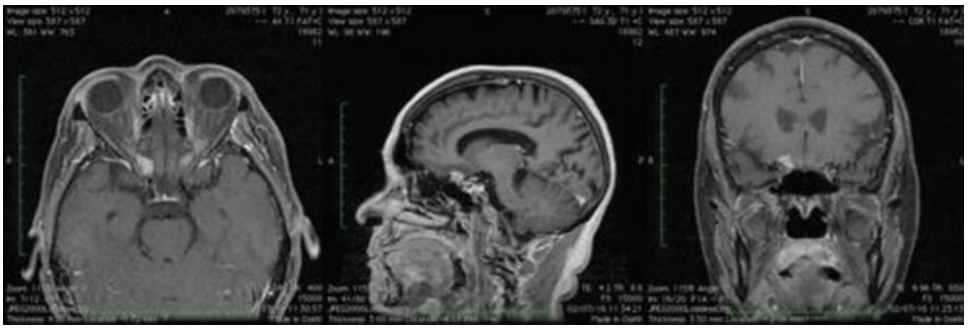


Fig. 1 Thickening with signs and enhancement by contrast of the sheaths of the optic nerve. An expansive lesion with intense homogeneous contrast enhancement in the right optic nerve with apparent implantation base on the sphenoid bone adjacent to the optic canal, measuring 1.3 × 0.9 cm.

Introduction

Sarcoidosis is a chronic multisystemic disease of unknown etiology in which there is an accumulation of non-caseating granulomas in the various tissues of the human body. It is a rare disease, and involvement of the central nervous system occurs in 5% to 10% of the cases. Therefore, the suspicion of involvement of the central nervous system should be considered in all patients diagnosed. However, according to Stern et al, in ∼ 48% of the cases of neurosarcoidosis, the symptomatology started with neurological alterations without previous diagnosis of sarcoidosis. Thus, the mass effect as the cause of the pathology is the only information available, which makes the diagnosis a challenge in the medical practice. Sarcoidosis lesions may resemble brain tumors, especially meningioma, so this pathology should be taken into consideration for the differential diagnosis of brain lesions. We report a case of neurosarcoidosis in a 79-year-old patient whose first symptom was progressive visual loss.

Case Story

A female patient, 79 years old, previously hypertensive, with hypothyroidism and depression, who was also being treated for Parkinson disease, started with a progressive picture of decrease in visual acuity to the right in the previous four years. Upon physical examination, the patient had: a score of 15 on the Glasgow scale; mydriatic pupils; amaurosis on the right, counting fingers to the left; decreased campimetry in the nasal field of the left eye, without other cranial nerve injuries; tremor in the right hand; bradykinesia to the right greater than to the left; bilateral Babinski sign; non-sustained clonus on the right; bilateral dysdiadochokinesia; preserved tactile, painful and vibratory sensibility and absence of meningism.

The patient was submitted to an investigation with computed tomography (CT) of the skull and magnetic resonance imaging (MRI) of the orbits (►**Fig. 1**), which evidenced an expansive lesion in the anterior fossa, obliterating the optic canal to the right. The lesion was initially treated as optic neuritis, and corticotherapy was performed. Lost in the follow-up, the patient presented worsening of the condition within 1 year, and a new investigation was necessary. In this interval, the patient presented complete loss of vision to the right and partial loss to the left, and underwent imaging exams that evidenced a nodular lesion to the right and hypersignal in the sheaths of the optic nerves bilaterally.

An investigation with cerebrospinal fluid (CSF) collection and a serological survey was performed, none of which evidenced alterations. The patient was submitted to the microsurgical approach of the lesion. Intraoperatively, a whitish lesion was observed near the optic nerve, with important adhesion and infiltration of the nerve, and we opted for partial resection. The anatomopathological analysis with classic non-caseating granulomas, consisting of densely arranged epithelioid cells associated with Langhans giant cells and/or foreign-body giant cells, was compatible with neurosarcoidosis (►**Fig. 2**).

Magnetic Resonance of the Skull

Histology

Discussion

Also called Heerfordt syndrome, sarcoidosis is a chronic granulomatous disease of unknown etiology that affects

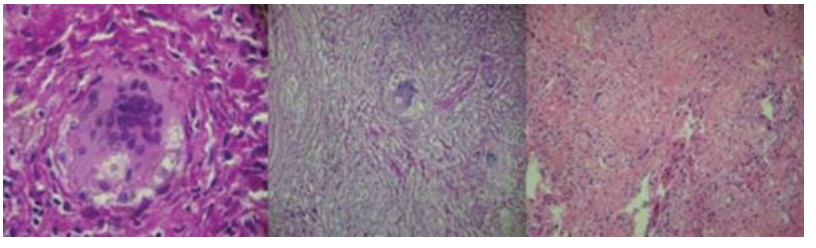


Fig. 2 Classic non-caseating granulomas consisting of densely-arranged epithelioid cells associated with Langhans giant cells and/or foreign-body giant cells.

young adults and reaches the nervous system in the systemic form in ~ 5% of the patients.[1]

The neurological manifestations described are paralysis of the cranial nerves, aseptic meningitis, peripheral neuropathy and myopathy.[2] Histologically, the development of granulomas, the activation of T cells and macrophages occur by a pathway mediated by the classic histocompatibility II complex, with an excessive Th1 response, leading to an overproduction of tumor necrosis factor-α (TNF-α) and interferon-gamma (IFN-γ), as well as interleukin-2 (IL-2) and interleukin-15 (IL-15), and the development of varying degrees of non-caseous necrosis.[3]

Clinically, the patients present diabetes insipidus, hypopituitarism and hyperprolactinemia due to hypothalamic involvement. According to a study by Fritz et al,[4] all cranial nerves may be affected, but the facial nerve and optic nerve present a higher prevalence, and unilateral involvement accounts for up to 65% of the cases, and bilateral involvement accounts for 35%.[4]

In association with these manifestations, vasculitis, convulsive seizures and hearing loss may occur.[5] Granulomas can coalesce, forming isolated intraparenchymal masses that are differential diagnoses of gliomas, Guillain-Barré syndrome, as well as HIV infection, mononucleosis, syphilis, acute porphyria, amyloidosis and multiple sclerosis.[3]

Usually, in neurosarcoidosis there is involvement of basal leptomeninges, causing abnormalities in the cranial nerves or hydrocephalus.[6,7] It is important in these cases to perform the differential diagnosis with carcinomatous meningitis and syphilis.[6,7] Neurosarcoidosis rarely presents itself solely mimicking a brain tumor, such as a meningioma.[8–10] Complementary exams, such as dosing of angiotensin-converting enzyme, serum alkaline phosphatase, and liquor and serum calcium, help in the diagnosis, but they are unspecific. The CSF has a mononuclear pleocytosis pattern, elevated proteins, and the presence of oligoclonal bands.[5] Imaging exams, such as cranial CT and MRI, may reveal hydrocephalus, meningeal enhancement and parenchymal mass, but are unspecific for the diagnosis.[3] Lesions with increased intensity in T2 at the junction of the gray and white substances are highly suggestive of this diagnosis, especially when associated with the enhancement of the meninges and with the hypothalamus lesion.[7,8,10] Only a minority of cases need histological confirmation with non-caseating granulomas in the affected nervous system tissue.[4,9] The diagnosis is of exclusion, but a probable diagnosis is defined as evidence of inflammation of the nervous system on the MRI or CSF with high protein and cellularity, G index of immunoglobin or the presence of oligoclonal bands in combination with evidence of systemic sarcoidosis with histological confirmation.[4,9]

Isolated cranial nerve abnormalities and aseptic meningitis present low risk of progression, with the exception of occasional cases of progressive optic neuropathy, and they respond well to corticosteroids.[7] However, patients with mass lesions, with leptomeningeal involvement with multiple anomalies of the cranial nerves, with spinal cord disease and with hydrocephalus often require high doses and prolonged course of corticoids associated with immunosuppressants.[7] Among the immunosuppressants used are methotrexate (MTX), azathioprine (AZA) and mycophenolate mofetil (MMF), which are equally efficient. Infliximab is a monoclonal antibody, but with caveats for oncologic patients and the possibility of increased risk of tuberculosis reactivation.[7] The diagnosis and management of neurosarcoidosis are still challenging aspects of the disease, as well as its recognition as a differential diagnosis.

It is important to consider the possibility of neurosarcoidosis in the differential diagnosis of brain expansive lesions pre- and intraoperatively. Thus, recognizing this condition leads to the proper clinical treatment with corticosteroids, avoiding an unnecessary extensive surgical treatment.

Conflict of Interests
The authors have none to declare.

References

1 da Costa Machado MA Jr, Goyanna A, Gomes LM, Goyanna F, Matos AS, Vieira LC. Neurossarcoidose: relato de caso. Arq Neuropsiquiatr 2001;59(2-A):266–269
2 Ema Alexandra Rosa Grilo. Sarcoidose e suas formas de apresentação clínica Artigo de revisão. Março 2009
3 Dutra LA, Braga-Neto P, Oliveira RA, Pedroso JL, Abrahão A, Barsottini OG. Neurosarcoidosis: guidance for the general neurologist. Arq Neuropsiquiatr 2012;70(04):293–299
4 Fritz D, van de Beek D, Brouwer MC. Clinical features, treatment and outcome in neurosarcoidosis: systematic review and meta-analysis. BMC Neurol 2016;16(01):220
5 Shimizu K, Yuki K, Sadatomo T, Kurisu K. Isolated neurosarcoidosis presenting with multiple cranial nerve palsies. Surg Neurol Int 2016;7:44
6 Elias WJ, Lanzino G, Reitmeyer M, Jane JA. Solitary sarcoid granuloma of the cerebellopontine angle: a case report. Surg Neurol 1999;51(02):185–190
7 Jackson RJ, Goodman JÇ, Huston DP, Harper RL. Parafalcine and bilateral convexity neurosarcoidosis mimicking meningioma: case report and review of the literature. Neurosurgery 1998;42(03):635–638
8 Weil RJ. Meningeal neurosarcoidosis mimicking convexity meningioma. Case illustration. J Neurosurg 2001;94(06):1013
9 Pawate S, Moses H, Sriram S. Presentations and outcomes of neurosarcoidosis: a study of 54 cases. QJM 2009;102(07):449–460
10 Ahn SW, Kim KT, Youn YÇ, Kwon OS, Kim YB. Isolated spinal cord neurosarcoidosis diagnosed by cord biopsy and thalidomide trial. J Korean Med Sci 2011;26(01):154–157

Brain Abscess Caused by Nocardia: Case Report and Literature Review

Abscesso Cerebral causado por Nocardia: Relato de Caso e Revisão da Literatura

Guilherme Finger[1] Maria Eduarda Conte Gripa[2] Tiago Paczko Bozko Cecchini[2] Tobias Ludwig do Nascimento[1]

[1] Neurosurgery Department, Hospital Cristo Redentor, Porto Alegre, RS, Brazil
[2] Universidade Luterana do Brasil, Canoas, RS, Brazil

Address for correspondence Guilherme Finger, MD, Rua Domingos Rubbo, 20, Porto Alegre, RS, 91040-000, Brazil (e-mail: guilhermefingermd@gmail.com).

Arq Bras Neurocir 2021;40(3):e280–e283.

Abstract

Nocardia brain abscess is a rare clinical entity, accounting for 2% of all brain abscesses, associated with high morbidity and a mortality rate 3 times higher than brain abscesses caused by other bacteria. Proper investigation and treatment, characterized by a long-term antibiotic therapy, play an important role on the outcome of the patient. The authors describe a case of a patient without neurological comorbidities who developed clinical signs of right occipital lobe impairment and seizures, whose investigation demonstrated brain abscess caused by *Nocardia spp*. The patient was treated surgically followed by antibiotic therapy with a great outcome after 1 year of follow-up.

Keywords
- brain abscess
- nocardia
- infection

Resumo

Abscesso cerebral por Nocardia é uma entidade rara, correspondendo a 2% dos abscessos cerebrais. Quando comparada a abscessos causados por outras bactérias, apresenta morbimortalidade 3 vezes maior. Adequada investigação e tratamento, caracterizado por antibioticoterapia prolongada, são cruciais para desfecho favorável dos pacientes. Os autores descrevem um caso de uma paciente sem comorbidades neurológicas prévias que apresentou sinais de comprometimento do lobo occipital direito e crises convulsivas, cuja investigação demonstrou tratar-se de abscesso cerebral por *Nocardia spp*. A paciente foi tratada cirurgicamente seguida de antibioticoterapia prolongada, com ótima evolução ao longo de 1 ano de acompanhamento.

