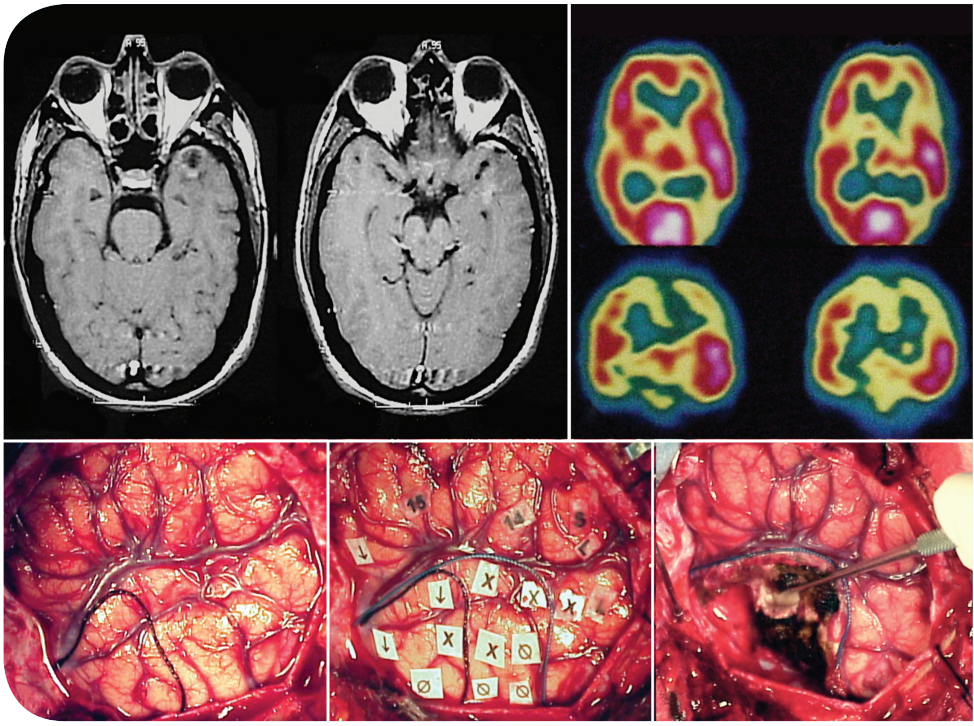
ISSN 0103-5355

Brazilian Neurosurgery

Arquivos Brasileiros de Neurocirurgia

Number 2 • Volume 43 • Pages 87–156 • June 2024



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ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

ISSN 0103-5355

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

Volume 43, Number 2/2024

Brazilian Neurosurgery
Arquivos Brasileiros de Neurocirurgia

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(Garcia LAO, Giannetti AV. Assessment of the Benefit of Intraoperative Cortical Stimulation in Patients with Lesions within Eloquent Brain Regions. Arq Bras Neurocir 2024;43(2):93–101)

 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.

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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

Endovascular Treatment of Basilar Artery Stenosis

Tratamento endovascular de estenose de artéria basilar

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Arq Bras Neurocir 2024;43(2):e87–e92.

Abstract

Objective To analyze epidemiological characteristics and therapeutic evolution of patients with basilar artery (BA) stenosis who underwent endovascular therapy in a reference service.

Methods Observational retrospective study of a case report of individuals with BA stenosis who underwent endovascular therapy in an endovascular neurosurgery reference service, between November 2005 and May 2018.

Results The prevalence was higher among male patients, with 60% of the cases. As for age, it ranged from 18 to 81 years old, with a mean of 60.2 years old. In terms of comorbidities, systemic arterial hypertension was found in 93% of the patients, and dyslipidemia in 86.7%. The initial symptoms were previous history of ischemic cerebrovascular accident (CVA) in 43.3% of the cases and dizziness in 46.7%. The degree of stenosis ranged from 90 to a 98% of obstruction, with a mean of 92.8%. Neurological deficit was observed in 23.3% of the cases postoperatively, and the postoperative death rate was 10% (3/30). There were no intraoperative adverse events.

Conclusion The applicability of endovascular stenting therapy in high-grade BA stenosis proved to be a safe and effective technique with lower morbimortality rates and faster recovery.

Keywords
- basilar artery
- stenosis
- dizziness
- endovascular
- case report

Resumo

Objetivo Analisar as características epidemiológicas e a evolução terapêutica de pacientes com estenose de artéria basilar (AB) submetidos a terapia endovascular em serviço de referência.

Metodologia Estudo retrospectivo observacional de trinta pacientes com estenose de AB submetidos à terapia endovascular em serviço de referência em neurocirurgia endovascular de Blumenau, SC, Brasil, no período de novembro de 2005 a maio de 2018.

Resultados O sexo masculino foi o mais prevalente, com 60% dos casos. A idade variou de 18 a 81 anos, sendo a média de 60,2 anos. Quanto à presença de comorbidades, observou-se que a hipertensão arterial sistêmica esteve presente em

Palavras-chave
- artéria basilar
- estenose
- tontura
- endovascular
- angioplastia

received
March 20, 2023
accepted
June 21, 2023
article published online
October 31, 2023

DOI https://doi.org/10.1055/s-0043-1776271.
ISSN 0103-5355.

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

93% dos casos e a dislipidemia em 86,7% dos casos. As sintomatologias iniciais observadas foram história prévia de AVE isquêmico em 43,3% dos casos e tontura em 46,7%. O grau de estenose variou de 90 a 98% de obstrução, com a média de 92,8%. Os stents de balão expansíveis foram os mais utilizados, sendo o da marca Pro-Kinect Energy o mais utilizado (60%). Por fim, em 23,3% dos casos, observou-se déficit neurológico no pós-operatório, e a taxa de óbito foi de 10% (3/30) no pós-operatório. Não ocorreu nenhum evento adverso intraoperatório.

Conclusão A aplicabilidade da terapia endovascular com utilização de stent em quadros de alto grau de estenose de AB mostrou-se técnica segura e eficaz com menores taxas de morbimortalidade e recuperação mais rápida.

Introduction

Cerebrovascular diseases, especially ischemic cerebrovascular accident (CVA), are important causes of death worldwide. A total of 20% of ischemic cerebral events involve the posterior circulation.[1,2] The basilar artery (BA), originating at the junction point of the vertebral arteries, usually at the level of the bulbopontine sulcus, supplies arterial blood to most of the brainstem, the thalamus, and the occipital lobes, and to part of the cerebellum. Thus, it is the most important artery of the posterior cerebral circulation.[2]

The ischemic event caused by BA stenosis and acute occlusion has devastating effects. According to the degree of brain stem involvement, the symptoms may range from isolated cranial nerve palsy, hemiplegia, and locked-in syndrome, to coma.[3] The morbimortality rate of an acute basilar artery occlusion event is $\sim$ 80%, with a worse prognosis when compared with ischemic events of the anterior circulation.[3]

Intracranial atherosclerotic disease and cardioembolic stroke are considered the main causes of BA stenosis. Approximately 60% of the posterior circulation ischemic events are due to atherosclerosis.[4] This condition is more frequently found in males, Asians, and African Americans, mainly between the 6th and 7th decades of life.[5]

The clinical presentation of BA stenosis may vary, with transient and intermittent symptoms, which may simulate otitis interna, with dizziness and headache.[5] Despite advances allowed by mechanical thrombectomy for ischemic events, mainly in the anterior circulation, and although studies such as ENDOSTROKE showed a high rate of revascularization after endovascular thrombectomy, its efficacy and safety remain uncertain when compared with drug treatment.[6] Endovascular treatment, based on the use of stents and balloons, has shown better outcomes than microsurgery, especially in patients whose stenosis is $>$ 70% and in whom conservative treatment has failed. Angioplasty is indicated for stenosis between 50% and 69%.[7] In stenosis $<$ 50%, medical treatment is the priority, aimed at managing risk factors and achieving secondary prevention of new events.[7]

The aim of the present study is to study the recanalization of BA stenosis through endovascular therapy with stents, as well as to analyze its clinical behavior in individuals who underwent endovascular treatment in a reference endovascular neurosurgery service.

Methods

Observational and retrospective study based on data collection and analysis of electronic medical records from a group of 30 participants seen in the endovascular neurosurgery reference service. All individuals who had failed clinical treatment events (acetylsalicylic acid 200mg/day, clopidogrel 75mg/day, and statin 80mg/day) presenting new cerebrovascular events and underwent endovascular therapy with angioplasty for stenosis $\geq$ 70% of the basilar artery between November 2005 and May 2018 were included in the study.

Insufficient medical data, such as loss to follow-up within 30 days, absence of radiological reports, platelets $<$ 100,000, previous neurosurgery or severe head trauma in the last 30 days and patients with RNI $\geq$ 1,7 using warfarin were considered exclusion factors. Endovascular treatment-related medical and epidemiological variables were studied, such as age, gender, pre-existing comorbidities, symptoms on admission, preoperative imaging tests, endovascular technique, stenosis characteristics, and 30-day postoperative follow-up.

The BA stenosis site was classified according to Archer et al. into proximal (from the vertebrobasilar junction to the origin of the anterior inferior cerebellar artery), middle (from the origin of the anterior inferior cerebellar artery to the origin of the superior cerebellar artery) and distal (distal to the origin of the superior cerebellar artery).[8] Stenosis degree was measured during digital cerebral arteriography using the Allura Xper FD10 hemodynamic machine (Philips Medical Systems, Veenpluis, Netherlands).

All procedures were performed by a neurosurgeon specialized in neurointervention with $>$ 15 years of experience and $>$ 2,000 intra- and extracranial angioplasties performed. All procedures were performed through femoral artery access, reaching the subclavian, the vertebral, and the BA (in order), using a 0.0014 size microguide compatible with the type of stent and balloon used. The technique and stent used were chosen by the surgeon. Due to the short time of procedure (average of 1 hour), most of cases were performed under sedoanalgesia and local anesthesia. Few patients were operated on under general anesthesia (20%). Follow-up

imaging tests were performed according to medical criteria. The magnetic resonance imaging (MRI) exam was not used after endovascular treatment.

All patients received dual antiaggregant therapy with clopidogrel 75 mg and acetylsalicylic acid 200 mg for at least 72 hours prior to the procedure. The time factor was very relative since each case was assessed individually according to clinical treatment failure. During the procedure, all patients received a bolus of heparin 5,000 IU. After the procedure, the protocol was clopidogrel 75 mg daily for 3 months and acetylsalicylic acid 300 mg daily continuously.

The project followed current ethical standards, approved by the local ethics committee, Comitê de Ética na Pesquisa em Seres Humanos da Universidade Regional de Blumenau, under CAAE: 80423017.7.0000.5370. The Informed Consent Form (ICF) was presented and made available to the study participants. Written informed consent was obtained from all subjects before the study.

Statistical Analysis

The data were organized in descriptive tables showing, as appropriate, absolute and relative frequencies, means, standard deviations (SDs), and estimates. Analyses were tabulated using Microsoft Excel 2020 (Microsoft Corporation, Redmond, WA, USA) and analyzed using the SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

The mean age among the study subjects was 60.2 years old (18 to 81 years old), with 60% of male patients. Dizziness and prior ischemic CVA were among the most prevalent symptoms (46.7 and 43.3%, respectively). There was rarely an association with gait alteration, but it was not possible to characterize it as ataxia. The least reported symptom was headache (13.3%). Regarding comorbidities, 93.3% of the patients had systemic arterial hypertension (SAH), which is the most prevalent comorbidity among the study subjects; 86.7% had dyslipidemia, and 26.7% had diabetes mellitus (DM). Five individuals had a history of active or previous smoking (16.7%). The mean preoperative modified Rankin scale[8] (mRS) was 2.1 (1 to 3) (►**Table 1**).

The mean degree of stenosis was 92.8%, as shown in ►**Fig. 1**. The middle segment of the BA was the most affected site (56.7%), followed by the proximal (30%) and distal segments (13.3%). Nine individuals had an ulcerated plaque (30%). Regarding the use of stents, as they have lower restenosis rates, balloon-expandable stents were most used, mainly the Pro Kinetic Energy (Biotronik, Bülach, Switzerland) (60%). The restenosis rate was low and not relevant to the study. All subjects underwent diagnostic digital cerebral arteriography during angioplasty, preceded by angioresonance or cerebral angio-computed tomography (CT) (33.3 and 26.7%, respectively) (►**Table 2**).

There were no intraoperative adverse events. Postoperative events included limb monoparesis (23.3%), dysphasia, and hemiplegia (13.3% each). Three individuals died within weeks of the procedure (10%). One of them had progressive lowering of the level of consciousness due to the severity of his previous condition. One had bleeding in the fourth ventricle and the other had a rupture of a pseudoaneurysm in the right deep femoral artery. The mean mRS after 30 days was 1.25 (1 to 2) (►**Table 3**).

Table 1 Clinical and epidemiological characteristics ($n = 30$)

Mean age (IQR) – years old	60.2 (18–81)
Gender, female – total *nr.* / Nr. (%)	9/30 (30)
Symptoms – total nr. / Nr. (%)	
iCVA	13/30 (43.3)
TIA	7/30 (23.3)
Dizziness	14/30 (46.7)
Headache	4/30 (13.3)
Pre-existing comorbidities – total nr. / nr. (%)	
Diabetes mellitus	8/30 (26.7)
Systemic arterial hypertension	28/30 (93.3)
Smoking	5/30 (16.7)
Dyslipidemia	26/30 (86.7)
Heart disease	6/30 (20)
Preoperative mRS	**2.1 (1–3)**

Abbreviations: iCVA, ischemic cerebrovascular accident; IQR, interquartile range; mRS, modified Rankin Scale; TIA, transient ischemic attack.