Palavras-chave
- abscesso cerebral
- nocardia
- infecção

Introduction

Nocardia is a genus of the Nocardiaceae family, described by Edmon Nocard as aerobic filamentous Gram-positive, weak-acid bacteria. Nocardia species live worldwide as soil saprophytes specially in organic detritus area, and include *Nocardia farcinica, Nocardia brasiliensis*, *Nocardia transvalensis* and *Nocardia otitidiscaviarum*.[1,2] However, the species most associated with human infection is *Nocardia asteroides*.[3] Although nocardia brain abscess is a rare clinical entity, accounting for only 2% of all brain abscesses, it is associated with high morbidity, and the mortality is 3 times higher than brain abscesses caused by other bacteria.[4,5] Mortality rate is even higher in patients with multiple abscesses or with immunosuppressive conditions.[5,6]

Nocardia is considered an opportunistic infection, associated with defects in cell-mediated immunity.[3] Risk factors for this condition include male, autoimmune diseases, alcohol abuse, innutrition, chronic pulmonary disease and all the

received
August 25, 2020
accepted
September 25, 2020
published online
November 26, 2020

DOI https://doi.org/10.1055/s-0040-1719124.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

situations that affect the immune system, such as HIV infection, transplantation, cancer (mainly hematological) and long-term corticosteroid use.[1,3] Patients who have received solid-organ transplants are also at higher risk.[7]

The pathogen is not transmitted personally, it may be inhaled through the respiratory tract,[1] especially on dust particles, or may be directly inoculated into the skin or subcutaneous tissues. Subsequent hematogenous dissemination may lead to infection in any organ, with a particular predilection for the central nervous system (CNS).[1,5]

The development and severity of the disease depend on the interaction between the bacteria (pathological invasive potential) and the immune system of the host. There are 6 different forms of nocardial infection disease: pulmonary nocardiosis; systemic nocardiosis (involving two or more body sites); CNS nocardiosis; extrapulmonary nocardiosis; cutaneous and actinomycetoma.[2] Cerebral nocardiosis constitutes the most severe form of infection; it can be either an isolated lesion, without evidence of extracranial involvement, or be part of a disseminated disease. Current data states that 71% of nocardial infections affecting the CNS are part of a disseminated infection, specially associated with pulmonary or cutaneous diseases.[8,9]

The authors present a case report of a patient who evolved with visual deficits and seizure, whose investigation diagnosed a brain abscess secondary to *Nocardia spp*. The patient was submitted to surgical resection of the lesion and prolonged antibiotic therapy with a great outcome after 1 year of follow-up.

Case Report

A 67-year-old female was admitted at the emergency department after fainting at home. The patient had no personal nor family history of neurological diseases or seizures. During hospital admission, the patient was confused but had no signs of motor or sensitive deficits, no aphasia nor dysarthria, superficial and deep reflexes were normal and symmetrical, there was no signs of cerebellar or brainstem compromise. The patient had no fever and there was no sign of neck stiffness. After 30 minutes of hospital admission, the patient described visual alteration that was followed by a seizure that was promptly controlled after 10 mg of diazepam infusion. A brain computed tomography (CT) was performed, demonstrating a lesion in the right occipital lobe with vasogenic edema, whose lesion had a peripheric enhancement after contrast infusion (►**Fig. 1**). The patient was transferred to the neurosurgery department, whose neurological exam evidenced a left homonymous hemianopsia, with no other deficits. The investigation was complemented with a magnetic resonance (MRI), which demonstrated a right occipital lobe lesion measuring 36 mm anteroposteriorly, 24 mm laterolaterally and 31 mm craniocaudally. On T1 weighted images, the lesion was hypointense with a circular enhancement after gadolinium infusion; fluid-attenuated inversion recovery (FLAIR) and T2 weighted images demonstrated a vasogenic edema surrounding the lesion, and diffusion images demonstrated an important restriction inside the lesion. The characteristics presented in the MRI suggested a case of brain abscess (►**Fig. 2**).

The patient was submitted to blood tests (including blood culture), chest X-ray and pulmonary angiotomography, but all exams were normal (no bacteria in the blood culture samples were identified, no signs of arteriovenous shunts in the lungs or heart. The medical history of the patient included hypertension, controlled with losartan and anlodipin.

A neurosurgical procedure was performed, with a right occipital craniotomy, aspiration of the lesion content (which was sent for Gram analysis and culture) and the capsule was removed. The patient presented a good recovery after surgery, remaining with the left homonymous hemianopsia, but no other neurological deficits.

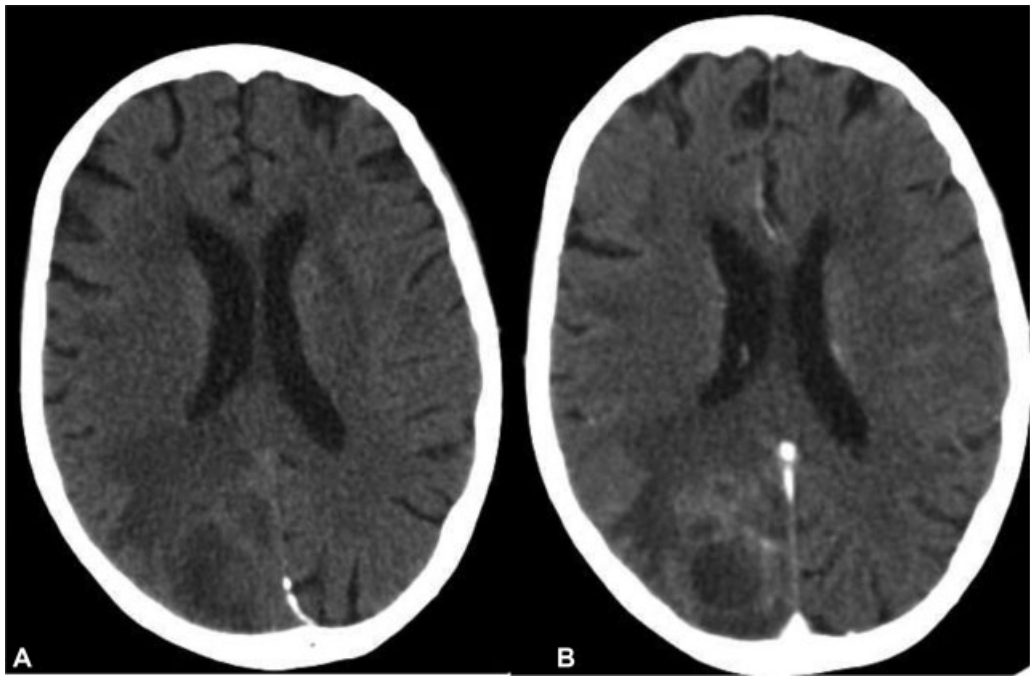


Fig. 1 Computed tomography images. Computed tomography in axial images, without contrast infusion (**A**) and after contrast infusion (**B**).

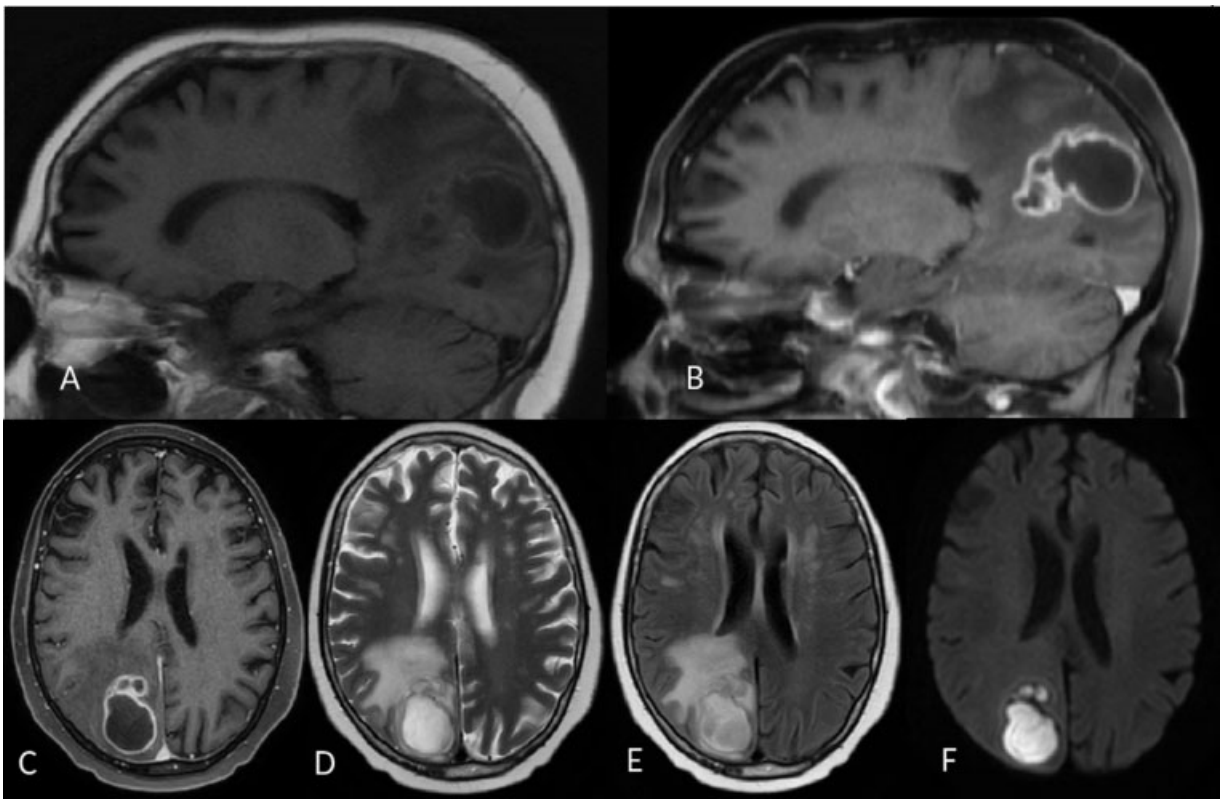


Fig. 2 Magnetic resonance images. Magnetic resonance images on sagittal plain without gadolinium infusion (**A**) and after gadolinium infusion with a peripheral enhancement (**B**). Axial imagens in T1 weighted with gadolinium (**C**), T2 weighted (**D**), FLAIR (**E**) and diffusion (**F**).

The Gram stain did not demonstrate any pathogens; however, the culture identified the growth of *Nocardia spp*. The patient was treated in the hospital with trimethoprim/ sulfamethoxazole and imipenem during 4 weeks, presenting a good neurological and clinical recovery (remaining only with the left homonymous hemianopsia), being discharged under the treatment of trimethoprim/sulfamethoxazole twice a day for 1 year. During the follow-up, the patient had no complaints, with no neurological nor systemic compromise. The cerebral computed tomography (CT) scan performed after 1 year of follow-up showed no signs of residual abscess and the patient was released back to primary care.

Discussion

Unlike primary pulmonary and cutaneous infections, which may be self-limiting, lesions of disseminated nocardiosis progress unless treated.[3] Central nervous system abscess can be isolated or multiple; the number of abscesses and their location will clinically determine the neurological manifestation.[1] Solitary abscess is the most common finding; however, multiple lesions are not uncommon, being reported in 38% of the cases.[10]

During investigation, lumbar puncture is not part of diagnosis procedures for brain abscess, and should be performed only when there is clinical suspicion of meningitis or abscess rupture into the ventricular system and there is no contraindications for lumbar puncture.[7]

The diagnosis of brain abscess can be suggested by image exams, especially MRI. On MRI, pyogenic brain abscess is characterized by a hypointense lesion surrounded by a capsule that enhances after gadolinium infusion on T1 weighted series; diffusion-weighted series show a hyperintense signal within the abscess and hypointense on apparent-diffusion-coefficient imaging.[7] Diffusion-weighted imaging has a sensitivity and specificity of 96% to differentiate brain abscess and tumor, with a positive predictive value of 98% and negative predictive value of 92%.[11] Nocardial brain abscess has similar features of a pyogenic abscess on MRI.

When the physician has suspicion of brain abscess, it is reasonable to postpone the therapy until the neurosurgical procedure is performed, as long as the patient is clinically stable and the surgery can be performed soon. If the patient has systemic disease (pulmonary or skin, for example), the sample can be retrieved from any of those places. If *Nocardia spp.* is identified and the patient is clinically stable with brain lesion < 2 cm, the neurosurgeon is authorized to indicate antibiotic therapy alone.[10] Under this therapy, stereotactic aspiration is recommend if the clinical condition deteriorates or if the lesion does not decrease within 1 month of antibiotic treatment.[12]

In patients with CNS nocardiosis, the treatment protocol depends on the condition of the immune system of the patient. Immunocompetent patients presenting one of the following situations: intracranial abscess > 2.5cm, multiple abscesses, cerebellum or posterior fossa involvement, lesion growth after 2 weeks of antibiotic treatment, failure to reduce size within 1 month, should undergo a neurosurgical resection.[8] Immunocompetent patients without those criteria may be submitted to stereotactic biopsy and wait for the identification of the pathogen, which facilitates an early and accurate diagnosis with an

antimicrobial sensitivity profile specific to the intracranial lesion.[12]

Immunocompromised patients should always be submitted to neurosurgical procedure, because they are more likely to have atypical infections and neoplasms, multiple intracranial lesions and a higher mortality rate.[12,13]

Nocardia spp. usually grows in regular means of bacteriological culture. However, cultural diagnosis requires a longer period for bacterial isolation, once it is a slow-growing pathogen and the laboratory is often unable to identify the microorganism using routine techniques. Therefore, the laboratory should be notified about the suspicion of *Nocardia spp.* infection, so the culture will be accompanied for a longer period.[1,5,6]

Because of its excellent CNS penetration, trimethoprim-sulfamethoxazole remains the first line treatment, except in patients with known hypersensitivity to it.[12] The prescription of trimethoprim-sulfamethoxazole in high parenteral doses (15 mg/kg trimethoprim and 75 mg/kg sulphamethoxazole daily) is recommended for 6 weeks, after which the therapy can be reduced or changed depending on the clinical and radiological responses, followed by oral therapy. Central nervous system nocardiosis should be treated for a total of 12 months[5] and monitored for at least a further year after completion of treatment.[8] Herrero Martínez et al. recommend lifetime secondary prophylaxis for patients with unrecoverable immunocompromised states.[1]

Nocardia spp. is generally resistant to penicillin,[6] and second line agents include minocycline, imipenem, and third-generation cephalosporins combined with aminoglycoside.[14,15]

The mortality rate is 20% for immunocompetent and 55% for immunocompromised patients.[10] The recognized factors leading to a good outcome are: early diagnosis, institution of appropriate antimicrobial therapy, lack of underlying systemic disease, and limited disease caused by *Nocardia spp*.[12]

The present article has some weakness that must be stated. First, it is a case report, which, in a scientific point of view, does not have the same power of evidence as other most sophisticated study designs. Second, the incidence of primary brain abscess has diminished in the last decades; therefore, Nocardia brain abscess (which represents 2% of all brain abscesses) will not be expected to be frequent among neurosurgical cases. Third, the investigation algorithm of brain abscess remains the same, and should not be changed to try to identify a bacterium that accounts for $< 5\%$ of cases.

However, the article has some strengths that deserve to be highlighted. The literature review presented embraces important information about Nocardia (including biological characteristics, which are usually unknow by doctors) and the different types of human affection by this bacterium, demonstrating that brain abscess is one of the types of human infection by *Nocardia spp*. Also, the discussion brings information about proper investigation and therapy of brain abscesses in general, describing when antibiotic therapy should be promptly prescribed or when a surgical procedure is required prior to the antibiotic therapy. Finally, the case report and the review have two main notes. The first one is that brain abscess caused by *Nocardia spp.* is curable and can be treated with a single antibiotic (trimethoprim-sulfamethoxazole). The second significant information is that proper treatment requires a long-term therapy with antibiotic, which must be maintained for, at least, 1 year; or during the lifetime in immunocompromised patients.

Conclusion

Even though the incidence of brain abscess due to *Nocardia spp.* is rare and have a higher morbidity and mortality when compared with other pyogenic abscesses, its diagnosis and optimized surgical and antibiotic therapy may cure the patient without neurological deficits.

Note

The patient has consented to the submission of the case report to the journal.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Herrero Martínez JA, Gómez Gómez J, García Vázquez E, Hernández Torres A. Nocardiosis. Med - Programa Form Médica Continuada Acreditado [Internet]. 2014;11(58):3412–3418. Available from: http://linkinghub.elsevier.com/retrieve/pii/S03045412147 07930

2 Beaman BL, Beaman L. Nocardia species: host-parasite relationships. Clin Microbiol Rev 1994;7(02):213–264

3 Lerner PI. Nocardiosis. Clin Infect Dis 1996;22(06):891–903, quiz 904–905

4 Tamarit M, Poveda P, Barón M, Del Pozo JM. Four cases of nocardial brain abscess. Surg Neurol Int 2012;3:88http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3463145/

5 Kennedy KJ, Chung KHC, Bowden FJ, et al. A cluster of nocardial brain abscesses. Surg Neurol 2007;68(01):43–49, discussion 49

6 Yaakup NA, Rahmat K, Ramli N, Sia SF. Cerebral nocardiosis in an immunocompetent patient: A diagnostic dilemma. Eur J Radiol Extra 2009;71(02):47–51

7 Brouwer MC, Tunkel AR, McKhann GM II, van de Beek D. Brain abscess. N Engl J Med 2014;371(05):447–456http://www.nejm.org/doi/abs/10.1056/NEJMra1301635

8 Kilincer C, Hamamcioglu MK, Simsek O, et al. Nocardial brain abscess: review of clinical management. J Clin Neurosci 2006;13(04):481–485http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16678731

9 Malincarne L, Marroni M, Farina C, et al. Primary brain abscess with Nocardia farcinica in an immunocompetent patient. Clin Neurol Neurosurg 2002;104(02):132–135

10 Mamelak AN, Obana WG, Flaherty JF, Rosenblum ML, Holtom PD. Nocardial brain abscess: treatment strategies and factors influencing outcome. Neurosurgery 1994;35(04):622–631

11 Reddy JS, Mishra AM, Behari S, et al. The role of diffusion-weighted imaging in the differential diagnosis of intracranial cystic mass lesions: a report of 147 lesions. Surg Neurol 2006;66(03):246–250, discussion 250–251

12 Fleetwood IG, Embil JM, Ross IB. Nocardia asteroides cerebral abscess in immunocompetent hosts: report of three cases and review of surgical recommendations. Surg Neurol 2000;53(06):605–610

13 Embil JM, Halliday WC, Nath A. Primary cerebellar T-cell lymphoma with acquired immunodeficiency syndrome. J Neurovirol 1997;3(03):229–232

14 Chen ST, Tang LM, Ro LS. Brain abscess as a complication of stroke. Stroke 1995;26(04):696–698

15 Börm W, Gleixner M. Nocardia brain abscess misinterpreted as cerebral infarction. J Clin Neurosci 2003;10(01):130–132

Microsurgical Resection of Glioblastoma in a Patient Infected with Covid-19: A Case Report

Ressecção microcirúrgica de glioblastoma em um paciente infectado com COVID-19: Relato de caso

Lívio Pereira de Macêdo[1] Kauê Franke[1] Auricélio Batista Cezar-Junior[1,2] Igor Vilela Faquini[1,2] Eduardo Vieira de Carvalho Júnior[1] Nivaldo S. Almeida[1] Hildo Rocha Cirne Azevedo-Filho[3]

[1] Department of Neurosurgery, Hospital da Restauração, Recife, PE, Brazil
[2] Department of Neurosurgery, Instituto de Medicina Integral Professor Fernando Figueira (IMIP), Recife, PE, Brazil
[3] Chairman of Department of Neurosurgery, Hospital da Restauração, Recife, PE, Brazil

Address for correspondence Lívio Pereira de Macêdo, MD, Rua João Fernandes Vieira, 544, Boa Vista, Recife, PE, 50050-200, Brazil (e-mail: livio21@gmail.com).

Arq Bras Neurocir 2021;40(3):e284–e287.

Abstract

The COVID-19 pandemic has affected a large number of patients in all countries, overwhelming healthcare systems worldwide. In this scenario, surgical procedures became restricted, causing unacceptable delays in the treatment of certain pathologies, such as glioblastoma. Regarding this tumor with high morbidity and mortality, early surgical treatment is essential to increase the survival and quality of life of these patients. Association between COVID-19 and neurosurgical procedures is quite scarce in the literature, with a few reported cases. In the present study, we present a rare case of a patient undergoing surgical resection of glioblastoma with COVID-19.

Keywords
- neurosurgery
- COVID-19
- SARS-CoV-2
- glioblastoma

Resumo

A pandemia de COVID-19 afetou um grande número de pacientes em todos os países, sobrecarregando os sistemas de saúde em todo o mundo. Nesse cenário, os procedimentos cirúrgicos tornaram-se restritos, causando atrasos inaceitáveis no tratamento de algumas patologias, como o glioblastoma. Em relação a esse tumor com alta morbimortalidade, o tratamento cirúrgico precoce é fundamental para aumentar a sobrevida e a qualidade de vida desses pacientes. A associação entre COVID-19 e procedimentos neurocirúrgicos é bastante escassa na literatura, com poucos casos relatados. No presente estudo, apresentamos um caso raro de paciente com COVID-19 submetido à ressecção cirúrgica de glioblastoma.

Palavras-chave
- neurocirurgia
- COVID-19
- SARS-CoV-2
- glioblastoma

Introduction

Officially declared as a global pandemic by the World Health Organization (WHO) on 11 March 2020, the Coronavirus Disease 2019 (COVID-19) outbreak has evolved at an unprecedented rate. It presents as a severe acute respiratory syndrome (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which was first reported in the city of

received
June 22, 2020
accepted
August 24, 2020
published online
November 26, 2020

DOI https://doi.org/10.1055/s-0040-1718998.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Wuhan, China, in December 2019. Despite efforts to contain this virus, it quickly turned into a pandemic with an exponentially increasing number of patients being diagnosed. Therefore, COVID-19 has overwhelmed healthcare systems worldwide.[1–9] However, operative procedures have become restricted in hospitals due to that infection. Therefore, this may lead to unacceptable delays in the treatment of patients with certain types of pathologies with high morbidity and mortality such as glioblastoma (GBM).

Glioblastoma is the most aggressive type of brain tumor. The median survival time after diagnosis is only 12 to 15 months, with $<$ 3 to 7% of patients surviving for $>$ 5 years. It is well-established that early surgical treatment, associated with adjuvant treatment, is essential to increase survival and quality of life in these patients. In this scenario, management protocols recommend early surgical treatment for newly diagnosed or recurrent high-grade gliomas.[9,10] Association between COVID-19 and neurosurgical procedures is quite scarce in the literature, with a few reported cases. In the present study, we present a rare case of a patient undergoing surgical resection of GBM with COVID-19, in the Hospital da Restauração, Recife, state of Pernambuco, Brazil.

Case Report

A 70-year-old male patient, with no comorbidities, was admitted to the neurosurgical emergency at Hospital da Restauração, on April 2020. He presented with headache, left sided hemiparesis and gait disturbances, for 3 days. There was no previous history of respiratory symptoms. A cranial computed tomography (CT) scan showed a right heterogeneous parietal lesion, with mass effect, irregular hypodense center and enhancement of its margins. A cerebral magnetic resonance imaging (MRI) revealed a heterogeneous lesion in the right parietal convexity, with extension to the ipsilateral ventricular atrium, irregular-enhancing margins and a central necrotic core, suggestive of high-grade glioma (HGG) (►**Fig. 1**). On physical examination, he was alert, oriented, with an incomplete and asymmetric left hemiparesis (grades III and IV on the lower and upper limbs, respectively).