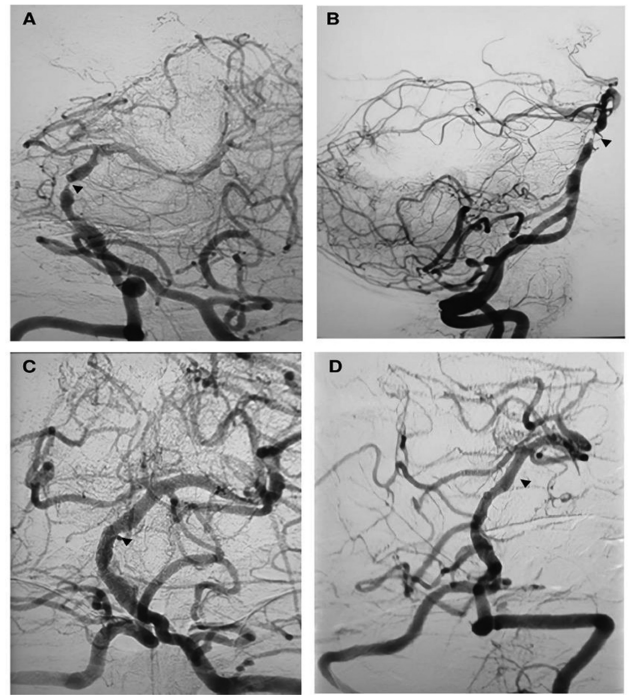

Fig. 1 An 81-year-old male patient with acute stroke due to critical basilar artery stenosis. (A-B), left vertebral artery angiogram shows an occlusion (arrow) at the distal segment of the basilar artery. C-D, left vertebral artery angiogram obtained after intracranial angioplasty and stent placement (arrow) shows complete recanalization of the basilar artery with great distal perfusion.

Table 2 Stenosis characteristics, stents, and preoperative tests ($n = 30$)

Mean stenosis degree % (IQR)	92.8 (90–98)
Stenosis characteristics – nr. / total nr. (%)	
Dissection	1/30 (3.3)
Site	
Proximal segment	9/30 (30)
Middle segment	17/30 (56.7)
Distal segment	4/30 (13.3)
Ulcerated plaque	9/30 (30)
Stent type – nr. / total nr. (%) *Balloon-expandable Stent*	
Coroflex Blue	3/30 (10)
Micro Drive	3/30 (10)
Pro Kinetic Energy	18/30 (60)
Liberte	2/30 (6.7)
Drive	2/30 (6.7)
Self-expanding Balloon	
Enterprise	1/30 (3.3)
Resolute Integrity	1/30 (3.3)
Neuroimaging – nr. / total nr. (%)	
Brain MRI	7/30 (23.3)
Brain CT	6/30 (20)
Digital cerebral arteriography	30/30 (100)
Cerebral Angio-CT	8/30 (26.7)
Carotid Doppler test	6/30 (20)
Cerebral Angio-MRI	**10/30 (33.3)**

Abbreviations: CT, computed tomography; IQR, interquartile range; MRI, magnetic resonance imaging.

Table 3 Intraoperative events, outcome, and complications ($n = 30$)

Mean mRS after 30 days (IQR)*	1.25 (1–2)
Intraoperative adverse events nr. / total nr. (%) Postoperative adverse events nr. / total nr. (%)	0/30 (0)
Dysphagia	4/30 (13.3)
Hemiplegia	4/30 (13.3)
Monoparesis	7/30 (23.3)
Puncture site bleeding	2/30 (6.7)
DeathΔ	**3/30 (10)**

Abbreviation: IQR, Interquartile range;
ΔDeath, in weeks following the procedure.

Discussion

In the present study, basilar stenosis affects patients between the 6th and 7th decades of life (►**Fig. 2**) who also have DM as one of the most prevalent comorbidities, which is consistent with the literature.

In the present study, the prevalence of hypertensive (30% higher) and dyslipidemic patients (50% higher) was higher than in the study of the American and Chinese populations.[9,10] The study found dizziness and iCVA as the main initial symptoms, corroborating the basic literature; therefore, these are characterized as classic clinical presentations of basilar artery stenosis. On the other hand, the study found a lesser significance of headache, which was 29% less prevalent than in the literature. This difference is attributed to the fact that the population of the present study has headache as a secondary symptom, that is, it is present concomitantly with other symptoms.[11]

In an observational study with 40 patients, Ciríaco et al observed that 28 patients (70%) had stenosis grades $\geq$ 90%; these patients underwent endovascular therapy.[5] In the present study, all patients who underwent angioplasty had stenosis $>$ 90%.

Samaniego et al. point out that, in basilar stenosis, the middle segment was the most affected site, with 54.9% of cases.[12] The authors observed a greater association between smoking and middle segment stenosis, but they do not associate its site with worse on admission or follow-up mRS. The higher prevalence of one site was also reported in the study by Shu et al., with 41.2% of 51 patients presenting with middle segment stenosis.[9] Among the 187 patients evaluated in the study by Sun et al., the authors observed greater involvement of the proximal segment (55.6%), with 28.9% for the middle segment.[13] The present study showed greater middle segment involvement, in 56.7% of cases, with 4 of 5 smoking patients having middle segment stenosis, but not associated with worse outcomes.

In a long-term follow-up of 30 individuals with $\geq$ 70% stenosis of vertebral and BAs who underwent endovascular therapy, Djurdjevic et al. reported 7 deaths, 3 of which related to vascular events, 1 intraoperative death with basilar artery rupture, and the other 2 related to gangrene and intraparenchymal hemorrhage, 5 and 7 years after the procedure, respectively. In his long-term follow-up, Djurdjevic highlights stable treatment outcomes, indicating that endovascular treatment can be beneficial to appropriately selected patients with intracranial stenosis.[14]

In a study on revascularization techniques in BA occlusion, Siebert et al. noted that while the outcome remained unfavorable, the endovascular technique proved effective and relatively safe. The authors reported a mortality rate of 36.8%.[7] In a multicenter study, Kang et al. describe that endovascular therapy is safe and effective in recanalizing acute basilar artery occlusion.[10] In an analysis of 27 individuals who also underwent endovascular technique, Antunes Dias et al. found a mortality rate of 37% of the cases.[15] In the present study, a low mortality rate of 10% was observed, with 3 deaths per 30 treated patients. According to the mRS, there was an improvement in quality of life in all cases. The patients were monitored on an outpatient basis by the same neurosurgeon and underwent imaging exams after 1 year for control.

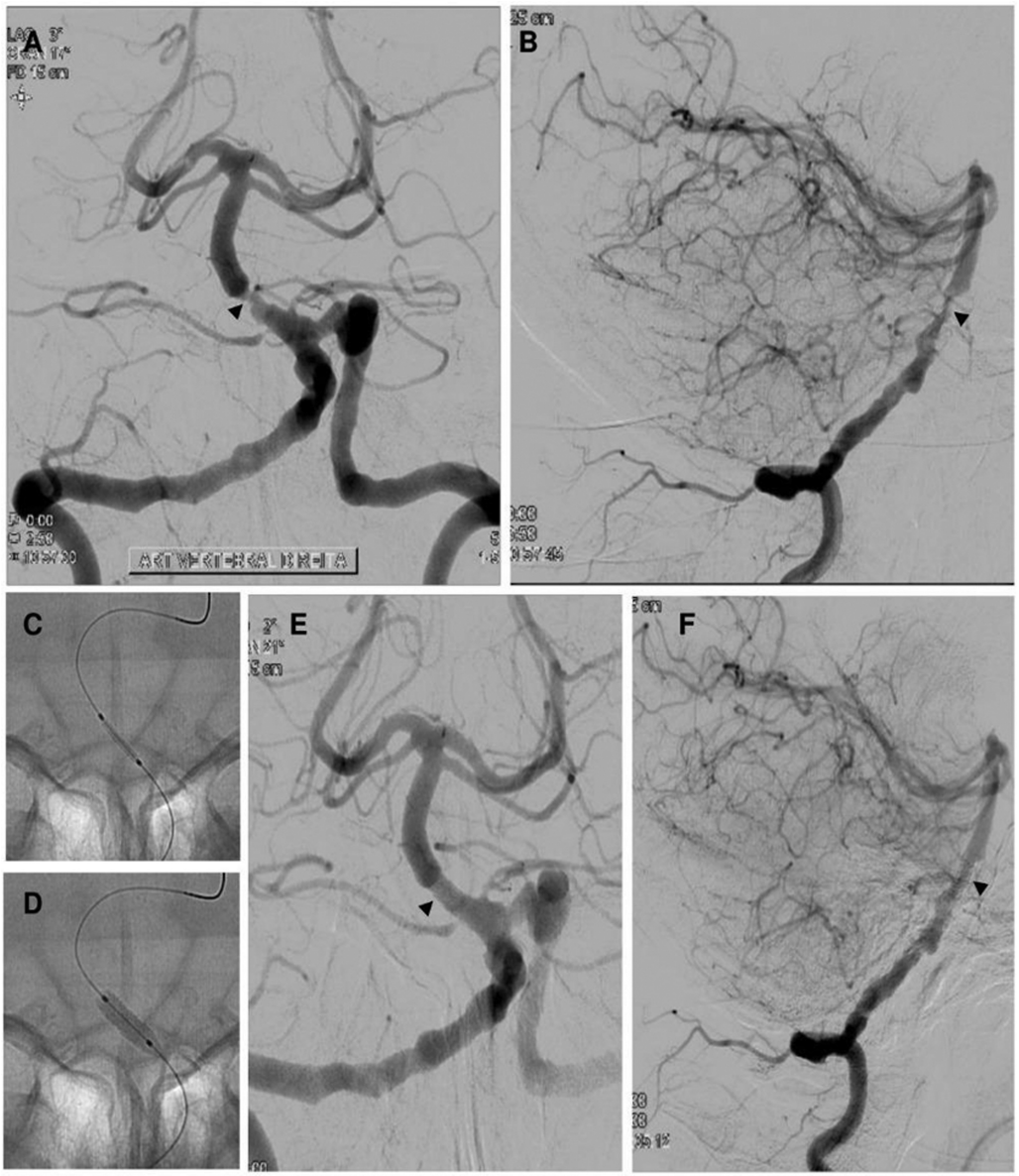

Fig. 2 A 58-year-old male patient with acute due to basilar artery stenosis. (A-B), left vertebral artery angiogram shows a stenosis (arrow) at the distal segment of the basilar artery. (C-D), show balloon expandable stent angioplasty. (E-F), left verterbal artery angiogram obtained after intracranial angioplasty and stent placement (arrow) shows complete recanalization of the basilar artery with great distal perfusion.

According to the study by Kang et al., in the case of the 212 individuals they analyzed, younger patients, lower National Institutes of Health Stroke Scale (NIHSS) on admission, absence of DM as a comorbidity and absence of parenchymal hematoma were significant factors for a more favorable outcome after endovascular procedure.[16] In the study by Antunes Dias, the authors pointed out that being female, having a lower NIHSS on admission, mild to moderate symptoms, and a lower posterior collateral circulation score were considered predictors of a better outcome.[15] The present study found a higher prevalence of male subjects (70%) with a mean age of 60.1 years and a mean mRS on admission of 2.1, with no DM as an aggravating factor. One of the 3 patients who died was a 46-year-old female with subarachnoid hemorrhage (SAH); one was a 64-year-old male, smoker, with SAH; and the third was a 54-year-old male with SAH, smoker, dyslipidemic.

Despite dealing with a considerable database on endovascular therapy for basilar stenosis, the present study faced a few limitations, including its retrospective nature. Multicenter prospective studies and randomized clinical trial studies with control groups are needed to better determine clinical and radiological characteristics, as well as to confirm the safety and efficacy of intracranial angioplasty of BA stenosis compared with other treatments. Sample calculation was not done and should be considered as a limitation of the present study.

Conclusion

The outcomes of the present study, such as the low postoperative morbimortality rate, support the use of the endovascular technique, especially for the BA.

Ethics Approval

Ethical approval for the present study was obtained from the Comitê de Ética na Pesquisa em Seres Humanos of FURB, under CAAE: 80423017.7.0000.5370.

Disclosures

No potential conflict of interests relevant to this article was reported.

Sources of Funding

Own financing, there wasn't financial supporter. The present study was free of costs.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgments

We thank Hospital Santa Isabel, Blumenau, Santa Catarina, Brazil, for providing structural support for the procedures.

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Assessment of the Benefit of Intraoperative Cortical Stimulation in Patients with Lesions within Eloquent Brain Regions

Avaliação do benefício da estimulação cortical intraoperatória em pacientes com lesões em áreas cerebrais eloquentes

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Arq Bras Neurocir 2024;43(2):e93–e101.

Abstract

Objective The present study sought to evaluate the benefits of intraoperative cortical stimulation (CS) for reducing morbidity in neurosurgery.

Method A total of 56 patients were submitted to neurosurgical procedure with the aid of CS. Initially, surgical exposure and planned resection were based on anatomy and imaging exams, which were followed by CS. According to the findings, the patients were divided into two groups. In group 1 the previous surgical strategy had to be altered, while in group 2 the surgical planning did not suffer any interference. Patients were also divided into subgroups according to the underlying disease: gliomas or other etiologies. Transient and definitive deficits occurrence were compared between groups 1 and 2 and subgroups of etiologies. The real benefit of CS technique was calculated by a specific formula.

Results There were 20 patients (37.5%) whose surgical strategy was changed based on CS findings. Furthermore, 65% of group 1 patients had transient deficit, in comparison to 30.5% of patients in group 2 ($p = 0.013$). As for the definitive deficit, it occurred in 15.0% of group 1 patients versus 8.3% of patients in group 2 ($p = 0.643$). Definitive deficits with no statistical difference ($p = 0.074$) were found in 17.2% of patients with gliomas, while none were found in the other etiologies subgroup. The rate of real benefit of intraoperative CS was 30.4%. Considering the subgroups of gliomas and other etiologies, the benefit rates were 25.7% and 38.1%, respectively.

Conclusions The surgical decision was influenced by CS in 35.7% of the cases and prevented definitive deficit in 30% of patients.

Keywords
- intraoperative neurophysiological monitoring
- gliomas
- brain mapping
- neuronal plasticity
- surgery
- direct electrical stimulation

received
March 9, 2023
accepted
June 21, 2023
article published online
October 31, 2023

DOI https://doi.org/10.1055/s-0043-1776280.
ISSN 0103-5355.

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

Resumo

Objetivos O presente estudo procurou avaliar os benefícios da estimulação cortical (EC) intraoperatória na redução da morbidade em neurocirurgias.

Métodos Um total de 56 pacientes foram submetidos ao procedimento neurocirúrgico com ajuda da EC. Inicialmente, a exposição cirúrgica e o panejamento da ressecção eram baseados nos achados de anatomia e imagem, que eram seguidos pela EC. De acordo com os achados neurofisiológicos, os pacientes foram divididos em dois grupos. No grupo 1, a estratégia cirúrgica teve que ser modificada, enquanto no grupo 2, o planejamento cirúrgico não foi alterado. Os pacientes foram ainda divididos em dois subgrupos de acordo com a doença subjacente: gliomas ou outras etiologias. A ocorrência de déficits transitórios e definitivos foram comparadas entre os grupos 1 e 2 e entre os subgrupos de etiologias. O benefício real da técnica de estimulação cortical foi calculado por uma fórmula específica.

Resultados A estratégia cirúrgica foi alterada em 20 (37,5%) pacientes após a estimulação cortical. Além disso, 65% dos pacientes do grupo 1 tiveram déficits transitórios, em comparação com 30,5% dos pacientes do grupo 2 ($p = 0{,}013$). Quanto ao déficit definitivo, este ocorreu em 15% dos casos do grupo 1 contra 8,3% dos pacientes do grupo 2 ($p = 0{,}643$). Déficit definitivo sem diferença significativa ($p = 0{,}074$) foi observado em 17,2% dos pacientes com gliomas, enquanto nenhum foi encontrado no subgrupo de outras etiologias. A taxa de benefício real da EC intraoperatória foi de 30,4%. Considerando os subgrupos de gliomas e outras etiologias as taxas de benefício foram 25,7% e 38,1%, respectivamente.

Conclusões A EC influenciou a decisão cirúrgica em 35,7% dos casos. Embora 90% dos pacientes não tenham cursado com déficits a longo prazo, a estimulação cortical preveniu tais déficits em cerca de um terço deles.

Palavras Chaves

- monitorização neurofisiológica intraoperatória
- gliomas
- mapeamento cerebral
- plasticidade neuronal
- cirurgia
- estimulação elétrica direta

Introduction

Studies have shown that quality of life and mean survival correlate with the extent of lesion resection, especially in gliomas.[1–4] However, the aim is to dry out the lesion as much as possible, taking care to preserve cortical functions. Identification of eloquent areas in the cerebral cortex is important to minimize the morbidity associated with resection of abnormal brain tissue. Techniques used for this localization have been adapted over the years for epilepsy, tumors, and vascular surgeries involving the eloquent cortex and subcortical white matter.[1,5,6]

The treatment for these lesions involves proper preoperative planning, imaging exams, and functional identification during surgery. Techniques for identifying eloquent areas are varied, with an emphasis on direct intraoperative cortical stimulation. The use of cortical electrical stimulation in neurosurgery began in 1930 with Forster, then Penfield described the motor and sensory homunculus in 1937.[5] Then, it spread across America and Europe.[7,8] The principle of this technique is based on depolarization of local neurons, inducing excitation or inhibition.[6] This technique is efficacious, cost-effective, and easy to apply, being recommended for tumors, cavernomas, arteriovenous malformations, and epilepsy. Furthermore, it has changed the concept of "inoperable lesion" by reducing the sequelae rate described in the literature from 6.5 to 17%.[9]

Cortical and subcortical electrical stimulation allow resection to the point where functional response occurs.[6,10] This technique can be used to identify descending subcortical motor fibers when resection extends below the cortical surface, such as during resection in additional motor areas or insular regions. It is believed that intraoperative cortical stimulation has contributed to a wider and safer removal of lesions, improving patient survival, and preserving the functional area. Nevertheless, there are no randomized and controlled studies that determine the impact of this technique concerning surgical safety and survival of patients. Most of the published articles present case series without comparative groups. On the other hand, metanalyses reinforce assumption that it is difficult, if not impossible for ethical reasons, to recruit a control group of patients with infiltrative lesions in eloquent areas of the brain to undergo resection surgery without intraoperative cortical stimulation.[1,6,11–15]

The present study aimed to evaluate the benefit of this technique in surgical resection of brain lesions in eloquent areas of the brain.

Method

From 2002 to 2016, 63 patients were operated at the Hospital das Clínicas of the Federal University of Minas Gerais (Belo Horizonte, Brazil), for presenting brain lesions near or involving

Table 1 Degree of resection and histological findings of 56 patients

Degree of resection	N	%
Total	34	60.7%
Partial	22	39.2%
Etiology		
Low-grade gliomas	25	44.6%
High-grade gliomas	10	17.8%
Metastasis	5	8.9%
Cortical dysplasia	3	5.3%
Radionecrosis	3	5.3%
Lymphomas	2	3.5%
Neurotoxoplasmosis	2	3.5%
Meningiomas	1	1.8%
Ependymoma	1	1.8%
Dysembryoplastic tumor	1	1.8%
Abscess	1	1.8%
Cavernoma	1	1.8%
Vascular malformation	1	1.8%
Total	56	100%

one or more brain eloquent areas, such as motor, sensory, or language. All of them were submitted to intraoperative cortical stimulation. Of this total, 7 patients were excluded due to having a follow-up period lower than 3 months or because of incomplete medical record data. Thus, 56 patients were selected and retrospectively evaluated. There were 31 men (55.3%) and 25 women (44.6%), with a mean age of 39 years, ranging from 9 to 79 years. After chart review, patients were called for a new consultation, and their data were checked and updated. Furthermore, a new neurological examination was done, and the imaging exams were analyzed. Patients were followed for a mean of 228.4 months (3 to 120 months). ►**Table 1** presents the degree of resection and lesion etiologies.

All patients were operated by the same surgeon, using the same technique. If only motor stimulation was necessary, the patient underwent general anesthesia. In cases where language and/or sensory stimulation were necessary, sedation alone was used at the beginning of the series to obtain satisfactory arousal during neuropsychological tests. As anesthetic technique improved, the "asleep-awake-asleep" strategy was applied, in which the patient undergoes general anesthesia, the airway is protected with a laryngeal mask or orotracheal tube, and patient is awakened during the tests after airway clearance. After cortical stimulation, patients were submitted again to general anesthesia with the laryngeal mask and the surgical procedure was completed as usual. Craniotomy was used to expose the entire lesion (►**Fig. 1C**) as well as the adjacent cortex. For that purpose, preoperative images, craniometric references, stereotactic system (for small lesions), neuronavigation, intraoperative ultrasound, and electrocorticography (for refractory epilepsy cases) were used (►**Table 2**). Once the lesion was delimited (►**Fig. 1D**, **2B**, **3B**, **4B**), the area to be resected or incised was marked with a silk thread. These anatomical parameters alone were used, and when the functional register was not possible, and a photographic record was made. Then, the cortical stimulator equipment (biphasic current, 60 Hz, 1 millisecond, starting from 2A and increasing based on the response) was used to perform stimulation over the adjacent cortex and the area to be operated. Once the eloquent area was identified, the medical professionals decided if the previous planning would be modified or not. The alternatives were reduction (►**Fig. 2C**) or increase in the area to be removed (►**Fig. 4C**), or incision on another topography (►**Fig. 3C**). A new photographic record was made at this point, as well as at the end of the main surgical procedure (►**Fig. 1F**, **2D**, **3D**, **4D**).

Considering cortical stimulation findings, patients were divided into two groups, with (group 1) and without (group 2) changes in surgical strategy due to cortical stimulation . The changes in surgical tactics for group 1 were increasing or reducing the area to be resected, or alteration in corticectomy. The patients were further divided into two subgroups according to the underlying disease: gliomas and other etiologies. They were also compared for transient and permanent deficit, as well as for change in surgical strategy. Furthermore, patients were periodically monitored and reevaluated; the rates of transient and definitive neurological deficits were recorded and compared statistically. Transient deficits were defined as those that appeared or suffered aggravation during postoperative period but regressed up to the date of the last clinical evaluation. Permanent deficits, regardless of magnitude, were those neurological deficiencies that did not exist during preoperative period and remained up to the last clinical evaluation.

The real benefit of the cortical stimulation technique was calculated by dividing the number of patients who needed a change in strategy after mapping and who did not present late deficit by the total of patients multiplied by 100. This assessment was also performed for the etiology subgroups.

To estimate homogeneity among the groups, regarding the variables of this study, and to compare the deficits between the groups, the Fisher exact and the Chi-square tests were used.[16] The software employed in the analysis was R (R Foundation for Statistical Computing, Vienna, Austria) version 3.3.2. The statistical significance level established was 5%. A *p*-value lower than 0.05 generates evidence for rejection of the null hypothesis of the test.

The present study was approved by the university's ethics and research committee (CAAE - 53468716.5.0000.5149). The free and informed consent form was signed by all patients, ensuring the secrecy and confidentiality of collected data. When a patient was considered unable to sign the consent form, this function was delegated to a caregiver or family member.

Results

Regarding the surgical technique and stimulation variables (►**Table 2**), it is important to note that most of the individuals

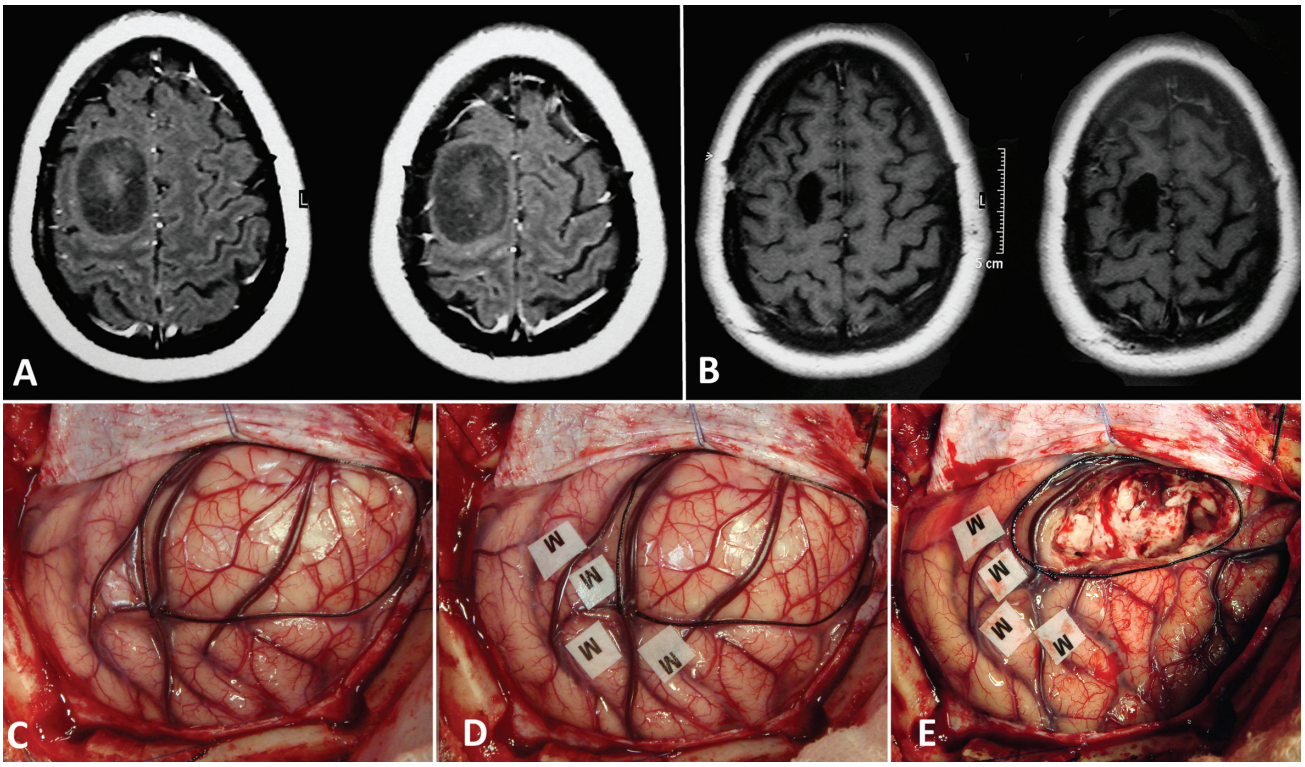

Fig. 1 (A) Preoperative, contrast-enhanced T1-weighted MRI: Hypointense, fairly enhancing, slightly insufflated image located in the right frontal region whose posterior border is close to or encompassing the motor area. (B) Postoperative, contrast-enhanced MRI showing complete lesion resection. (C) Intraoperative photo: Wide craniotomy with exposure of the cortex infiltrated by the disease and a silk thread demarcating the planned resection area. (D) Intraoperative photo after mapping: motor cortex (M) is outside the planned resection area. (E) Intraoperative photo: final appearance after tumor resection, demonstrating that initially planned surgical strategy was performed without the influence of cortical stimulation.