Preoperative laboratory tests and cardiologic evaluation were normal, including the SARS-CoV2 real-time polymerase chain reaction (RT-PCR), which was negative. The surgical procedure was performed within 72 hours. Personal protective equipment (PPE) was appropriately used by the surgical team, following the recommendations established for COVID-19 suspected or confirmed surgical patients.[1,2,5,11,12] Gross Total Resection (GTR) was performed. At the end of the procedure, mechanical ventilation could not be removed due to the patient̀s low oxygen saturation, despite the high fraction of oxygen offered (FiO2). The postoperative cranial CT scan showed GTR of the tumor (►**Fig. 2**). A chest CT scan exhibited multilobed ground-glass opacities, compatible with SARS-CoV2 infection (►**Fig. 3**). The patient was moved to the

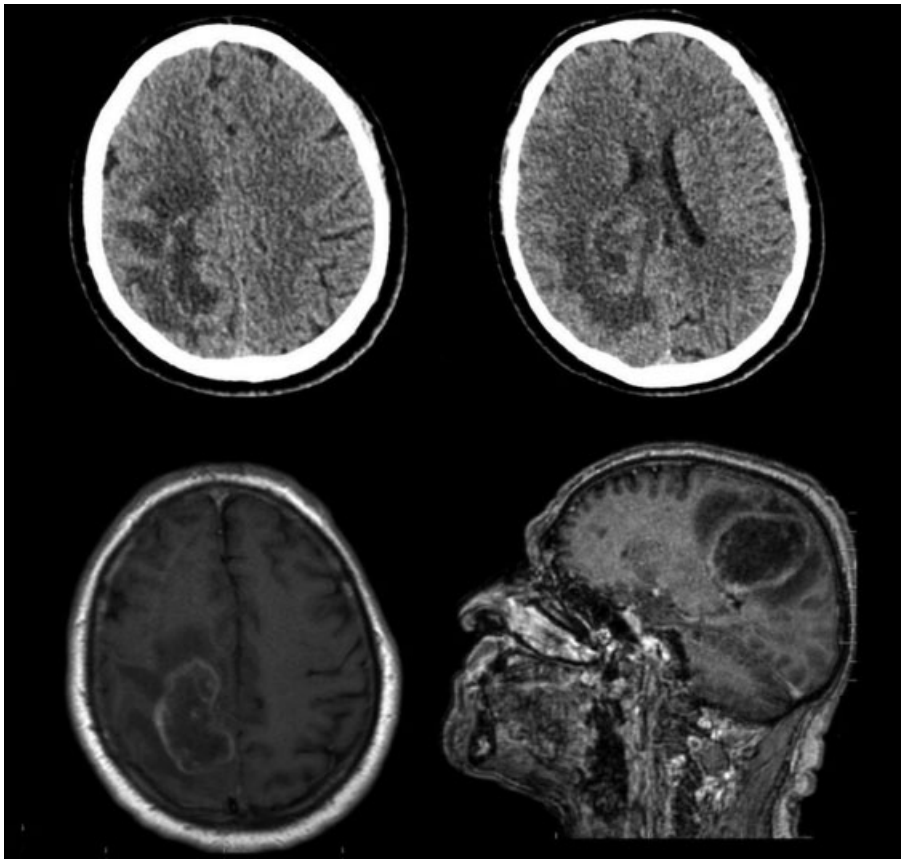


Fig. 1 Axial cranial computed tomography scan (upper) and axial brain magnetic resonance imaging (lower) with paramagnet contrast showing a heterogeneous lesion in the right parietal convexity, with extension to the ipsilateral ventricular atrium, irregular-enhancing margins and a central necrotic core.

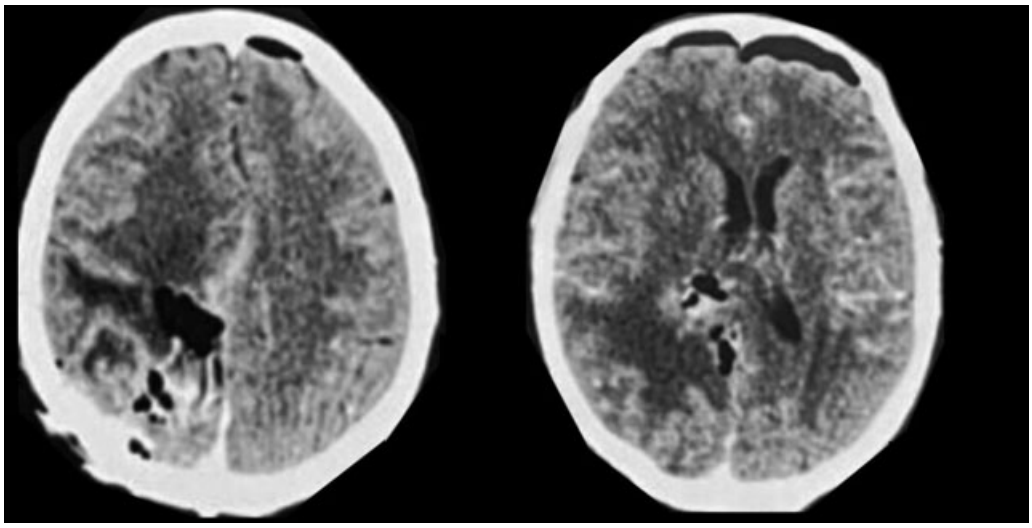


Fig. 2 Postoperative axial cranial computed tomography scan showing gross total resection of the tumor.

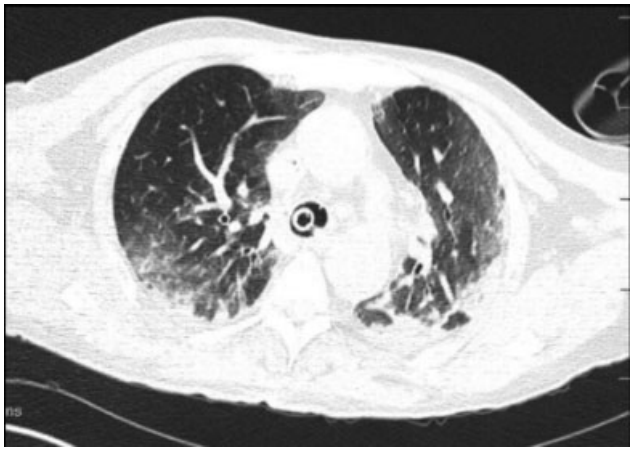


Fig. 3 Postoperative axial chest computed tomography scan exhibiting multilobed ground-glass opacities, suggestive of SARS-CoV2 infection.

intensive care unit (ICU), and another nasopharyngeal swab RT–PCR test was performed postoperatively, which was positive for SARS-CoV2 infection. During the hospitalization, respiratory symptoms were treated with ceftriaxone, azithromycin, oseltamir and hydroxychloroquine. After 12 days of mechanical ventilation, and 15 days of ICU, the patient was allocated to the infirmary. He showed improvement of his previous neurological deficits (showing left hemiparesis grade IV +). He was discharged after 19 days of hospitalization, with resolution of the respiratory condition and improvement of the functional status (modified Rankin Scale [mRS] of 3). The histological analysis diagnosed GBM (WHO grade IV), and the patient was referred to the clinical oncology department for planning adjuvant therapy.

Discussion

Recommendations and guidelines for the best neurosurgical practices in the COVID-19 era are still ongoing.[11] The case described in the present study was a suspected HGG in a patient infected with SARS-CoV-2. Due to the presence of neurological deficits (left hemiparesis) and radiologic evidence of malignancy, associated with the fact that the patient had no respiratory symptoms and negative RT-PCR on admission, we opted for early surgical treatment, following precautions recommended by the WHO. As described by Zoia et al.[13] in Lombardy (Italy), screening protocols were performed to support or contraindicate neurosurgical procedures. Thus, patients requiring immediate surgical treatment were classified as Class A ++; as Class +, those requiring treatment within a maximum of 7–10 days; and as Class A, those requiring surgery within a month. Patients with intracranial tumors with mass effect or with progressive neurological deficits, as reported in the present study, should be treated within a maximum of 7–10 days (Class A +). Moreover, according to the Centers for Medicare and Medicaid Services (CMS), all non-essential surgical procedures should be postponed and only urgent procedures must be performed. However, neurological surgeries should not be delayed if they are essential in reducing mortality and in preserving neurological function. The same recommendation is applied to patients with intracranial hypertension and risk of death.[14]

It is known that patients diagnosed with COVID-19 who underwent surgical procedures had worse outcomes and a higher mortality rate, requiring a longer ICU stay and hospitalization, compared to uninfected patients.[2,15] On this account, for COVID-19 patients, the in-hospital mortality rate is, regrettably, high, at 28% overall; however, it is much greater, at $>$ 50%, among those requiring mechanical ventilation.[1] Endorsing the higher mortality rate in neurosurgical patients, Ozoner et al.[2] reported their recent data from the University of Brescia (Italy). According to this study, the mortality related to chronic subdural hematoma surgical drainage was 80% in COVID-19 (+) patients. This rate was reported as 3.7% in the control group treated before the pandemic. The case described in our study showed a longer hospital stay and consequent delay in starting adjuvant treatment, which may cause a negative impact on the outcome of a patient with HGG. However, the patient reported that he recovered well. Although the mechanism of SARS-CoV-2 cerebral invasion is not fully understood, COVID-19 appears to demonstrate neuroinvasive potential. Viral encephalitis,

hemorrhagic necrosis involving mesial brain structures such as the mesial temporal lobes and thalami have been reported to date and may affect neurosurgical results.[16] Moreover, according to a recent meta-analysis including nearly 1,800 COVID-19 patients, lower platelet count was associated with severe COVID-19. Thus, thrombocytopenia can lead to postoperative rebleeding that results in a poor outcome.[15] Similarly, in SARS-CoV-2 infected and asymptomatic patients, surgical intervention could impair the immune system, leading to progression of the respiratory disease and to a worse outcome.[17,18]

Since the infection is asymptomatic in some cases, the authors of the present study believe screening for COVID-19 is essential in all patients before surgery. In addition, it contributes to healthcare professional safety. A higher mortality risk is well-demonstrated in COVID-19 patients who were submitted to surgical procedures.[2] Therefore, asymptomatic surgical candidates are screened for SARS–CoV2 RT-PCR on hospital admission. However, the case reported in the present study showed a preoperative negative test. According to Kucirka et al.,[19] the false-negative rate for SARS-CoV-2 RT-PCR testing is highly variable, highest within the first 5 days after exposure (up to 67%), and lowest on day 8 after exposure (21%). Therefore, it is questionable which is the best screening test on preoperative asymptomatic patients. Thus, there is still no standard protocol to guide the screening tests of neurosurgical patients.

In the literature, there are few cases reported of neurosurgery in patients diagnosed with COVID-19.[2,20] As shown by Wen et al.,[6] microsurgery for a ruptured cerebral aneurysm clipping was performed in a patient with suspected SARS-Cov-2 infection. In this case, RT-PCR testing was negative, despite the possibility of being a false negative, which impacts to reduce registered cases. Therefore, we reported in our study a rare confirmed case of patient infected with SARS-CoV-2 undergoing neurosurgical operation. Despite prolonged hospitalization, a good outcome was obtained, with a mRS of 3 on discharge.

Conclusion

The SARS-CoV-2 pandemic has caused changes in the routines of healthcare systems worldwide. Many surgeries have been postponed, so there are few reported cases of neurosurgery performed in patients diagnosed with COVID-19. The possibility of false negative SARS–CoV2 RT-PCR screening test might contribute to the reduced registered cases. Although these patients have worse results and a high mortality rate, the reported patient managed to recover well. Therefore, the present study showed a rare case of a patient with COVID-19 undergoing neurosurgical procedure. Although the management of these patients is still uncertain, the value of surgical treatment must be balanced with risks and benefits.