Table 2 Absolute and relative descriptive frequency of variables

Variables		N	%
Anesthesia	General	35	62.5%
	Awake	21	37.5%
Identification method	MRI	51	91.7%
	Ultrasonography	17	30.3%
	Stereotactic	8	14.2%
	Electrocorticography	7	12.5%
	CT scan	5	8.9%
	Neuronavigation	2	3.5%
Stimulation	Motor	53	94.6%
	Language	13	23.2%
	Sensitive	9	16.1%

Abbreviations: CT, computerized tomography; MRI, Magnetic resonance image.

(62.5%) underwent general anesthesia. More than one localization method was used in most patients, and magnetic resonance imaging was used in 91% of the cases. Motor stimulation was the most frequent modality (94.6%).

Among the patients who presented a surgical strategy change, this alteration occurred in three ways: resection was smaller or larger than planned, or the corticectomy site was modified. These changes occurred in 20 of the 56 cases, making up 35.7% of surgical interventions. Among the 20 patients who had the surgical tactics altered due to intraoperative cortical stimulation, 16 (80.0%) obtained a smaller resection than expected (►**Table 3**).

There was a significant difference in transient deficit ($p = 0.013$) between the groups: 65.0% of group 1 patients had transient deficit, compared with 30.5% of those in group 2. Regarding definitive deficit, it is possible to say, with no statistical difference ($p = 0.643$), that it occurred in 15.0% of group 1 patients versus 8.3% of group 2 patients (►**Table 4**).

The subgroups were divided by underlying disease etiologies. The group of patients with gliomas had 83.4% of transient deficits ($p = 0.005$) and all late deficits (►**Table 5**). Furthermore, when the surgical strategy changed, the transitory deficits rate was 83.3% ($p = 0.024$) for this subcategory (►**Table 6**).

Permanent deficits, with no statistical difference ($p = 0.074$), were observed in 17.2% of the patients with gliomas and in none of those in the other etiologies subgroup (►**Table 5**).

The real benefit rate of intraoperative cortical stimulation was obtained by dividing the number of patients with technique changes and without long-term deficit[17] by the total of patients (n = 56), and the result was multiplied by 100, thus obtaining a value of 30.4%. In the gliomas subgroup, this result was of 25.7%, and in the other etiologies subgroup it was of 38.1%.

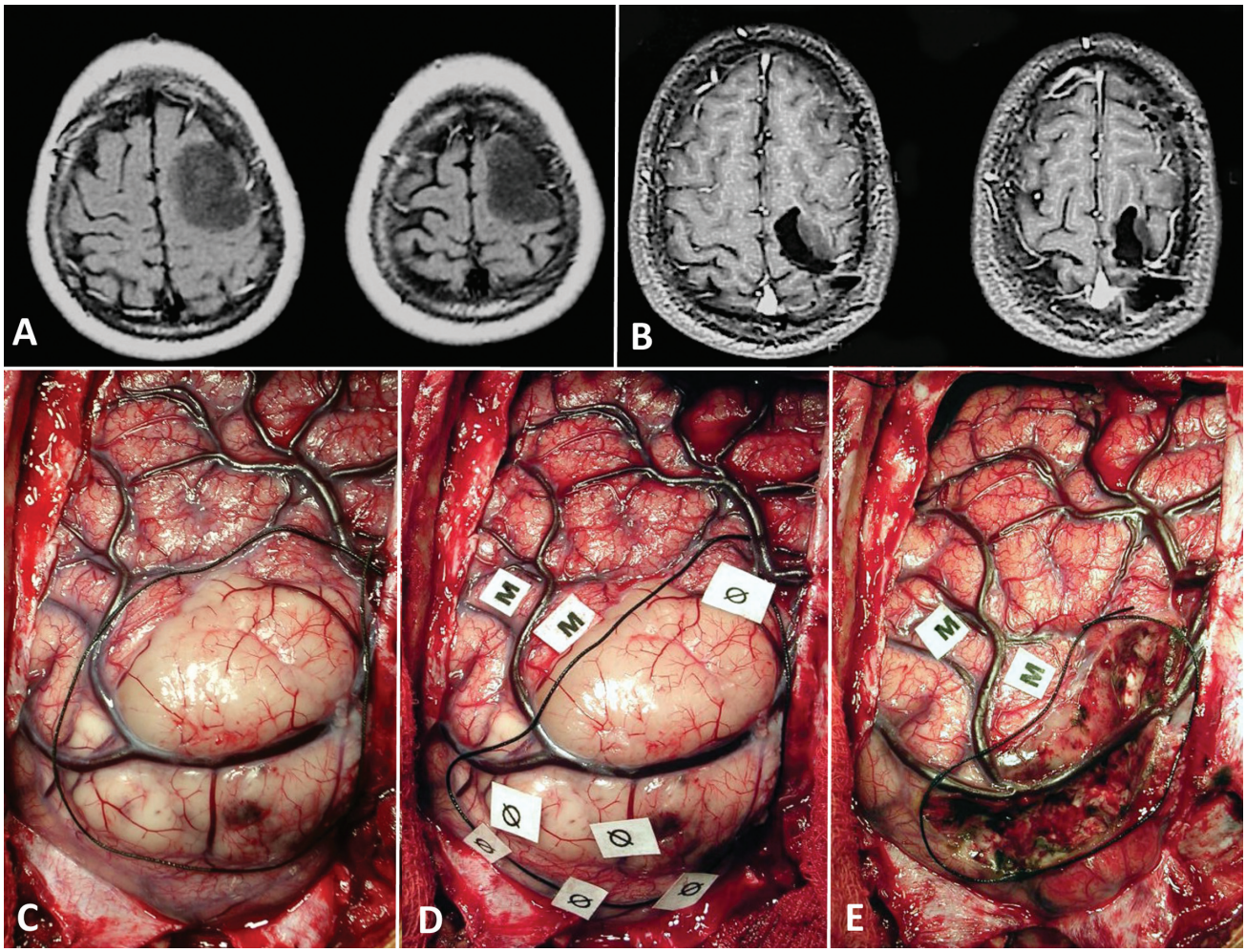

Fig. 2 (**A**) Preoperative, contrast-enhanced T1-weighted MRI: Hypointense, no-enhancing, slightly insufflated image located in the left frontal region whose posterior border is close to or encompassing the motor area. (**B**) Postoperative, contrast-enhanced MRI showing incomplete lesion resection. The tumor residue site corresponds to the motor strip (hand). (**C**) Intraoperative photo prior cortical stimulation: a silk thread demarcates the planned resection area based on anatomical and imaging data. (**D**) Intraoperative photo after mapping: motor response (M) was obtained at anterior and lateral border of the lesion. The silk thread had to be moved medially. Ø represents areas of no response. (**E**) Intraoperative photo after lesion resection. It is observed that the final resection was smaller than the initially planned one. The patient had no definitive deficit.

In regards to the relation between development of neurological deficits and anesthetic strategy, there was no significant difference ($p > 0.050$) in any of the variables (►**Table 6**).

Discussion

The present study sought to verify the effectiveness of direct cortical stimulation in postoperative outcomes, mainly regarding the presence of transient and permanent deficit stratifying patients among comparable groups regarding the alteration or not of the previously outlined surgical strategy (as result of the stimulation). The results were then analyzed considering two diseases subgroups: gliomas and other etiologies.

Aiming to compare results between two groups, in which all patients were submitted to direct cortical stimulation, a control group (group 2) was simulated, with patients whose surgical strategy was not altered as a function of the experimented technique. This control group was then compared with group 1, in which stimulation altered the surgical strategy.

The comparison performed in the present efficacy evaluation study is unprecedented, with most of the available literature constituting case series.[5,10–12] Scientific literature, in general, does not provide data for comparative calculations. Most published studies are case series without control groups. Furthermore, assembling a patient control group and submitting them to surgery without intraoperative cortical stimulation goes against medical ethics, since the benefit of the technique is considered relevant despite the absence of class 1 studies.

Mapping by cortex stimulation procedures can be performed under general anesthesia or while the patient is awake. In this study, motor stimulation was performed in 94.6% of the patients and in association with stimulation of the language area in 17.8% of them.

The motor stimulus evaluation can be performed under general anesthesia and in awake patients. The adopted anesthetic strategy did not affect surgical planning changes or the resection degree in the present study. Therefore, when the

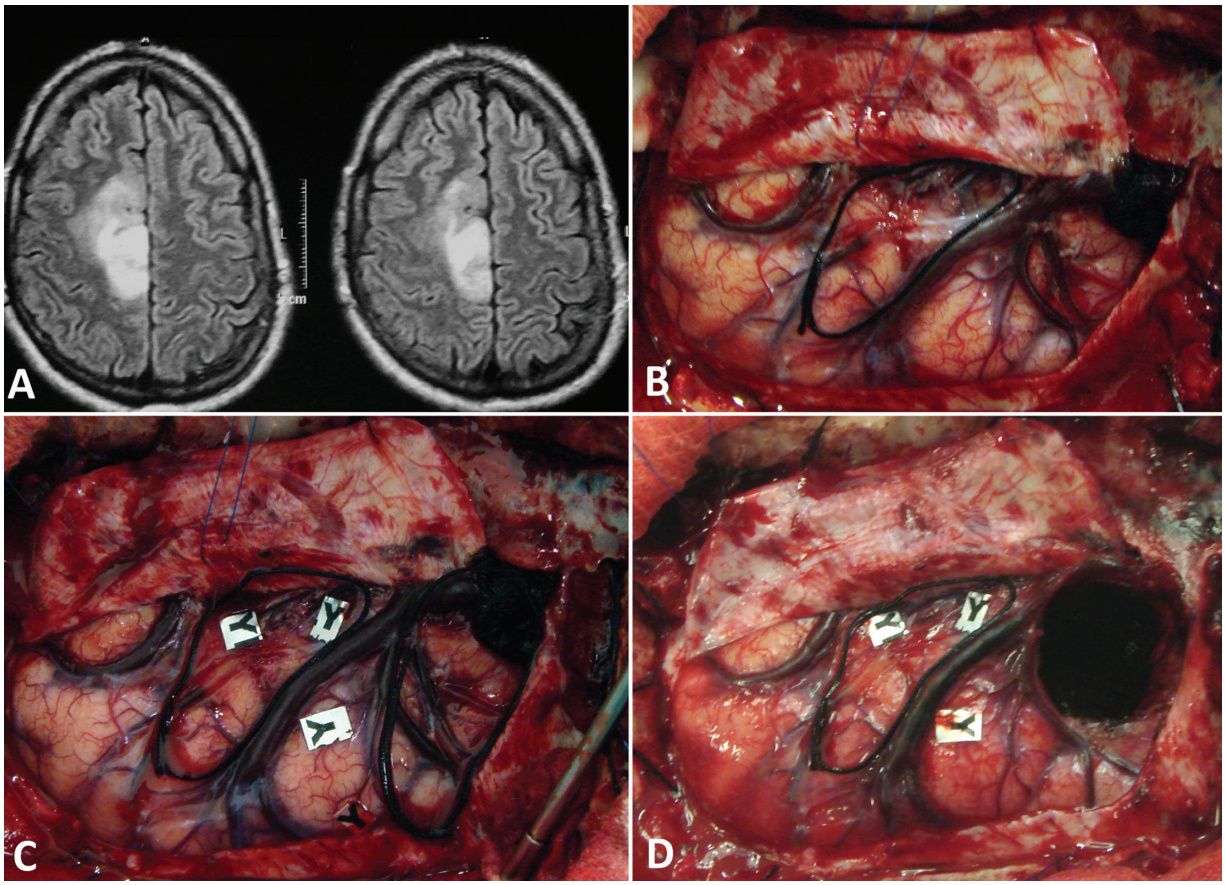

Fig. 3 (**A**) Preoperative Flair-sequenced MRI revealing an irregular, hyperintense right frontoparietal lesion. (**B**) Intraoperative photo: Exposure and planning of the resection before mapping. (**C**) Intraoperative photo: cortical mapping with functional areas detected inside the surgical planning site. (Y; motor stimulus areas). (**D**) Intraoperative photo: site of the corticectomy and lesion approach was moved anteriorly due to intraoperative cortical stimulation.

motor area is being evaluated alone, the plan with general anesthesia and airway protection should be prioritized, since it is safer and has a similar efficacy. However, mapping with the patient awake is fundamental in language evaluation, being the only strategy capable of evaluating this brain function. Language stimulation was performed in 23.2% of the patients, as its deficit (evaluated during intraoperative stage) can have different nuances. Both speaking and understanding language involve complex interface mechanisms and distinct association pathways, and specific neuropsychological tests are needed to detect each language deficit. Coordination between surgeon and neuropsychologist demands technical knowledge to identify semantic, phonological, phonetic, phonemic, and visual paraphasias, as well as to adapt the nature of the test applied to the patient intraoperatively with the surgical site and the more probabilistically resection-damaged path of association.[14]

A meta-analysis published by Hamer et al. showed that, in 75 publications, the rate of patients without permanent neurological deficit of any severity after resections of low-grade gliomas in eloquent areas was of 92.9% with the use of direct cortical stimulation.[12] The present study, although not exclusively composed of patients with gliomas, obtained a similar result (89.3%). In another study involving 8,091 adult patients with supratentorial infiltrative gliomas, the use of direct cortical stimulation mapping resulted in a 3.4% incidence of definite neurological deficits , and 8.2% without its use.[15] However, these analyzes did not managed to consider the number of patients who would be successful in surgery even without the utilization of the technique.