Patient Consent

The patient and relatives have consented to the submission of the present case report to the journal.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Tsermoulas G, Zisakis A, Flint G, Belli A. Challenges to Neurosurgery during the COVID-19 pandemic. World Neurosurg 2020
2 Ozoner B, Gungor A, Hasanov T, Toktas ZO, Kilic T. Neurosurgery Practice During Coronavirus Disease. 2019 (COVID-19) Pandemic. World Neurosurg. 2020 May;
3 Flemming S, Hankir M, Ernestus RI, et al. Surgery in times of COVID-19-recommendations for hospital and patient management. Langenbecks Arch Surg 2020;405(03):359–364
4 Moriguchi T, Harii N, Goto J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. Vol. 94, International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020:55–8
5 Grelat M, Pommier B, Portet S, et al. Covid-19 patients and surgery: Guidelines and checklist proposal. World Neurosurg 2020
6 Wen J, Qi X, Lyon KA, Liang B, Wang X, Feng D, et al. Lessons from China When Performing Neurosurgical Procedures During the Coronavirus Disease 2019 (COVID-19) Pandemic. World Neurosurg2020
7 Ng Kee Kwong KC, Mehta PR, Shukla G, Mehta AR. COVID-19, SARS and MERS: A neurological perspective. J Clin Neurosci 2020;77:13–16
8 Paybast S, Emami A, Koosha M, Baghalha F. Novel coronavirus disease (COVID-19) and central nervous system complications: What neurologist need to know. Acta Neurol Taiwan 2020;29(01):24–31
9 Ramakrishna R, Zadeh G, Sheehan JP, Aghi MK. Inpatient and outpatient case prioritization for patients with neuro-oncologic disease amid the COVID-19 pandemic: general guidance for neuro-oncology practitioners from the AANS/CNS Tumor Section and Society for Neuro-Oncology. J Neurooncol 2020;147(03):525–529
10 Bernhardt D, Wick W, Weiss SE, et al. Neuro-oncology Management During the COVID-19 Pandemic With a Focus on WHO Grade III and IV Gliomas. Neuro-oncol 2020:noaa113
11 Germanò A, Raffa G, Angileri FF, Cardali SM, Tomasello F. Coronavirus Disease 2019 (COVID-19) and Neurosurgery: Literature and Neurosurgical Societies Recommendations Update. World Neurosurg 2020;139:e812–e817
12 Liu Z, Zhang Y, Wang X, et al. Recommendations for Surgery During the Novel Coronavirus (COVID-19) Epidemic. Indian J Surg 2020:1–5
13 Zoia C, Bongetta D, Veiceschi P, et al. Neurosurgery during the COVID-19 pandemic: update from Lombardy, northern Italy. Acta Neurochir (Wien) 2020;162(06):1221–1222
14 D'Amico RS, Baum G, Serulle Y, et al. A Roadmap to Reopening a Neurosurgical Practice in the Age of COVID-19. World Neurosurg 2020;139:289–293
15 Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta 2020;506:145–148
16 Wilson MP, Jack AS. Coronavirus disease 2019 (COVID-19) in neurology and neurosurgery: A scoping review of the early literature. Clin Neurol Neurosurg 2020;193:105866
17 O'Dwyer MJ, Owen HC, Torrance HDT. The perioperative immune response. Curr Opin Crit Care 2015;21(04):336–342
18 Torrance HDT, Pearse RM, O'Dwyer MJ. Does major surgery induce immune suppression and increase the risk of postoperative infection? Curr Opin Anaesthesiol 2016;29(03):376–383
19 Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure. Ann Intern Med 2020;173(04):262–267
20 Carrabba G, Taricciotti L, Guez S, Calderini E, Locatelli M. Neurosurgery in an infant with COVID-19. Lancet 2020;395(10234):e76

Minimally Invasive Mini-orbitozygomatic Approach for Clipping an Anterior Communicating Artery Aneurysm: Virtual Reality Surgical Planning

Abordagem mini-orbitozigomático minimamente invasiva para clipagem de um aneurisma da artéria comunicante anterior: planejamento cirúrgico de realidade virtual

Nicolás González Romo[1] Franco Ravera Zunino[1]

[1] Department of Neurosurgery, Hospital Regional Rancagua, Rancagua, Chile

Address for correspondence Nicolás González Romo, MD, Department of Neurosurgery, Hospital Regional Rancagua, Rancagua, Chile (e-mail: ngonzalezr@ug.uchile.cl).

Arq Bras Neurocir 2021;40(3):e288–e293.

Abstract

Virtual reality (VR) has increasingly been implemented in neurosurgical practice. A patient with an unruptured anterior communicating artery (AcoA) aneurysm was referred to our institution. Imaging data from computed tomography angiography (CTA) was used to create a patient specific 3D model of vascular and skull base anatomy, and then processed to a VR compatible environment. Minimally invasive approaches (mini-pterional, supraorbital and mini-orbitozygomatic) were simulated and assessed for adequate vascular exposure in VR. Using an eyebrow approach, a mini-orbitozygomatic approach was performed, with clip exclusion of the aneurysm from the circulation. The step-by-step process of VR planning is outlined, and the advantages and disadvantages for the neurosurgeon of this technology are reviewed.

Keywords
- virtual reality
- intracranial aneurysm
- microsurgery
- skull base

Resumo

A realidade virtual (RV) é uma ferramenta cada vez mais utilizada na prática neurocirúrgica. Apresentamos um caso de aneurisma da artéria comunicante anterior (AcoA) sem rompimento com planejamento cirúrgico por RV. Os dados da angiografia por tomografia computadorizada (ATC) DICOM foram usados para a criação de um modelo 3D da anatomia vascular e da base do crânio do paciente, seguido de análise em um ambiente compatível com RV. Abordagens minimamente invasivas (mini-pterional, supraorbital e mini-orbitozigomática) foram simuladas e avaliadas quanto à exposição vascular adequada na RV. Utilizando uma abordagem pela sobrancelha, foi realizada uma abordagem mini-orbitozigomática, com exclusão do aneurisma da circulação. O processo passo a passo do planejamento da RV foi descrito e foram revisadas as vantagens e desvantagens desta tecnologia.

Palavras-chave
- realidade virtual
- aneurisma intracraniano
- microcirurgia
- base do crânio

received
April 11, 2020
accepted
August 24, 2020
published online
November 26, 2020

DOI https://doi.org/10.1055/s-0040-1719004.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Surgical planning is a critical step in cerebrovascular surgery. Appropriate selection of surgical approaches, angle of attack, and potential clip configuration may be optimized by meticulous assessment of the patient angiographic images.

Virtual reality (VR) has increasingly been adopted as a technology with potential benefits for neurosurgery, allowing a reduced learning curve of complex procedures, improved visuospatial skills, and understanding of complex anatomical relationships.[1,2]

Digital imaging and communications in medicine (DICOM) data from computed tomography angiography (CTA) can be used to create accurate and individualized 3D models of the patient skull base and vascular anatomy. These 3D models can later be transferred to a virtual reality environment, obtaining in this process "stereopsis"[3], which is a sense of depth from binocular vision that translates to optimized visuospatial interpretation.

Using VR, the neurosurgeon can have a more accurate, preoperative interaction with the patient's unique anatomy. In the VR environment, different surgical approaches can be simulated, and surgical strategy rehearsed.

Our goal is to outline our step-by-step process of VR surgical planning, including DICOM data processing and creation of VR models of different surgical approaches, applied successfully in the case of a patient with an unruptured anterior communicating artery (AcoA) aneurysm treated at our center, and briefly point the advantages and disadvantages of this technology.

Case

A 64-year-old female patient with medical history of arterial hypertension was admitted to our center because of headache of acute onset and was diagnosed an unruptured saccular AcoA aneurysm. The patient was neurologically intact. On CTA, the dimensions of the aneurysm were 3-mm neck and 5-mm diameter, with an anteroinferior projection, and counter clockwise rotation of the A2 fork. This case was considered favorable for a minimally invasive approach.

VR Planning

DICOM CTA (1.0-mm thickness volumetric acquisition) was processed using the open-source DICOM software Horos version 3.3.6 (Nimble LLC, Purview in Annapolis, MD, USA). Using "grow segmentation tool," two different regions of interest (ROIs) of the polygon of Willis and of the skull bone were created. Next, in the 3D volume rendering mode, with the "scissor tool" 3 surgical approaches suitable for the case were simulated (mini-pterional, supraorbital and mini-orbitozygomatic). In the 3D surface rendering mode, red color labeling was assigned to the arterial ROI, and white color to the bone ROI. The 3D model was converted and exported to a VR compatible file.

Using Sketchfab (http://www.sketchfab.com) free online VR editor, the file was uploaded, and the texture was processed.

Using a VR headset (Zeiss Vr Oneplus headset), the resulting models were assessed using the first-person VR mode.

Results

A VR simulation of minimally invasive cranial approaches was performed from the side of A1 dominance (left side).

Mini-pterional Approach (https://skfb.ly/6QsxC)

A frontotemporal curvilinear skin incision behind the line of hair implantation, is followed by interfascial dissection of the temporalis muscle. A subfascial or myocutaneous dissection can be performed as well. A fronto-temporo-sphenoidal craniotomy, as described by Figueiredo et al.,[4], includes bone removal from the keyhole region, posterior to the frontozygomatic suture, lateral to the superior temporal line and anterior to the stephanion (►**Fig. 1.A**, **B**).

Supraorbital Approach (https://skfb.ly/6Qt6w)

After an eyebrow incision, following the description of Perneckzy,[5] frontal bone removal begins in the keyhole region and continues parallel to the supraorbital rim curving backward lateral to the supraorbital notch, avoiding entering the frontal sinus. The orbital roof is flattened with a cutting or diamond burr (►**Fig. 1C**, **D**).

Mini-orbitozygomatic Approach (https://skfb.ly/6Qtos)

This approach can be performed both from an eyebrow incision, or after a frontotemporal curvilinear incision behind the hairline insertion. Interfascial of subfacial dissection of the temporalis muscle is required. A proper MacCarty keyhole is followed by removal of a 3×3-cm bone flap that includes frontal bone, frontal process of the zygomatic bone, part of the orbital roof, and the supraorbital rim.[6] (►**Fig. 1 E**, **F**)

Neurovascular Anatomy, Approach Selection, and Dissection Strategy

The left A1 was dominant and had a trajectory directed first posteriorly and then curved back anteriorly into the AcoA complex. The A2 fork was rotated counterclockwise to the left side. The contralateral A1 joined the AcoA complex posteriorly. Because of the lack of contrast enhancement, the perforators and recurrent artery of Heubner were not represented in the VR model.

The aneurysm originated form the AcoA and projected inferiorly into the chiasmatic groove of the sphenoid (►**Fig. 2**). Optimal exposure of the aneurysm neck was obtained with a view axis almost perpendicular to the orbital roof. For this reason, a mini-orbitozygomatic approach was selected because it offered a better trajectory, perpendicular to the aneurysm neck, creating a corridor unobstructed by the orbital roof, and also offered an increased upward view angle toward the A2. Dissection strategy included exposure of optic-carotid and interoptic space. Because of a curved and deep trajectory of the ipsilateral A1, an arterial exposure

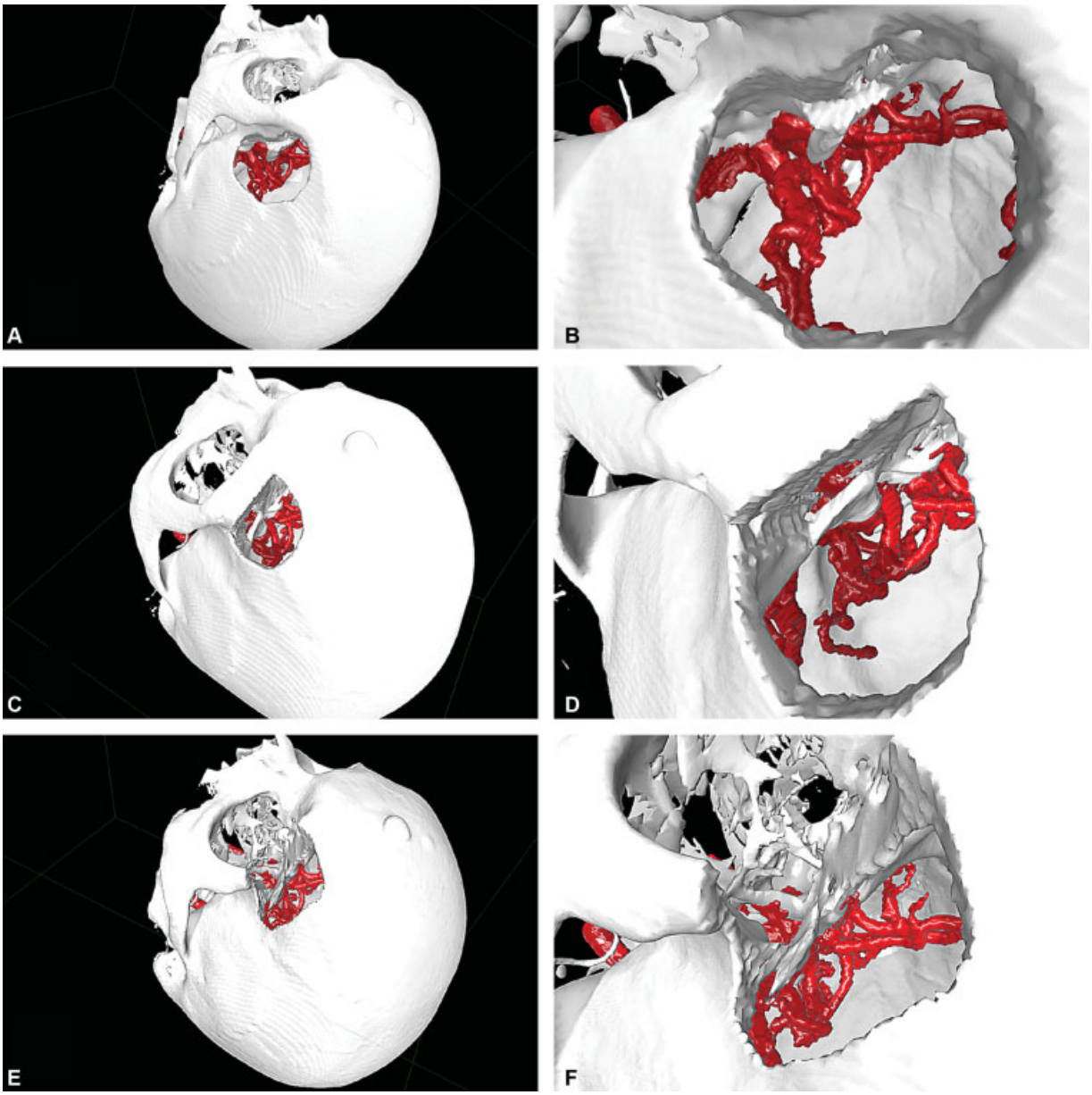


Fig. 1 Virtual reality simulation of surgical approaches. (A, B) Mini-pterional craniotomy. (C) (D) Supraorbital craniotomy. (D, E) Mini-orbitozygomatic osteotomy.

proximal to the AcoA complex was planned. Exposure of bilateral A2's required inter-hemispheric fissure dissection. Clipping with a straight clip configuration perpendicular to the aneurysm neck was considered an optimal exclusion strategy.