In the group of patients with a resection area unaltered by cortical stimulation (group 2), it is speculated that stimulation had no benefit in the direction of resection. For patients whose strategy was modified by stimulation findings (group 1), but presented deficits, it can be also considered the technique did not bring benefits. Thus, it is inferred that only those who did not have long-term deficits and whose stimulation findings altered the surgical strategy benefited. Therefore, to calculate the benefit rate, we divided the number of benefited patients (those who had changed strategy and no deficit) by the total of participants multiplied by 100. By this formula, there was a 30.4% overall benefit rate of the cortical stimulation technique. When gliomas alone were analyzed, this rate is reduced to 25.7%, whereas at the other etiologies subgroup the benefit rate was 38.1%. All calculations were made using the same formula.

According to the literature, cortical stimulation allows resection of more extensive areas in 74.9% of the cases.[12] However, when the results obtained in the present study are analyzed, among the group of patients who underwent a

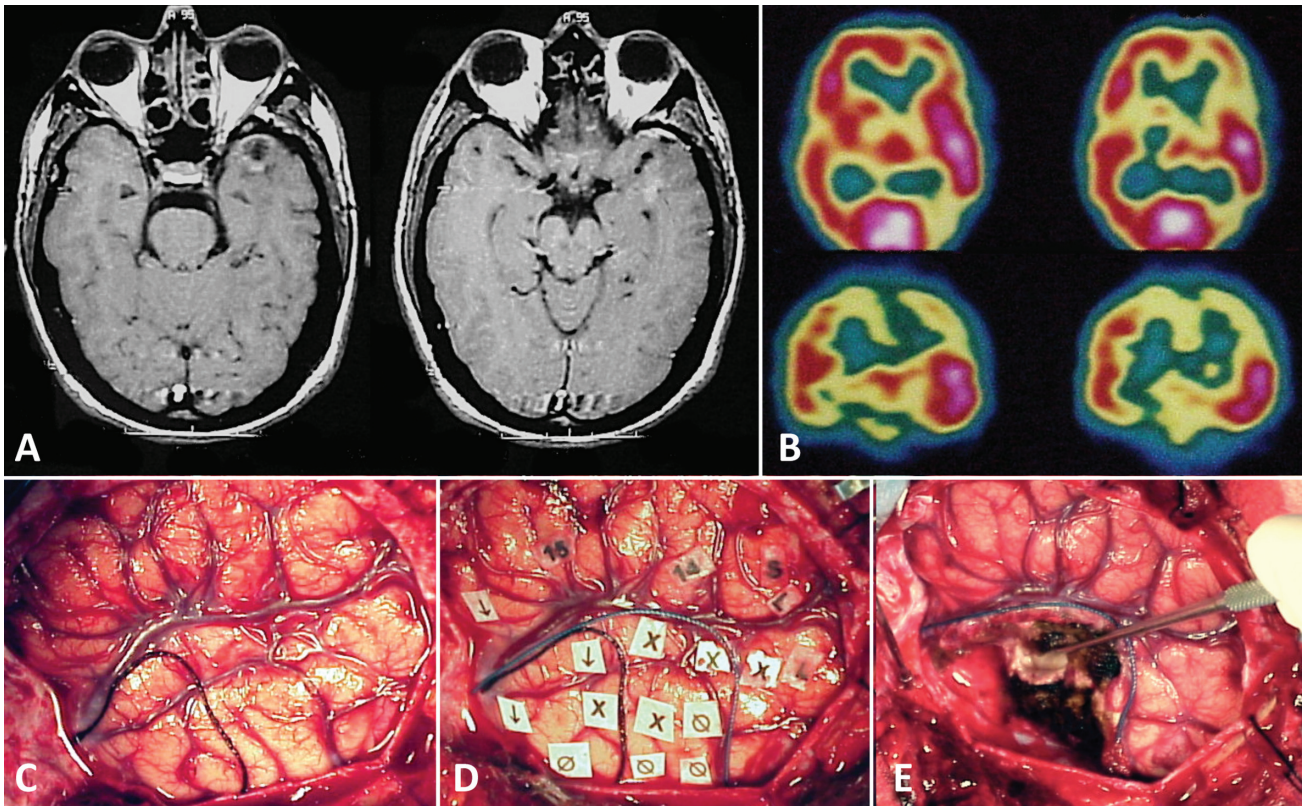

Fig. 4 (A) Preoperative, contrast-enhanced T1-weighted MRI reveals hypointense lesion in left temporal lobe pole of patient with refractory epilepsy. (**B**) Ictal aspect scan showing a bright area at the left temporal lobe. (**C**) Intraoperative photo: Exposure with delimitation of the area to be resected with silk thread. (**D**) Intraoperative photo: After electrocorticography registry was performed, discharges (X) were noted beyond the tumor site. Since the language areas (L) were more posterior, a 5 cm temporal cortex resection could be made from its pole. ↓: attenuation; Ø: normal electrographic tracing. (**E**) Intraoperative photo: final aspect, revealing an increase of the resected area compared with the initial planning. The patient became seizure free with no transitory or definitive deficit.

Table 3 Number of patients whose surgical strategy changed and type of alteration

Change	Number of cases (%)	Type of change	Number of cases (%)
No	36 (64.3%)		
Yes	20 (35.7%)	Minor resection	16 (80%)
		Major resection	1 (5%)
		Corticectomy site	3 (15%)

Table 4 Neurological deficits frequencies according to change on surgical strategy after cortical stimulation

Change (N)	Transitory deficit number (%)		Definitive deficit number (%)	
	Yes	No	Yes	No
No (36)	11 (30.6%)	25 (69.4%)	3 (8.3%)	33 (91.7%)
Yes (20)	13 (65.0%)	7 (35.0%)	3 (15.0%)	17 (85.0%)
Total (56)	24 (42.9%)	32 (57.1%)	6 (10.7%)	50 (89.3%)
p-value	0.013		0.643	

[a]Chi-square test.

Table 5 Comparison of deficits in relation to gliomas subgroups and other etiologies

Transitory deficit (N)	No (%)	Yes (%)	Value-p[a]
Gliomas (35)	15 (46.9)	20 (83.4)	0.005
Other etiologies (21)	17 (53.1)	4 (16.6)	
Definitive deficit (N)	**No (%)**	**Yes (%)**	**Value-p[a]**
Gliomas (35)	29 (58.0)	6 (100.0)	0.074
Other etiologies (21)	21 (42.0)	0 (0.0)	

[a]Fischer exact test.

surgical strategy change as a function of cortical stimulation (group 1), the results conflicted with those in the literature. These patients were subdivided into three other categories according to the nature of the alteration obtained through cortical stimulation: corticectomy change (15%), minor resection (80%), and major resection (5%). This evidence shows that cortical stimulation, when surgical procedure was changed, was not responsible for a larger than expected resection, but a smaller one. This data confronted the literature in countless works.[10–12,17]

The use of cortical stimulation usually assists in obtaining total or subtotal resections in 75% of patients using the technique, whereas this rate falls to 58% without its use.[12,18]

Table 6 Comparison of transitory and definitive deficits in relation to the studied pathology etiology, stratified by the change or not of the surgical strategy:

	Transitory deficit	Change in surgical strategy		*p*-value[a]
Gliomas		No (%)	Yes (%)	
	No	13 (56.5%)	2 (16.6%)	0.0238
	Yes	10 (43.5%)	10 (83.3%)	
Other etiologies	No	11 (84.6%)	6 (75.0%)	0.586
	Yes	2 (15.3%)	2 (25.0%)	
	Definitive deficit	**Change in surgical strategy**		***p*-value[a]**
Gliomas		No (%)	Yes (%)	
	No	20 (87.5%)	9 (75.0%)	0.391
	Yes	3 (12.5%)	3 (25.0%)	
Other etiologies	No	13 (100.0%)	8 (100.0%)	1.000
	Yes	0 (0.0%)	0 (0.0%)	

[a]Fischer exact test.

Table 7 Comparison between the anesthetic technique and the presence of transitory or definitive deficits:

VARIABLES / ANESTHESIA		Awake	General	*p*-value[a]
		N (%)	N (%)	
Transitory deficit	No	13 (61.9%)	19 (54.3%)	0.604
	Yes	8 (38.1%)	16 (45.7%)	
Definitive deficit	No	19 (90.5%)	31 (88.6%)	0.801
	Yes	2 (9.5%)	4 (11.4%)	

[a]Chi-square test.

The most accepted theory that explains such findings is that functional areas of the brain diverge topographically as a function of individual variations in physiological-cortical organization and anatomical distortion caused by injury—as well as by neuroplasticity, which is especially present in slow-growing lesions such as low grade gliomas.[18,19] This phenomenon occurs through a functional reorganization of motor areas and language, or through a recruitment of latent neuronal circuits.[20]

In their series of cases, Southwell et al. observed neuroplasticity in 33.3% of patients, through stimulation of eloquent cortical points in repeated oncologic surgeries.[20] In a 2017 study, Sanai et al. reported that the change in positive cortical focus for function in repeated surgeries of low-grade gliomas, occurred in 40.9% of cases.[18] The detection of this change in functional area through direct cortical stimulation would allow the resection of areas infiltrated by neoplasia, but considered (by the classic studies) eloquent in "nondiseased" brains. Larger resections are facilitated by his technique, so that surgery would be interrupted only when positive cortical stimulation points are identified intraoperatively, instead of being based on anatomical knowledge alone.[13,19,21,22]

As this is a retrospective study, where events occurred in the past, there were difficulties related to data collection, most of which sums up to medical record errors and information losses in physical records. In an attempt to minimize these pitfalls, patients were called to the clinic and a new interview with neurological examination and image analysis was performed. At this point, the limitations of some patients were observed in thoroughly describe facts that had occurred at the time of diagnosis and the instituted surgical treatment (memory bias). Furthermore, the allocation of different etiologies with different oncological behaviors (such as metastases and gliomas) at a single group, as well as to generalize the results from the cortical stimulation benefit rate, was another considerable limitation. To exclude this bias, the groups were stratified according to the underlying disease etiology (gliomas and other etiologies), and the rate was calculated individually for the described subgroups.

Conclusions

The present study concludes that the real benefit rate of the intraoperative cortical stimulation technique for the mapping of eloquent areas in brain lesion surgeries was 30.4%.

Cortical stimulation influenced the surgical decision in 35.7% of the cases. For the most part, the change in strategy was for a smaller resection of the lesion. Although almost 90% of patients had no long-term deficits, it is believed that intraoperative cortical stimulation prevented it in one third of them. This number is sufficiently important to justify the adoption of this operative technique.

The anesthetic strategy had no influence on patients' final evolution, since there was no significant difference in definitive deficit between awake patients or those submitted to general anesthesia.

Conflict of Interests

The authors have no conflict of interests to declare.

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Comparison of Prognostic Performance between Fisher and Modified Fisher Scales for Patients with Aneurysmal Subarachnoid Hemorrhage

Comparação do desempenho prognóstico entre as escalas Fisher e Fisher modificada para pacientes com hemorragia subaracnóidea aneurismática

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Arq Bras Neurocir 2024;43(2):e102–e106.

Abstract

Objective The present study aims to assess and compare the prognostic value of these two scales for predicting mortality.

Method We reviewed 172 patients with aneurysmal subarachnoid hemorrhage, who were followed-up for 6 months. The Fisher and modified Fisher scales were evaluated for the prediction of mortality using logistic regressions.

Results The Fisher scale was associated with mortality (odds ratio [OR]: 2; 95% confidence interval [CI]: 1.09–4.05) in the multivariate analysis. The modified Fisher scale was not associated with mortality in the multivariate analysis (OR: 1.39; 95% CI: 0.9–2.29), nor in the univariate analysis (OR: 1.24; 95%CI: 0.87–1.86). There was no significant association between Fisher score and unfavorable functional outcomes (mRS >2) in the univariate analysis (OR: 1.33; 95%CI: 0.92–1.92), nor in the multivariate analysis (OR: 1.37; 95%CI: 0.92–2.05). There was no significant association between modified Fisher scores and unfavorable functional outcomes in the univariate analysis (OR: 1.16; 95%CI: 0.88–1.52). There was also no significant association in the multivariate analysis (OR: 1.18; 95%CI: 0.88–1.57).

Conclusion Only the Fisher scale was associated with mortality. Neither of the two scales was associated with unfavorable functional outcomes (mRS >2).

Keywords
- fisher
- modified fisher
- subarachnoid hemorrhage
- intracranial aneurysm
- prognosis

received
April 14, 2023
accepted
July 5, 2023
article published online
October 27, 2023

DOI https://doi.org/10.1055/s-0043-1776275.
ISSN 0103-5355.

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

Resumo

Objetivo O presente estudo tem como objetivo avaliar e comparar o valor prognóstico dessas duas escalas para predizer mortalidade.

Método Revisamos 172 pacientes com hemorragia subaracnóidea aneurismática, acompanhados por 6 meses. As escalas de Fisher e modificada de Fisher foram avaliadas para a previsão de mortalidade usando regressões logísticas.

Resultados A escala de Fisher foi associada à mortalidade (odds ratio [OR]: 2; intervalo de confiança [IC] 95%: 1.09–4.05) na análise multivariada. A escala Fisher modificada não foi associada à mortalidade na análise multivariada (OR: 1.39; IC95%: 0.9–2.29), nem na análise univariada (OR: 1.24; IC95%: 0.87–1.86). Não houve associação significativa entre o escore de Fisher e resultados funcionais desfavoráveis (mRS >2) na análise univariada (OR: 1.33; IC95%: 0.92–1.92), nem na análise multivariada (OR: 1.37; IC95%: 0.92–2.05). Não houve associação significativa entre os escores modificados de Fisher e resultados funcionais desfavoráveis na análise univariada (OR: 1.16; IC95%: 0.88–1.52). Também não houve associação significativa na análise multivariada (OR: 1.18; IC95%: 0.88–1.57).

Conclusão Apenas a escala de Fisher foi associada à mortalidade. Nenhuma das duas escalas foi associada a resultados funcionais desfavoráveis (mRS >2).

Palavras-chave

- escala fisher
- escala fisher modificada
- hemorragia subaracnóidea
- aneurismas intracranianos
- prognóstico

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) has serious consequences. One of the main causes of the problems is cerebral ischemia, and the presence of vasospasm, another clinical consequence, might make the ischemia worse. Vasospasm is characterized by a focal or diffuse artery constriction that can be noticed on vascular imaging.[1] Due to its role in lowering cerebral blood flow, vasospasm is strongly associated with delayed ischemic neurologic impairments in patients.[2–4]

There are a few approaches to classify vasospasm and to attempt to forecast its progression; the Fisher Scale is typically used for the latter.[5] The Fisher Scale is the best method for categorizing the magnitude of subarachnoid hemorrhage shown on computed tomography (CT) scans. It is very effective for predicting when and how severe cerebral vasospasm may occur.

Another method for grading subarachnoid hemorrhage is the modified Fisher Scale. This is a more logical tool than the original Fisher scale, because in this scale, the chance of developing vasospasm increases with each grade; in contrast, the risk in the original Fisher scale peaks at grade 3 and then decreases for grade 4.[6]

The Fisher and modified Fisher scales were, therefore, developed for the classification of aSAH and to predict the occurrence of vasospasm. In the present study, we intend to evaluate a possible correlation between these scales and mortality.

Methods

Study

We performed a retrospective cohort study that reviewed 172 consecutive patients with aSAH between January 2018 and July 2019.

Eligibility Criteria

We included patients with aSAH whose CT scans, Fisher, and Modified Fisher scores were described by the attending neuroradiologist, with an adequate register of follow-up. Patients who did not have an aSAH, did not accept to participate, or were lost to follow-up were excluded.

Statistical analyses

Descriptive statistics are presented according to data type and normality checks (Shapiro-Wilk test). Logistic regressions evaluated covariates that could influence functional outcomes, and those significant in the univariate analyses ($p < 0.1$) were included in the multivariable models.

Logistic regression analyses were used to assess the prediction performance of the 2 scales for mortality within 6 months.

All tests were 2-tailed and statistical significance was pre-established at $p < 0.05$. Analyses were done using R software (R Foundation for Statistical Computing, Vienna, Austria). The local Ethics Committee approved the present study.

RESULTS

We reviewed the data of 172 patients who developed aSAH. The majority were female (114, or 75.5%), the mean age was 56.7 ($\pm$12.6) years old. The mean Glasgow Coma Scale (GCS) on admission was 11.62 ($\pm$4.5) and the Median Rankin T 6 months was 3 (5). ►**Table 1** summarizes demographic and clinical patient characteristics. These patients were classified according to Fisher and Modified Fisher scores (►**Table 2**). ►**Table 3** shows the classification of patients according to the Rankin Scale.

The second part of our study was the association between covariates and mortality. Covariates were evaluated in univariate regressions, including age, gender, hypertension,

Table 1 Population characteristics

Mean age (years old)	56.7 (±12.6)
Female	114 (75.5%)
Hypertension	61 (79.2%)
DM	32 (41.6%)
Smoker	46 (59.7%)
Mean GCS on admission	11.62 (±4.5)
Median Rankin 6 months	3 (5)

Abbreviation: GCS, Glasgow Coma Scale.

Table 2 Classification of patients according to the Fisher and Modified Fisher scales

Grade	Fisher scale	Modified Fisher scale
0		7 patients
1	9 patients	25 patients
2	25 patients	4 patients
3	55 patients	55 patients
4	83 patients	81 patients

Table 3 Classification of patients according to the Rankin Scale

Grade	Rankin
1	47
3	20
4	6
5	1
6	33

Table 4 Association between patient score in the Fisher grading system and mortality

	OR	95%CI
Univariate		
Fisher	1.63	0.98–2.89
Multivariate		
Age	1.04	1.0–1.08
Fisher	2.00	1.09–4.05

Abbreviations: CI, confidence interval; OR, odds ratio.

diabetes, and smoking status. Covariates significant at $p < 0.1$ in the univariate analysis were included in the final multivariable model.

Logistic regression analysis about the association between patient score in the Fisher grading system and mortality (►**Table 4**) showed that, in the multivariate analysis, the Fisher scale was associated with mortality (odds ratio [OR] 2; 95% confidence interval [CI]: 1.09–4.05). The modified Fisher scale was not associated with mortality in the multivariate analysis

Table 5 Association between patient score in the modified Fisher grading system and mortality

	OR	95%CI
Univariate		
Modified Fisher	1.24	0.87–1.86
Multivariate		
Age	1.04	1.00–1.09
Modified Fisher	1.39	0.9–2.29

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 6 Association between Fisher scores and unfavorable functional outcomes (mRS > 2)

	OR	95%CI
Univariate		
Fisher	1.33	0.92–1.92
Multivariate		
Age	1.02	0.99–1.05
Fisher	1.37	0.92–2.05

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 7 Association between modified Fisher scores and unfavorable functional outcomes (mRS > 2)

	OR	95%CI
Univariate		
Modified Fisher	1.16	0.88–1.52
Multivariate		
Age	1.02	0.99–1.05
Modified Fisher	1.18	0.88–1.57

Abbreviations: CI, confidence interval; OR, odds ratio.

(OR: 1.39; 95%CI: 0.9–2.29), nor in the univariate analysis (OR: 1.24; 95%CI: 0.87–1.86) (►**Table 5**).

►**Tables 6** and **7** show logistic regression analyses demonstrating the correlation between Fisher and modified Fisher scores with unfavorable functional outcomes (mRS > 2).

There was no significant association between Fisher score and unfavorable functional outcomes in the univariate analysis (OR: 1.33; 95%CI: 0.92–1.92). There was also no significant association in the multivariate analysis (OR: 1.37; 95%CI: 0.92–2.05).

There was no significant association between modified Fisher scores and unfavorable functional outcomes in the univariate analysis (OR: 1.16; 95%CI: 0.88–1.52). There was also no significant association in the multivariate analysis (OR: 1.18; 95%CI: 0.88–1.57).

The mortality per Fisher score was 20% in FS-1, 18.75% in FS-2, 25% in FS-3 and 40% in FS-4 (►**Fig. 1**), whereas in the

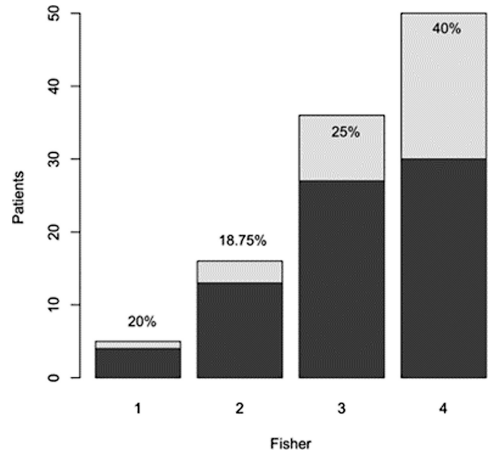

Fig. 1 Mortality per Fisher score.

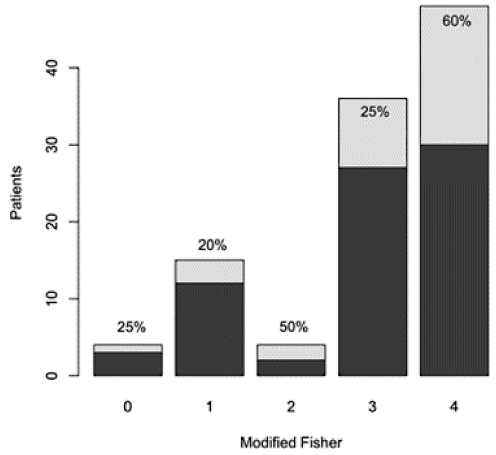

Fig. 2 Mortality per Modified Fisher Score.

Modified Fisher score the mortality was 25% in MFS-0, 20% in MFS-1, 50% in MFS-2, 25% in MFS-3, and 60% in MFS-4 (►**Fig. 2**).

DISCUSSION

Logistic regression data showed that the Fisher scale was associated with mortality in the multivariate analysis. On the other hand, the modified Fisher scale was not associated with mortality in any analysis. In our study, the mortality rate assessed by the Fisher scale increases as the grades of this scale increase, reaching a maximum at grade 4 (►**Fig. 1**). The mortality rate assessed by the modified Fisher scale showed a greater variation, being minimal in grade 1 and maximum in grade 4 (►**Fig. 2**).

According to Fisher et al.,[7] enough blood at specific regions in the subarachnoid space might be the only important etiological factor in vasospasm, being superior to age, sex, severity of the original illness, blood pressure, and headache. Therefore, the Fisher scale was devised to predict the occurrence of vasospasm. In our study, we aimed to compare the prognostic performance between the Fisher and modified Fisher scales for patients with aSAH.

The modified Fisher scale was proposed by Frontera et al.,[6] who concluded that it predicts symptomatic vasospasm following subarachnoid hemorrhage more accurately than the original Fisher scale. In our study, only the Fisher scale could predict mortality.

Lindvall et al.[8] analyzed the receiver operating characteristic (ROC) curve and demonstrated the significance of the Fisher scale grade as an outcome predictor. This result agrees with the results obtained in our study. Additionally, they suggest that the Fisher scale may need to be reevaluated because of the possibility that the increased resolution of modern CT scanners has altered the significance of the scale in predicting vasospasm and outcome. In one study about outcomes for surgical and endovascular management of intracranial aneurysms, Ogilvy et al.[9] demonstrated that, for both the endovascular and surgical categories, there is a strong association between outcome and density of hemorrhage graded by the Fisher scale.

Cedzich et al.[10] suggest that Fisher grade is very good for describing initial state of patients, but it is not a good tool for predicting the outcome of patients with ruptured intracranial aneurysms, highlighting the fact that a the initial clinical and morphological status of a patient may not always predict the outcome.

Strengths and limitations of the study

There are some limitations to our study. First, this is a retrospective study, limiting the obtaining of the sample and variable measuring. Second, in some patients, data about the Fisher and Modified Fisher scale could not be found. Third, the follow-up was lost in some patients, which may interfere with the clinical trial.

Conversely, there are also some strengths. First, we reviewed the data of 172 patients, which is a significant sample. Second, this is an original work. Third, the original description of these scales is for the prediction of vasospasm, and, in our study, we showed the correlation between these scales and mortality. This will help the clinic to be more confident in using the scales as a prognostic index as well.

Conclusion

The Fisher scale was associated with mortality. The modified Fisher scale was not associated with mortality. Neither of the two scales was associated with unfavorable functional outcomes (mRS >2).

Ethical Standards

The present research project was approved by the Ethics and Research Committee of the Hospital das Clínicas of FMUSP. Online registration CAPPesq: 15226 approved 06/20/2016. Approved on the Brazil platform CAAE number: 61719416.6.0000.0068

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in the present article.

Originality
I, Nícollas Nunes Rabelo, certify that this manuscript is a unique submission and is not being considered for publication with any other source in any medium.

Financial Support
None to declare.

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

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Paradoxical Air Embolism in Spinal Surgery: Case Report and Literature Review

Embolia gasosa paradoxal em cirurgia de coluna: Relato de caso e revisão de literatura

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Arq Bras Neurocir 2024;43(2):e107–e111.

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Abstract

Air embolism (AE) is a subtype of embolism, caused by the entry of air into the vascular system. It is a predominantly iatrogenic complication, and its symptomatic form is severe, although uncommon. In some cases, a venous thrombi may pass into the arterial system through a venous-arterial shunt, characterizing a paradoxical embolism. Here, we describe the case of a previously healthy 44-year-old female who underwent cauda equina decompression and lumbar epidural abscess drainage. The patient suffered a paradoxical AE intraoperatively and died after 4 days. The occurrence of AE in lumbar spine surgeries in the prone position is rare, but the surgical team must be attentive to its clinical signs and quickly institute initial management when necessary.