Surgical Technique

A left-sided mini-orbitozygomatic approach was performed. Under general anesthesia, the patient was positioned in a Mayfield head clamp. The head was extended and rotated ~ 30 degrees to the right side. Following an eyebrow incision laterally to the supraorbital notch, a fascial plane between the orbicularis oculi and the frontalis and temporalis muscles was identified. The supraorbital rim was exposed, and the supraorbital nerve was protected medially. Using a high-speed drill, a MacCarty keyhole was performed, exposing the periorbita and frontal dura. The periorbita was carefully separated from the orbital roof with a Penfield dissector. A one piece mini-orbitozygomatic bone flap was created with a craniotome, and the orbital roof was fractured with a chisel. The dura was opened in a curvilinear fashion and retracted with sutures (►**Fig. 3 A**). Without rigid retraction, the frontal lobe was gently mobilized posteriorly, exposing the optic-carotid cistern. Opening these cisterns allowed cerebrospinal fluid (CSF) release and brain relaxation. The supraclinoid carotid artery and optic nerve were identified (►**Fig. 3 B**). Further dissection revealed the aneurysm in the interoptic space projecting inferiorly into the chiasmatic groove (►**Fig. 3 C**). The dominant ipsilateral A1 was exposed in the posterior aspect of the AcoA, and both A2s where identified by dissection of the

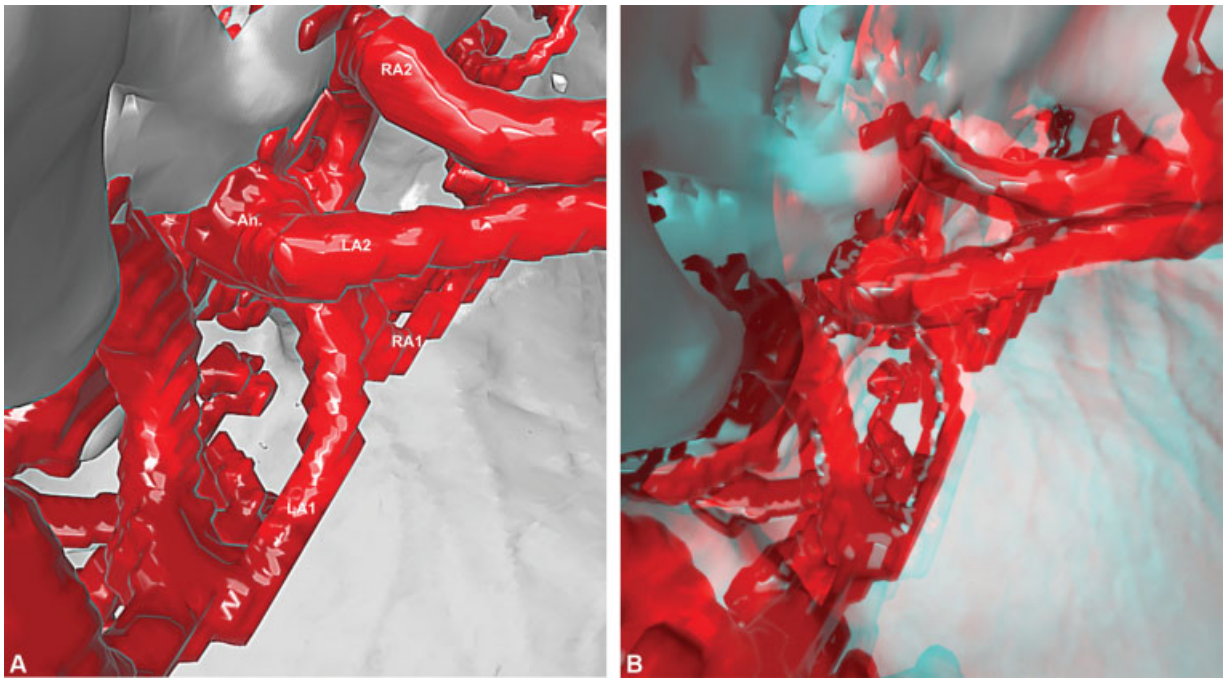


Fig. 2 Virtual reality model of vascular anatomy. (A) ICA: Internal carotid artery. LA1: left A1, RA1: right A1, AcoA: Anterior communicating artery, LA2: left A2, RA2: right A2, An: Aneurysm (B) Red/cyan anaglyph.

interhemispheric fissure, without the need of gyrus rectus resection. The ipsilateral recurrent artery was exposed at the A1–A2 junction. Two straight 7- and 9-mm Yasargil clips (Aesculap AG & Co., Tuttlingen, Germany) were used to exclude the aneurysm from the circulation (►**Fig. 3 C**). Indocyanine green (ICG) videoangiography confirmed aneurysm exclusion and patency of relevant vessels and perforators. The patient had a favorable postoperative course, without complications, and was discharged neurologically intact.

Discussion

Virtual reality is a technology that has increasingly been adopted in neurosurgery. Reports that related the use of VR in neurosurgery correspond to one of the following categories: education and resident training, morphological research, surgical planning, and use as an intraoperative surgical adjunct.[7–15]

In our study, we focused on the use of VR as a planning tool for cerebrovascular surgery. An eyebrow mini-orbitozygomatic approach was selected to treat an unruptured AcoA aneurysm after VR simulation, with favorable exposure and clinical outcome. This approach offered a perpendicular view to the neck of the aneurysm, compared with a more parallel axis view of the mini-pterional approach, and an increased upward view angle toward the A2 (by removal of the orbital rim and roof) compared with the supraorbital approach. These were subjective observations made in the VR simulation, and objective measurements would have made our study more robust, but our goal was to describe the process of VR simulation used and not to do a morphometric VR study comparing surgical approaches.

Virtual reality is a readily available technology, requiring a low-cost investment of a smartphone VR headset to be used. Stand-alone equipment exists that offers better image quality and interaction in the VR environment but at a higher cost. A computer station with a good graphics processor is also desirable.

In the VR environment, "stereopsis"[3], the sense of depth obtained from binocular vision, gives the surgeon the opportunity to asses complex spatial relationships of vascular structures before surgery and to establish a surgical plan, including patient positioning, surgical approach, vascular exposure, and aneurysm neck dissection strategy . In our opinion, the most important benefit of VR planning is observed during surgery, at which point a "déjà vu" feeling develops when exposing the relevant vascular anatomy, and the path to the aneurysm neck, as microsurgical dissection continues, is crystal clear from the beginning.

Disadvantages from our VR planning procedure include extra time required to process de DICOM images and conversion into VR files. Advanced knowledge of ROI creation and DICOM software use is required.

Soft-tissue layers, such as skin and muscle, cannot be visualized in VR. As a part of the simulation strategy, however, we took into consideration surgical steps related to soft-tissue dissection, such as skin incision and temporalis muscle dissection among others, to create a framework that is to be reproduced in surgery, and allowed us to make the decision about the best approach for the case.

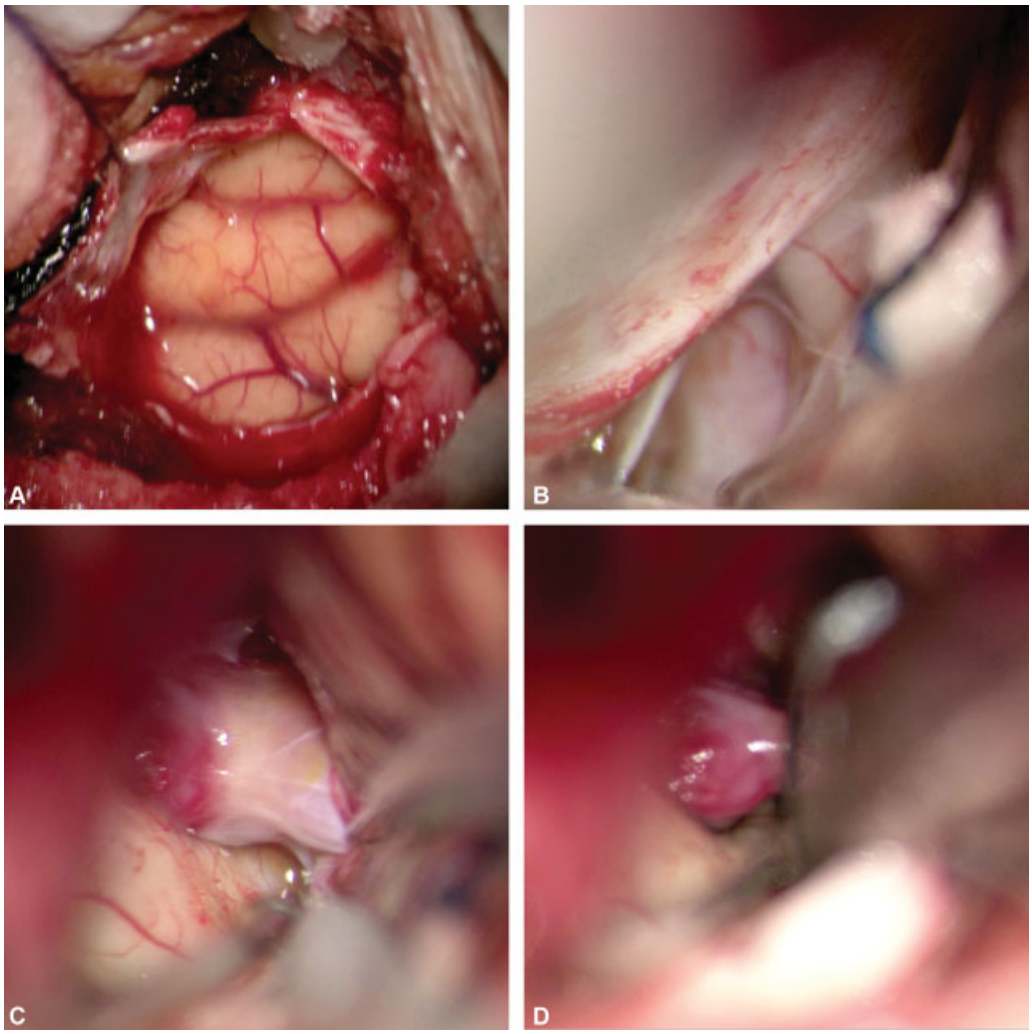


Fig. 3 Surgical Technique. (A) Dural opening. (B) Exposure of ipsilateral internal carotid artery and optic nerve. (C) Aneurysm dissection and neck exposure. (D) Clipping with straight clip.

The resulting VR model offers a gross representation of the vascular arterial anatomy and is a product of the ROI created from the vessels with contrast enhancement in CTA, so there may be artifacts, like venous vessels colored as arteries because of similar pixel values. Careful interpretation of the VR model is required. Perforators, due to lack of contrast enhancement, are usually not possible to observe in the VR model.