Keywords
- air embolism
- paradoxical embolism
- surgery
- spine
- prone position

Resumo

A embolia gasosa (EG) é um subtipo de embolia, causada pela entrada de ar no sistema vascular. É uma complicação predominantemente iatrogênica e sua forma sintomática é grave, embora incomum. Em alguns casos, um trombo venoso pode migrar para o sistema arterial através de um shunt venoso-arterial, caracterizando uma embolia paradoxal. Aqui, descrevemos o caso de uma mulher de 44 anos, previamente saudável, submetida a descompressão da cauda equina e drenagem de abscesso peridural lombar. A paciente sofreu uma EG paradoxal no intraoperatório e morreu 4 dias depois. A ocorrência de EG em cirurgias da coluna lombar em posição prona é rara, mas a equipe cirúrgica deve estar atenta aos seus sinais clínicos e, quando necessário, instituir o manejo inicial rapidamente.

Palavras-chave
- embolia gasosa
- embolia paradoxal
- cirurgia
- coluna
- posição prona

received
February 3, 2023
accepted
August 4, 2023
article published online
May 2, 2024

DOI https://doi.org/10.1055/s-0044-1779439.
ISSN 0103-5355.

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

Introduction

Air embolism (AE), a subtype of embolism that occurs when air enters the vascular system, has the potential to generate a severe and deadly clinical scenario.[1,2] It is a predominantly iatrogenic complication, usually secondary to medical procedures, such as central venous catheterization, endoscopy, hysteroscopy, laparoscopy, and hemodialysis, among others.[1–10] The clinical presentation varies according to the final destination of the air embolus, which can happen in a myriad of locations.[2,11,12] Paradoxical AE occurs when air transferred by the vascular system passes through the venous bed and into the arterial bed through a venous-arterial shunt, such as in cases of heart defect (right-to-left shunt) or pulmonary arteriovenous malformation. Patent foramen ovale (PFO) is an important cause of paradoxical embolism, especially due to its high prevalence in the population (up to 25%).[1–3]

Cerebral arterial AE (CAGE) is uncommon, but often has catastrophic results. It is sometimes caused by a paradoxical AE rather than the direct entry of air into the arterial bed. It has been described several times, but rarely associated with lumbar spine surgery or the prone position.[13–16] In this study, we describe the case of a patient undergoing surgical treatment for lumbar discitis who developed pulmonary AE and CAGE during the procedure.

Case Report

A previously healthy 44-year-old woman had persistent lower back pain that irradiated to both lower limbs for 3 months, with the use of common analgesics proving unsuccessful. The pain kept progressing, and about a week prior to admission, she developed walking impairment, fevers, and chills.

On admission, lumbar spine magnetic resonance imaging (MRI) was performed, evidencing lumbar spondylodiscitis at the L5-S1 level (►**Fig. 1**). Furthermore, the patient had sinus tachycardia (HR 120 bpm), increased capillary filling time and fever, in addition to paraparesis. An intensive care unit (ICU) bed was requested due to the diagnosis of systemic inflammatory response syndrome, and broad-spectrum antibiotic therapy (ceftriaxone, vancomycin, and metronidazole) was promptly initiated. A surgical procedure was sequentially indicated for cauda equina decompression and epidural abscess drainage. During the operation, the patient had an abrupt drop in O2 saturation (to 70%), followed by circulatory shock. The anesthesiologist rapidly brought up the possibility of air embolism, which was seen as the most probable cause by the entire team, and management was promptly initiated. The surgical field was immediately covered with compresses and immersed in saline solution to prevent new air entry, the O2 supply was increased to 100%,

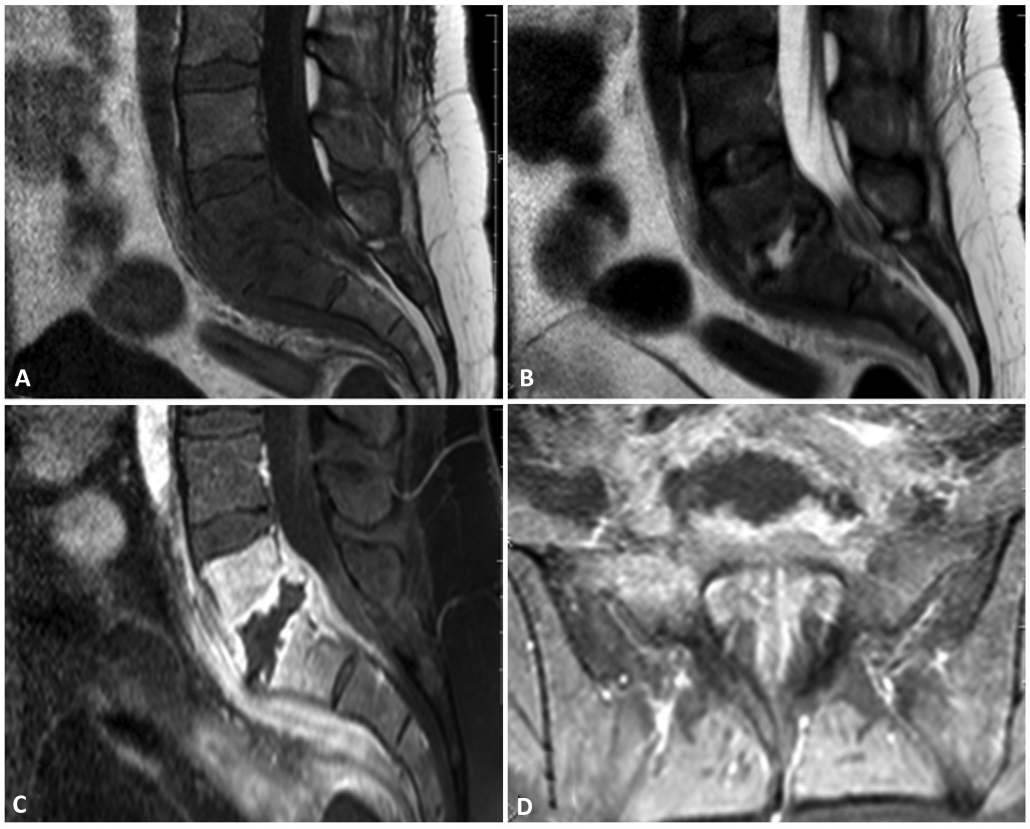

Fig. 1 Preoperative lumbar spine MRI. Spondylodiscitis L5-S1 with infiltration of adjacent soft tissues. The disc component generates compression of the anterior surface of the dural sac. (**A**), (**B**), and (**C**) are sagittal T1, STIR, and contrast enhanced T1 SPIR images, respectively; the involvement of the L5 and S1 vertebrae and the intervertebral disc can be seen, as well as the disc protrusion causing compression of the dural sac. (**D**) is a contrast-enhanced axial T1 SPIR image at the S1 level demonstrating involvement of paravertebral structures. **Abbreviations:** MRI, magnetic resonance imaging; STIR, short T1 inversion recovery; SPIR, spectral pre-saturation with inversion recovery.

and hyperventilation was performed until the condition stabilized. The patient did not have central venous access positioned for aspiration at the time.

In the immediate postoperative period, the patient did not awaken after the cessation of anesthetic medication. Neurological examination showed that she developed right hemiplegia and deviation of conjugated gaze to the left, so she was kept under sedation and mechanical ventilation. An emergency computed tomography (CT) of the head was performed, and multiple air bubbles were spotted within the lumen of the left internal carotid and left posterior cerebral arteries (►**Fig. 2**). Ventilation with 100% O2 was maintained for the management of AE. Hyperbaric therapy is not available at our center, and transfer to another hospital capable of offering this therapy was not feasible. The day after surgery, the patient developed fixed mydriasis and rostrocaudal degeneration. A new CT scan of the head was then performed, demonstrating multiple areas of bilateral ischemia. After further investigation, a transesophageal echocardiogram was performed, which demonstrated a 2 mm PFO. Although small, the PFO was the most probable explanation found for CAGE in this case, since other exams showed no alterations. The patient died after 4 days. Informed consent forms were acquired from the patient's family, as she died before the article was written.

Discussion

For air to enter the vascular system, there must be a direct communication between an air source and a vessel, as well as a pressure gradient that favors its entry.[3,11] The severity of AE depends on some key factors, in particular the amount of air entering the system, the rate of accumulation in the tissues and the patients' position on the surgical bed at the time of the event.[1,2,4,17,18]

Lumbar spine surgeries constitute an atypical clinical scenario for the occurrence of CAGE, which can lead to a delay in management. Nonetheless, this rare association has been described in the past.[13–16] The prone position can create the necessary conditions for the entry of air into the veins of the epidural plexus by generating the necessary gravitational gradient required (believed to be as little as 5 cm height difference between the operative site and the right atrium), as well as a pressure of up to -2.0 cmH2O in the

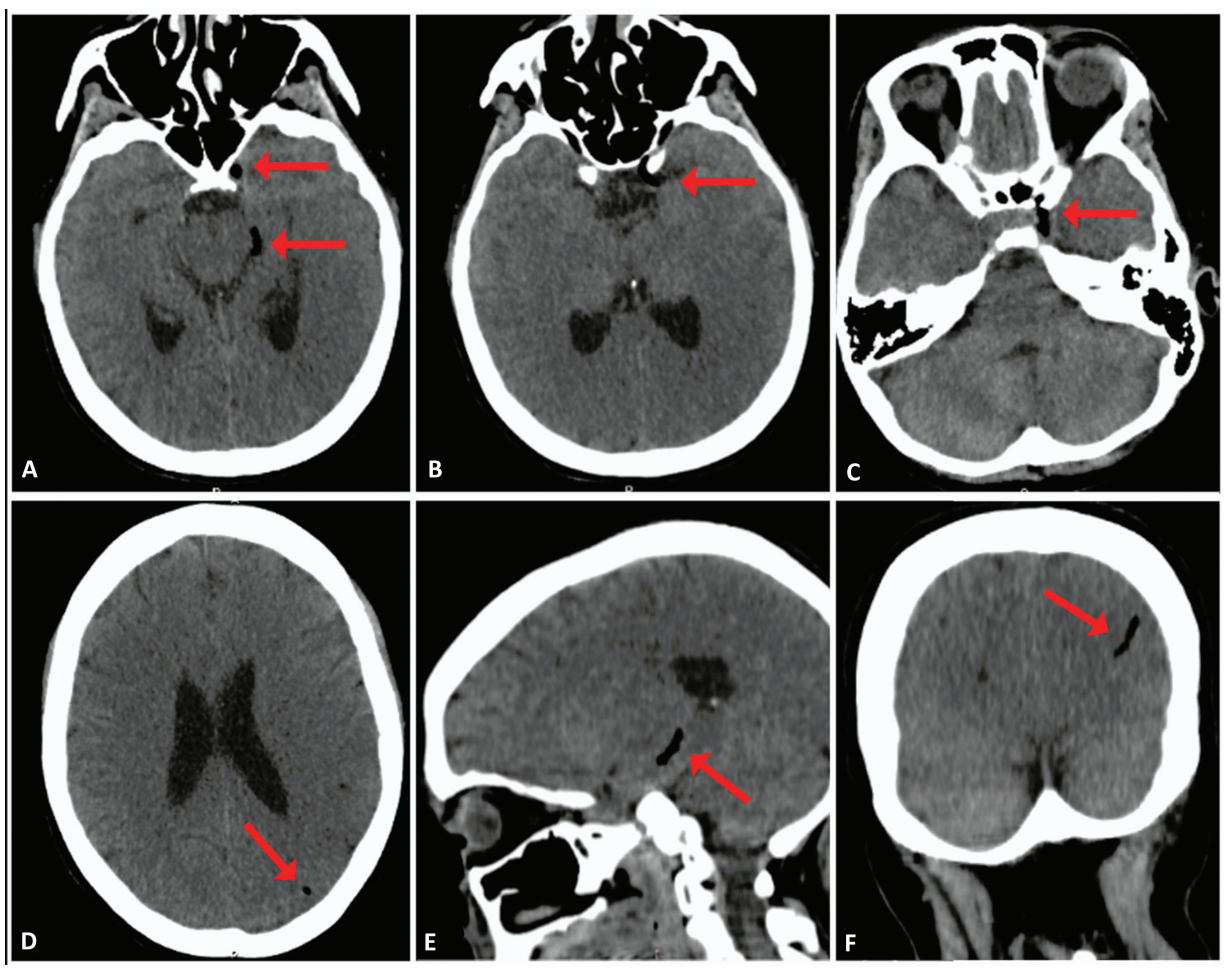

Fig. 2 Immediate post-operative CT scan of the head. Noncontrast CT of the head performed in the immediate postoperative period. In (**A**), density compatible with air is visualized in the left internal carotid and posterior cerebral arteries. (**B**) and (**C**) show air embolus in the left internal carotid artery, in the clinoid and cavernous segments, respectively. (**D**) Demonstrates air embolus in a distal cortical branch of the left posterior cerebral artery. (**E**) and (**F**) demonstrate intraluminal air in the left internal carotid artery and in a distal branch of the left posterior cerebral artery, in the sagittal and coronal sections, respectively. The red arrows point to the air emboli. **Abbreviation:** CT, computed tomography.

inferior vena cava, which creates relative emptying of the epidural veins and a suctioning effect.[12,15,17,19] When happening together, these scenarios can lead to AE. Therefore, despite its rarity, the surgical and anesthesiology teams should be aware that AE is possible and start management immediately after the patient turns symptomatic during surgery.