Overall, we believe that the advantages of this technology are superior to the disadvantages. Further studies with this technology are required to measure clinical benefit in terms of neurological outcomes

Conclusion

Virtual reality is a valuable tool for planning cerebrovascular surgery, optimizing patient positioning, surgical approach selection, dissection strategy, and clip selection.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Bernardo A. Virtual Reality and Simulation in Neurosurgical Training. World Neurosurg 2017;106:1015–1029
2 Bernardo A. Establishment of Next-Generation Neurosurgery Research and Training Laboratory with Integrated Human Performance Monitoring. World Neurosurg 2017;106:991–1000
3 Rubio RR, Bonaventura RD, Kournoutas I, et al. Stereoscopy in Surgical Neuroanatomy: Past, Present, and Future. Oper Neurosurg (Hagerstown) 2020;18(02):105–117
4 Figueiredo EG, Deshmukh P, Nakaji P, et al. The minipterional craniotomy: technical description and anatomic assessment. Neurosurgery 2007;61(05, Suppl 2):256–264, discussion 264–265
5 Fischer G, Stadie A, Reisch R, et al. The keyhole concept in aneurysm surgery: results of the past 20 years. Neurosurgery 2011;68(01, Suppl Operative)45–51, discussion 51
6 Yagmurlu K, Safavi-Abbasi S, Belykh E, et al. Quantitative anatomical analysis and clinical experience with mini-pterional and mini-orbitozygomatic approaches for intracranial aneurysm surgery. J Neurosurg 2017;127(03):646–659
7 de Faria JW, Teixeira MJ, de Moura Sousa Júnior L, Otoch JP, Figueiredo EG. Virtual and stereoscopic anatomy: when virtual reality meets medical education. J Neurosurg 2016;125(05):1105–1111

8 Bernard F, Gallet C, Fournier HD, Laccoureye L, Roche PH, Troude L. Toward the development of 3-dimensional virtual reality video tutorials in the French neurosurgical residency program. Example of the combined petrosal approach in the French College of Neurosurgery. Neurochirurgie 2019;65(04):152–157
9 Shao X, Yuan Q, Qian D, et al. Virtual reality technology for teaching neurosurgery of skull base tumor. BMC Med Educ 2020;20(01):3
10 Alaraj A, Luciano CJ, Bailey DP, et al. Virtual reality cerebral aneurysm clipping simulation with real-time haptic feedback. Neurosurgery 2015;11(Suppl 2):52–58
11 Bairamian D, Liu S, Eftekhar B. Virtual Reality Angiogram vs 3-Dimensional Printed Angiogram as an Educational tool-A Comparative Study. Neurosurgery 2019;85(02):E343–E349
12 Raabe C, Fichtner J, Beck J, Gralla J, Raabe A. Revisiting the rules for freehand ventriculostomy: a virtual reality analysis. J Neurosurg 2018;128(04):1250–1257
13 Peh S, Chatterjea A, Pfarr J, et al. Accuracy of augmented reality surgical navigation for minimally invasive pedicle screw insertion in the thoracic and lumbar spine with a new tracking device. Spine J 2020;20(04):629–637
14 Tai AX, Sack KD, Herur-Raman A, Jean WC. The Benefits of Limited Orbitotomy on the Supraorbital Approach: An Anatomic and Morphometric Study in Virtual Reality. Oper Neurosurg (Hagerstown) 2020;18(05):542–550
15 Morone PJ, Shah KJ, Hendricks BK, Cohen-Gadol AA. Virtual, 3-Dimensional Temporal Bone Model and Its Educational Value for Neurosurgical Trainees. World Neurosurg 2019;122:e1412–e1415

Author university affiliation

Apio Antunes[1]

[1] Neurosurgical Unit, University Hospital, Porto Alegre Medical School, Porto Alegre, Rio Grande do Sul, Brazil

Arq Bras Neurocir 2021;40(3):e294.

Address for correspondence Apio Antunes, MD, MSc, PhD, IFAANS, Neurosurgical Unit, Porto Alegre Medical School, University Hospital, Porto Alegre, Rio Grande do Sul, Brazil (e-mail: aantunes@hcpa.edu.br).

Dr. Eberval Figueiredo
Editor-in-Chief
Brazilian Journal of Neurosurgery
Dear Dr. Eberval:

In the recent volume 39(2) of the *Brazilian Journal of Neurosurgery*, we were deeply and negatively surprised with the finding in the article "Microsurgical and Endoscopic Anatomy of the Cavernous Sinus", coaoutohored by yourself. The first author aludded to be a member of our University (Universidade Federal do Rio Grande do Sul). Unless this was done by an improper digitation error, we, here, never found any position of this doctor in our Medical School. This being so, according to the possible legal and ethical responsibilities, we ask prompt manifestation of the authors or the journal for proper corrections and explanations.

Porto Alegre February 23, 2021
Apio Antunes
Apio Antunes, MD, MSc, PhD,IFAANS
Chairman of Neurosurgical Unit, University Hospital
Associate Professor of Neurosurgery
Porto Alegre Medical School

Conflict of Interest
The author has no conflicts to declare.

received
July 21, 2021
accepted
July 28, 2021

DOI https://doi.org/10.1055/s-0041-1735151.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Cavernous sinus triangles – correlation between cranial and endonasal visualization

Gustavo Rassier Isolan[1] Francisco Braga[2] Ricardo Lopes de Araújo[3]

[1] Department of Neurosurgery, School of Medicine and Postgradution Program in Surgery at Faculdade Evangélica Mackenzie do Paraná, The Center for Advanced Neurology and Neurosurgery, Porto Alegre, Brazil
[2] Department of Neurosurgery, The Center for Advanced Neurology and Neurosurgery, Porto Alegre, Brazil
[3] Weill Cornell University, New York City, New York, United States

Arq Bras Neurocir 2021;40(3):e295–e296.

Address for correspondence Gustavo Rassier Isolan, MD, PhD, Faculdade Evangélica Mackenzie do Paraná e CEANN, Curitiba, Brazil (e-mail: gustavo.isolan@fempar.edu.br).

Regarding the paper Microsurgical and Endoscopic Anatomy of the Cavernous Sinus (Arq Bras Neurocir 2020;39(2):83–94) published in the *Brazilian Neurosurgery Journal* last year, we would like to clarify that authors Gustavo Rassier Isolan, MD, Ricardo Lopes de Araújo, MD and Francisco Braga, MD, wrote this study at the time we were part of the postgraduate program in surgery at the Federal University of Rio Grande do Sul (Universidade Federal do Rio Grande do Sul – UFRGS). We want to assure that we no longer work at that university and our affiliations are following:

1. Gustavo Rassier Isolan, MD, PHD – Professor, School of Medicine and Postgradution Program in Surgery at Faculdade Evangélica Mackenzie do Paraná. Neurosurgeon – The Center for Advanced Neurology and Neurosurgery, Porto Alegre, RS, Brazil
2. Francisco Braga, MD – Neurosurgeon – The Center for Advanced Neurology and Neurosurgery, Porto Alegre, RS, Brazil
3. Ricardo Lopes de Araújo, MD – Doctoral Fellow, Weill Cornell University

Best Regards
Gustavo Isolan
Porto Alegre, March 20, 2021

DOI https://doi.org/10.1055/s-0041-1733996.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

ISSN 0103-5355

Instructions to Authors

Thank you for contributing to Brazilian NeuroSurgery (BNS). Please read the instructions carefully and observe all the directions given. Failure to do so may result in unnecessary delays in publishing your article. There are no submission charges to submit your manuscript to this journal..

Brazilian Neurosurgery (Arquivos Brasileiros de Neurocirurgia), an official journal of the Brazilian Society of N**eurosurgery (Sociedade Brasileira de Neurocirurgia) and Portuguese Language Neurosurgery Society (Sociedades de Neurocirurgia de Língua Portuguesa)**, aims to publish scientific works in Neurosurgery and related fields, unpublished and exclusive. As from January 2018, the journal **only publishes papers written in English with English and Portuguese abstracts**. Manuscripts must conform to acceptable English usage.

Submitted articles shall be placed as one of the following categories:

- ***Original:*** result of clinical, epidemiological or experimental research. Abstracts of theses and dissertations.
- ***Review:*** review and update synthesis of specific themes, with critical analysis and conclusions. Databases and the period range must be specified.
- ***Case Report:*** presentation, analysis and discussion of cases that present relevant interest.
- ***Technical Note:*** note on surgery techniques and/or surgical instruments.
- ***Miscellaneous:*** neurosurgery history, professional practice, medical ethics and other pertinent matters to the journal purpose.
- ***Letter to the Editor:*** critics and comments presented in a brief ethical and instructive manner about published content in this journal. The copyright is safe to authors of the aimed subject. Letters, when accepted, will be published with authors reply.

General standards for publishing

- Article files for publishing must be submitted to the Editor, via https://www.editorialmanager.com/bns/.
- All articles will have a double blinded peer-review process, and no Article Publishing Charge (APC) – society funded. More about Open Access at http://open.thieme.com.
- Only new unpublished manuscripts will be acceptable. Submitted articles **must not be** fully or partially submitted to any other journal.
- The editorial board may reject or suggest changes in order to improve the clarity and structure of the text and maintain uniformity with the journal policy.
- Copyrights of articles published in the journal will belong exclusively to the **Brazilian Neurosurgery and Thieme Revinter Publicações Ltda**. The reproduction of articles or illustrations without prior consent is prohibited.

Standards for submission

Authors must send the following files:

1. Pub Letter (formal text file) stating the article has not yet been published partially or fully or submitted concomitantly to other journal. Must contain Article Title, authors names in full (without abbreviations) and affiliations in ascending order of hierarchy and corresponding author (full address for correspondence, email, telephone).

2. Blind Manuscript (text file must contain article name in English, article name in Portuguese, abstracts in English and Portuguese, without identification of authors and affiliations).

3. Figures (*Tiff, Jpeg, Pdf, Indd*) sent in separate files with minimum resolution of 300 dpi.

4. Tables, charts and graphics (text file) sent separately.

Standards for articles structure

Articles must be structured with all the following items and paginated accordingly:

1. Title page: article title both in Portuguese and English; full name of all authors; academic or professional affiliation of each author; institutions names where the study took place; running title; corresponding author name, degree, full address, e-mail and phone number; followed by **ICMJE COI forms** (COI forms are available at: http://www.icmje.org/conflicts-of-interest/).

2. Abstract: original articles need structured abstract with 250 words at the most: **objective, methods, results and conclusions**; review articles, case reports, technical notes and miscellaneous need no structured abstract. Following the abstract comes keywords (six at the most), based on MeSH (Medical Subject Headings), published in Medline and available at: www.ncbi.nlm.nih.gov/mesh/.

3. Portuguese abstract: Portuguese version of title, abstract and keywords based on DeCS (Descritores em Ciências da Saúde, http://decs.bvs.br).

4. Main text: introduction; casuistry or material and methods; results; discussion; conclusion; acknowledgments.

5. References: number references as they are **first cited** in the text with Arabic numerals. Use Vancouver style; list all authors until the sixth, using *et al*. after the third when more than six; when reference authors are cited in the text cite the first and et al. for references with more that two authors; unpublished data or personal communication must be cited as such between parentheses and cannot be listed as reference; use journal abbreviation from *Index Medicus*; use the following examples:

Journal Article

Agner C, Misra M, Dujovny M, Kherli P, Alp MS, Ausman JI. Experiência clínica com oximetria cerebral transcraniana. Arq Bras Neurocir 1997;16(1):77–85

Book Chapter

Peerless SJ, Hernesniemi JA, Drake CG. Surgical management of terminal basilar and posterior cerebral artery aneurysms. In: Schmideck HH, Sweet WH, editors. Operative neurosurgical techniques. 3rd ed. Philadelphia: WB Saunders; 1995:1071–86.

Book

Melzack R. The puzzle of pain. New York: Basic Books Inc Publishers; 1973.

Theses and dissertations

Pimenta CAM. Aspectos culturais, afetivos e terapêuticos relacionados à dor no câncer. [thesis]. São Paulo: Escola de Enfermagem da Universidade de São Paulo; 1995.

Annals and other congresso publications

Corrêa CF. Tratamento da dor oncológica. In: Corrêa CF, Pimenta CAM, Shibata MK, editores. Arquivos do 7º Congresso Brasileiro e Encontro Internacional sobre Dor; 2005 outubro 19–22; São Paulo, Brasil. São Paulo: Segmento Farma. pp. 110–20.

Available Article in ahead of print

International Committee of Medial Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. Writing and editing for biomedical publication. Updated October 2007. Available at: http://www.icmje.org. Access in: June 12, 2008.

6. Tables and charts: numbered by Arabic numerals according to its citation in the text; edited in double space, using separate sheets per table/chart; title right above; note, abbreviations, legends must follow right under; introduce only essential tables and charts; files must come separately.

8. Figures: digital formats (TIFF, JPEG, PDF, Indd) with minimum resolution of 300 dpi (trim 7.5 or 15 cm).

9. Legends and captions: numbered by Arabic numerals according to its citation in the text; edited in double space, using separate files; identify eventual labels present in the figure (arrows,

characters, lines etc.); image previously published must have publisher authorization and credits.

10. Ethics standards: No data or image identifying a patient can be used without ***formal consent*** (**patient permission forms are available at: www.thieme.com/journal-authors**); studies using human beings or animal trials must follow ethical standards from the International Committee of Medical Journals Editors – ICMJE, as well as approval of original institution's Ethics Committee; conflicts of interest must have a ICMJE form filled in by all authors (available at: http://www.icmje.org/conflicts-of-interest/); commercial marks should be avoided; authors are the sole responsible for opinions and concepts in the published articles, as well as for the reference accuracy.

11. The editors and Thieme combat plagiarism, double publication, and scientific misconduct with the software CrossCheck powered by iThenticate. Your manuscript may be subject to an investigation and retraction if plagiarism is suspected.

12. Authors must disclose any financial relationship(s) at the time of submission, and any disclosures must be updated by the authors prior to publication. Information that could be perceived as potential confl ict(s) of interest must be stated. This information includes, but is not limited to, grants or funding, employment, affiliations, patents, inventions, honoraria, consultancies, royalties, stock options/ownership, or expert testimony.

13. Other information: PDF proof will be sent to corresponding author for eventual queries and/or approval within 72 hours; except measure units, acronyms must be spelled out after its first time mentioned.

Thieme Publishers
Acquisitions Editor
Ana Paula Canel Bluhm, MSc., PhD.
ana.bluhm@thieme.com.br

Editorial Production
Thieme Publishers - Production Coordinator
Gisele Múfalo
gisele.mufalo@thieme.com.br

Thieme Publishers - Junior Production Coordinator
Paula Di Sessa Vavlis
paula.disessa@thieme.com.br

ISSN 0103-5355

Instruções aos Autores

Muito obrigado por contribuir com a Arquivos Brasileiros de Neurocirurgia. Por favor, leia cuidadosamente as instruções a seguir. A falta de concordância com essas instruções pode causar atrasos desnecessários na publicação de seu artigo. Esta revista não cobra taxas de submissão e publicação de artigos.

Arquivos Brasileiros de Neurocirurgia, publicação científica oficial da **Sociedade Brasileira de Neurocirurgia** e das **Sociedades de Neurocirurgia de Língua Portuguesa**, destina-se a publicar trabalhos científicos na área de neurocirurgia e ciências afins, inéditos e exclusivos. **Serão publicados apenas trabalhos redigidos em inglês, com resumos em inglês e em português**. Os manuscritos devem ser escritos de forma clara e concisa.

Os artigos submetidos serão classificados em uma das categorias abaixo:

- ***Artigos originais:*** resultantes de pesquisa clínica, epidemiológica ou experimental. Resumos de teses e dissertações.
- ***Artigos de revisão:*** sínteses de revisão e atualização sobre temas específicos, com análise crítica e conclusões. As bases de dados e o período abrangido na revisão deverão ser especificados.
- ***Relatos de caso:*** apresentação, análise e discussão de casos que apresentem interesse relevante.
- ***Notas técnicas:*** notas sobre técnica operatória e/ou instrumental cirúrgico.
- ***Artigos diversos:*** são incluídos nesta categoria assuntos relacionados à história da neurocirurgia, ao exercício profissional, à ética médica e outros julgados pertinentes aos objetivos da revista.
- ***Cartas ao editor:*** críticas e comentários, apresentados de forma resumida, ética e educativa, sobre matérias publicadas nesta revista. O direito à réplica é assegurado aos autores da matéria em questão. As cartas, quando consideradas como aceitáveis e pertinentes, serão publicadas com a réplica dos autores.

Normas gerais para publicação

- Os arquivos dos artigos para publicação deverão ser enviados ao Editor, no endereço eletrônico http://www.editorialmanager.com/bns/.
- Todos os artigos serão avaliados pelo processo de revisão por pares do tipo duplo-cego, e não há cobrança de taxa pelo processamento da publicação (APC). Para saber mais sobre *Open Access*, acesse http://open.thieme.com.
- Serão aceitos apenas os artigos inéditos não publicados previamente. Os artigos, ou parte deles, submetidos à publicação em **Arquivos Brasileiros de Neurocirurgia** não deverão ser submetidos, concomitantemente, a outra publicação científica.
- Compete ao Corpo Editorial recusar artigos e sugerir ou adotar modificações para melhorar a clareza e a estrutura do texto e manter a uniformidade conforme o estilo da revista.
- Os direitos autorais de artigos publicados nesta revista pertencerão exclusivamente à **Arquivos Brasileiros de Neurocirurgia à Thieme Revinter Publicações Ltda**. É vetada a reprodução de artigos ou ilustrações publicadas nesta revista sem o consentimento prévio da Editora.

Normas para submeter os artigos à publicação

Os autores devem enviar os seguintes arquivos:

1. Carta formal ao Editor (arquivo de texto) explicitando que o artigo não foi previamente publicado no todo ou em parte ou submetido concomitantemente a outro periódico. Deve conter Título do artigo, nome completo dos autores, filiação em ordem crescente de hierarquia e autor correspondente.

2. Manuscrito Anônimo (arquivo de texto deve conter o nome do artigo em inglês, nome do artigo em português, resumos em inglês e português, sem identificação de autores e filiações).

3. Figuras (*Tiff, Jpeg, Pdf, Indd*), enviadas em arquivos individuais para cada ilustração, com resolução mínima de 300 dpi.

4. Tabelas, quadros e gráficos (arquivo de texto), enviados em **arquivos individuais**.

Normas para a estrutura dos artigos

Os artigos devem ser estruturados com todos os itens relacionados a seguir e paginados na sequência apresentada:

1. Página-título: título do artigo em português e em inglês; nome completo de todos os autores; sem abreviações, títulos universitários ou profissionais dos autores principais (máximo de dois títulos por autor); nomes das instituições onde o trabalho foi realizado; título abreviado do artigo, para ser utilizado no rodapé das páginas; nome, endereço completo, *e-mail* e telefone do autor responsável pelas correspondências com o Editor, juntamente com o **Formulário ICMJE** disponível em (http://www.icmje.org/conflicts-of-interest/).

2. Resumo: para **artigos originais**, deverá ser estruturado, utilizando cerca de 250 palavras, descrevendo **objetivo, métodos, principais resultados e conclusões**; para Revisões, Atualizações, Notas Técnicas e Relato de Caso o resumo não deverá ser estruturado; abaixo do resumo, indicar até seis palavras-chave, com base no MeSH (Medical Subject Headings), publicado pelo Medline e disponível em: www.ncbi.nlm.nih.gov/mesh/.

3. Abstract: título do trabalho em inglês; versão correta do resumo para o inglês; indicar até seis palavras-chave, com base no DeCS (Descritores em Ciências da Saúde), publicado pela Bireme e disponível em http://decs.bvs.br.

4. Texto principal: introdução; casuística ou material e métodos; resultados; discussão; conclusão; agradecimentos.

5. Referências: numerar as referências de forma consecutiva **de acordo com a ordem em que forem mencionadas pela primeira vez no texto**, utilizando-se números arábicos sobrescritos. Utilizar o padrão de Vancouver; listar todos os nomes até seis autores, utilizando "*et al*." após o terceiro quando houver mais de seis autores; as referências relacionadas devem, obrigatoriamente, ter os respectivos números de chamada indicados de forma sobrescrita, em local apropriado do texto principal; no texto, quando houver citação de nomes de autores, utilizar "*et al.*" para mais de dois autores; dados não publicados ou comunicações pessoais devem ser citados, como tal, entre parênteses, no texto e não devem ser relacionados nas referências; utilizar abreviatura adotada pelo *Index Medicus* para os nomes das revistas; siga os exemplos de formatação das referências (observar, em cada exemplo, a pontuação, a sequência dos dados, o uso de maiúsculas e o espaçamento):

Artigo de revista

Agner C, Misra M, Dujovny M, Kherli P, Alp MS, Ausman JI. Experiência clínica com oximetria cerebral transcraniana. Arq Bras Neurocir 1997;16(1):77–85

Capítulo de livro

Peerless SJ, Hernesniemi JA, Drake CG. Surgical management of terminal basilar and posterior cerebral artery aneurysms. In: Schmideck HH, Sweet WH, editors. Operative neurosurgical techniques. 3rd ed. Philadelphia: WB Saunders; 1995:1071–86.

Livro considerado como todo (quando não há colaboradores de capítulos)

Melzack R. The puzzle of pain. New York: Basic Books Inc Publishers; 1973.

Tese e dissertação

Pimenta CAM. Aspectos culturais, afetivos e terapêuticos relacionados à dor no câncer. [tese]. São Paulo: Escola de Enfermagem da Universidade de São Paulo; 1995.

Anais e outras publicações de congressos

Corrêa CF. Tratamento da dor oncológica. In: Corrêa CF, Pimenta CAM, Shibata MK, editores. Arquivos do 7º Congresso Brasileiro e Encontro Internacional sobre Dor; 2005 outubro 19–22; São Paulo, Brasil. São Paulo: Segmento Farma. p. 110–20.

Artigo disponível em formato eletrônico

International Committee of Medial Journal Editors. Uniform requirements for manuscripts

submitted to biomedical journals. Writing and editing for biomedical publication. Updated October 2007. Disponível em: http://www.icmje.org. Acessado em: 2008 (Jun 12).

6. Tabelas e quadros: devem estar numerados em algarismos arábicos na sequência de aparecimento no texto; devem estar editados em espaço duplo, utilizando folhas separadas para cada tabela ou quadro; o título deve ser colocado centrado e acima; notas explicativas e legendas das abreviaturas utilizadas devem ser colocadas abaixo; apresentar apenas tabelas e quadros essenciais; os arquivos devem ser submetidos separadamente do texto principal.

8. Figuras: elaboradas nos formatos TIFF, JPEG, PDF, Indd; a resolução mínima aceitável é de 300 dpi (largura de 7,5 ou 15 cm).

9. Legendas das figuras: numerar as figuras, em algarismos arábicos, na sequência de aparecimento no texto; editar as respectivas legendas, em espaço duplo, utilizando arquivos separados; identificar, na legenda, a figura e os eventuais símbolos (setas, letras etc.) assinalados; reprodução de ilustração já publicada deve ser acompanhada da autorização, por escrito, dos autores e dos editores da publicação original e esse fato deve ser assinalado na legenda.

10. Declaração de ética: Negrito nenhum dado ou imagem identificando um paciente pode ser utilizado sem consentimento formal (**os formulários de permissão do paciente estão disponíveis em: www.thieme.com/journal-authors**); estudos utilizando seres humanos ou animais devem obrigatoriamente seguir os padrões do ***International Committee of Medical Journals Editors* – ICMJE, bem como deve obter a aprovação do Comitê de Ética da Instituição onde foi realizado o trabalho; todos os autores devem assinar e anexar o seu próprio o formulário de conflitos de interesse (disponível em: http:// www. icmje. org/ conflicts-ofinterest/**); deve ser evitada a citação de marcas comerciais; os autores serão os únicos responsáveis pelas opiniões e conceitos contidos nos artigos publicados, bem como pela exatidão das referências bibliográficas apresentadas.

11. Os editores e Thieme combatem o plágio, dupla publicação, e má conduta científica atravé do uso do software CrossCheck distribuído por iThenticate. Seu manuscrito pode estar sujeito a investigação e retratação caso haja suspeita de plágio.

12. Os autores devem divulgar qualquer relação financeira no ato da submissão, e quaisquer divulgações devem ser atualizadas pelos autores antes da publicação. Informações que podem ser percebidas como potencial (is) separar conflito (s) de interesse deve ser declaradas. Esta informação inclui, mas não se limita a, subvenções ou financiamento, emprego, afiliações, patentes, invenções, honorários, consultorias, royalties, ou testemunho de especialista.

13. Outras informações: provas PDF serão enviadas aos autores correspondentes para resposta sobre eventuais dúvidas e/ou aprovação **dentro de 72 horas**; exceto para unidades de medida, abreviaturas devem ser evitadas; abreviatura utilizada pela primeira vez no texto principal deve ser expressa entre parênteses e precedida pela forma extensa que vai representar.

Thieme Publishers
Acquisitions Editor
Ana Paula Canel Bluhm, MSc., PhD.
ana.bluhm@thieme.com.br

Editorial Production
Thieme Publishers - Production Coordinator
Gisele Múfalo
gisele.mufalo@thieme.com.br

Thieme Publishers - Junior Production Coordinator
Paula Di Sessa Vavlis
paula.disessa@thieme.com.br