A high clinical suspicion is necessary to speed up the investigation and diagnosis of AE. The majority of cases are thought to go by unrecognized, as most patients are either asymptomatic or have nonspecific symptoms. The clinical presentation derives from the location of the embolus, which can lodge itself anywhere in the vascular system.[2,12] In CAGE, there is usually a multivessel occlusion, a classic feature of embolic stroke. Focal neurological signs and symptoms, as well as acute-onset decreased level of consciousness in a patient at risk for AE should raise suspicion of CAGE, followed by prompt investigation and treatment.[2,3] Transthoracic or transesophageal (preferred) echocardiography and CT scan of the affected region are the most efficient diagnostic tests in this case, as they can detect air bubbles within the vascular system (►**Fig. 2**). It is noteworthy that a negative CT scan does not completely exclude AE. Some other tests can be performed, but the findings are not specific.[1–3,8,20] Furthermore, the presence of CAGE or other arterial AE should raise the suspicion of a direct connection between the venous and arterial bed. Therefore, investigation is necessary in these cases.[1–3,8]

The treatment of AE must be instituted quickly to decrease ischemic damage. As it has already been described in detail elsewhere,[1–3,8,15,21] we shall briefly summarize it here. When AE is detected during surgery, the surgical site should be covered with compresses soaked in saline solution to prevent the entry of new emboli.[1,15] Then, in addition to hemodynamic support, good ventilation with 100% O2 must be ensured, since high concentrations of O2 help to reduce the nitrogen content of the embolus (thus decreasing its size). Hyperventilation can also be performed for the same purpose.[1–3,8,21] Positioning the patient in left lateral decubitus, and in the Trendelenburg position can also be useful, but not in cases of CAGE.[3] Immediate aspiration through a central venous catheter can be performed.[1,3,8] If available, hyperbaric oxygen therapy is recommended for the more severe cases.[1–3,8,21]

Conclusion

The occurrence of AE, especially CAGE, during lumbar spine surgery in the prone position is very rare, which hampers diagnosis and delays treatment. This clinical scenario has been described a few times in the past, and our case reinforces its existence and importance. Although rare, the surgical team must be attentive to its clinical signs and quickly institute management when necessary. The treatment of AE must be immediate, and even in situations where it is uncommon, the hypothesis must be raised and the initial treatment instituted until this diagnosis can be excluded. Unfortunately, even with the immediate recognition and management of AE in the present case, our patient died, which reinforces the severity of such a scenario.

Ethics Approval and Consent to Participate

Ethical approval was waived by the local Ethics Committee of the Faculdade Meridional - IMED in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. The study was conducted in accordance with the declaration of Helsinki.

Consent for Publication

Informed consent forms were acquired from the patient's family, as the patient died before the article was written.

Availability of Data and Material

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Each author made significant individual contributions to this manuscript. Miotto GJ: Main physician responsible for the patient's care and main surgeon; review of the manuscript's intellectual content; approval of the final version of the manuscript. Martio AE: Development and writing of the article; approval of the final version of the manuscript. Mesquita Filho PM: Development and writing of the article; approval of the final version of the manuscript. Karam OR: Physician responsible for the patient's care, auxiliary surgeon; writing of the article; approval of the final version of the manuscript. Padua WL: Critical review of the intellectual content of the manuscript; approval of the final version of the manuscript. Berres TO: Critical review of the intellectual content of the manuscript; approval of the final version of the manuscript. Ferreira Saltiél RM: Critical review of the intellectual content of the manuscript; approval of the final version of the manuscript.

Funding Statement

No funding was received in any phase of the article's production.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgments

None.

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Thermocoagulation in Multiple Targets to Treat Obsessive-Compulsive Disorder Associated with Drug Addiction: Case Report

Termocoagulação de múltiplos alvos para tratar transtorno obsessivo-compulsivo associado à drogadição: Relato de caso

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Arq Bras Neurocir 2024;43(2):e112–e116.

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Abstract

Substance-related disorders are chronic psychiatric conditions defined by substance abuse, and they compromise patients both clinically and functionally. Currently, pharmacotherapy, behavioral therapy, or an association of both are the treatments of choice for obsessive-compulsive disorder associated with drug addiction. However, the refractoriness to treatment, as a result of the high failure rates of these approaches, has led to the need to develop surgical techniques to treat severe cases of substance-related disorders. In the present article, we report the case of a patient who underwent neurosurgery through the stereotactic technique after refractoriness to the conventional treatment for drug addiction. The patient showed sustained improvement in his addiction to drugs. Despite the numerous reports on the effectiveness and applicability of neurosurgery in psychiatric disorders, some concerns regarding stereotactic surgery as a treatment for drug addiction still remain, especially in relation to its efficacy, safety, and ethical implications.

Keywords

- obsessive compulsive disorder
- drug addiction
- thermocoagulation
- case report

Resumo

Transtornos relacionados ao uso de substâncias são condições psiquiátricas crônicas definidas pelo abuso de substâncias, que deixam o paciente comprometido clínica e funcionalmente. Atualmente, a farmacoterapia, a terapia comportamental ou a associação de ambas são os tratamentos de escolha para o transtorno obsessivo-compulsivo associado ao vício em drogas. Contudo, a refratariedade ao tratamento, resultante das altas taxas de fracasso dessas abordagens, tornou necessário o desenvolvimento de técnicas cirúrgicas para tratar casos graves de transtornos relacionados ao uso de substâncias. Neste artigo, relatamos o caso de um paciente submetido a neurocirurgia pela técnica estereotáxica após fracasso do tratamento

Palavras-chave

- transtorno obsessivo-compulsivo
- dependência de drogas
- termocoagulação
- relato de caso

received
November 22, 2021
accepted
March 7, 2023
article published online
October 18, 2023

DOI https://doi.org/10.1055/s-0043-1774747.
ISSN 0103-5355.

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

convencional para drogadição. O paciente apresentou melhora sustentada do vício em drogas. Apesar dos inúmeros relatos sobre a eficácia e a aplicabilidade da neurocirurgia em transtornos psiquiátricas, ainda existem certa preocupação a respeito da cirurgia estereotáxica como tratamento para a drogadição, principalmente em relação à sua eficácia, segurança e implicações éticas.

Introduction

Substance-related disorders are chronic psychiatric conditions defined by substance abuse, and they compromise patients both clinically and functionally.[1] Patients affected by these disorders present with intense compulsive cravings for drugs, which persist despite the severe consequences they face because of their addiction.

In addition to the clinical and functional impairment of the patients, the problems associated with addiction are responsible for a huge economic and social burden on society. Even after prolonged periods of withdrawal, a high risk of relapse persists, due to the recall of memories associated with the addictive substance and exposure to stressful situations or those that trigger cravings.[2]

Currently, pharmacotherapy, behavioral therapy, or a combination of both are the main treatments for obsessive-compulsive disorder (OCD) associated with drug addiction.[3] Nevertheless, the high failure rates of these approaches have resulted in refractoriness to the treatments, making it necessary to develop surgical techniques to treat severe cases of substance-related disorders.[1]

In the present article, we report the case of a patient who underwent neurosurgery through the stereotactic technique after failure of the conventional treatment for drug addiction. The article aimed to describe possible treatment targets for OCD associated with drug addiction, as well as their indications and applications.

Case Report

A 25-year-old male patient sought treatment in our service after a 6-year history of drug addiction, which had begun when he was 19 years old. He first smoked cannabis and then started using cocaine. He used these drugs daily, and although the amount was variable, consumption was gradually increasing. The patient reported an attempt to end the dependence without any professional guidance, which resulted in irritability and anxiety during the periods of withdrawal; therefore, he also developed nicotine addiction. The patient made some attempts to quit the drugs by adopting a conservative treatment with the use of antidepressant medication as well as psychological treatment in rehabilitation clinics. As a result, he even went through a six-month period without constant drug use but experienced several relapses.

The patient had a history of depression, attempted suicide, and hypothyroidism. A psychiatric assessment was performed, and he was diagnosed with OCD associated with drug addiction. The patient filled out the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), a non-diagnostic scale to evaluate the severity of obsessive-compulsive symptoms, with scores ranging from 0 to 40, and he reached a total score of 16.

In 2019, the medical team and the patient's family, in consensus and following the protocol of the Brazilian Federal Council of Medicine, opted for the surgical procedure. Throughout the 30 days of drug withdrawal before the surgery, the patient presented nervousness, anxiety, and insomnia. He underwent thermocoagulation using a stereotactic technique, targeting the anterior limb of the internal capsule, the subgenual area, the nucleus accumbens, and the cingulate gyrus. Bilateral ablation of multiple targets was performed using an electrode with a 4-mm exposed tip at 70°C for 60 seconds.

In the first four months after the surgery, the patient underwent monthly follow-ups with our neurosurgery team, with subsequent follow-ups every three months, and then every six months. Another psychiatric evaluation was performed four months after surgery, when the patient was assessed once more using the Y-BOCS, with a total score of 3. The craving for cocaine ceased shortly after the surgical procedure. Nonetheless, the addiction to nicotine remained. Improvements in quality of life, sleep, and social, family, and professional functioning were observed since the first postoperative month. Although the patient reported slow reasoning and difficulty in articulating ideas in the first three postoperative months, his cognitive functions, especially memory, learning, and planning started showing improvement from three months onwards. He lost 20 kg after surgery but had no other major side effects.

The collection of data about the case was performed with the authorization of the patient, after he signed the Informed Consent Form, which was submitted to and approved by the Ethics in Research Committee of Pontifícia Universidade Católica de Goiás (CAAE: 39924920.6.0000.0037), following national and international guidelines.[4,5]

Discussion

Since ancient times, numerous attempts have been made to treat mental illnesses surgically. Trephination of the human skull, the oldest known neurosurgical procedure, has been used as part of the treatment of psychiatric disorders.[6,7] The first published account of an ablative surgery to treat psychiatric patients was made by Burkhardt in 1892.[8] Nevertheless, the popularization of neuropsychosurgery (NPS)

only occurred in 1935, with António Egas Moniz and Pedro de Almeida Lima, who performed the first frontal leucotomy, aiming to treat psychiatric patients with depression, anxiety, and aggressiveness.[7] Walter Freeman and James Watts further refined the leucotomy technique, enabling a more precise location of the lesion using anatomical landmarks.[9] Despite the effectiveness of the surgery, its indiscriminate application, associated with the emergence of pharmacological drugs, led to prejudice against leucotomy and the consequent decline in neurosurgical treatments for psychiatric disorders starting in the 1950s.[8,9]

As stereotactic surgery improved, the therapeutic targets have gradually become more precise.[10] In stereotactic surgical procedures, small lesions are created in specific targets, modifying neuronal activity without damaging the nervous system.[11] The selection of target points to be injured during the NPS procedure for the treatment of psychiatric disorders was greatly influenced by the description of the limbic system as the essence of human emotions.[12,13] As a consequence of the improvements in stereotactic techniques, the medial thalamic nucleus, the hypothalamic nucleus, and the amygdaloid nucleus, which make up the limbic system, and are considered the biological determining center of individual conduct, have become surgical targets for psychiatric disorders.[10]

Stereotactic neurosurgery as a treatment for drug addiction was first used between the 1960s and the 1970s.[11] Substance-related disorders are characterized by psychological and physical dependence.[14] Drug addiction is associated with OCD, a mental illness that is caused by a dysfunction in the dopaminergic inhibitory system, and its symptoms are the most important characteristics in chemically dependent people with psychological dependence.[14,15]

Neurosurgery has emerged as a therapeutic measure for substance dependence based on the understanding of the neurocircuitry of drug addiction and its recognition as a psychiatric disorder. As stereotactic procedures for drug addiction treatment evolved, multiple targets have been tested. Leucotomy was the first stereotactic neurosurgery used to treat substance dependence.[11] Subsequently, hypothalamotomy was reported as a surgical treatment for chemical dependency because it increased the patients' self-control. Nonetheless, it also produced serious side effects, such as amnestic syndrome, ophthalmic disorder, and vegetative crisis.[11,14]

Currently, NPS has gained ground in the treatment of psychiatric illnesses due to refractoriness to the conventional treatment, defined as the use of drugs for more than three years and at least three unsuccessful treatments.[16] The essential criteria used for the indication of neurosurgery in OCD include a diagnosis of at least five years; previous use of at least three serotonin reuptake inhibitors (clomipramine, mandatorily) and two effect enhancers at the maximum recommended doses for at least 12 weeks; a minimum of 20 hours of behavioral therapy; and rates of symptomatic improvement in the Y-BOCS lower than 25%.[17]

The theoretical foundation that supports the targets of surgical interventions in OCD is functional neuroimaging findings.[17] Resting computed tomography (CT) of patients with OCD shows increased activity in the orbitofrontal gyrus, cingulate gyrus, and caudate nucleus, unlike the images of patients without the disease. Furthermore, a normalization of activity is observed in these regions after clinical therapy in individuals who respond to conventional treatments.[18]

Although the drugs involved in substance-related disorders have different chemical structures and target sites, the main mechanism that culminates in drug addiction is the reward system.[19] In the 1950s, James Olds and Peter Milner discovered that, when stimulated, certain areas of the brain, identified as reward centers, provided a feeling of pleasure. Due to its numerous receptors for the neurotransmitter dopamine, known as the "pleasure molecule," the limbic system and the nucleus accumbens have become the main representatives of these centers.[20]

Psychoactive substances increase the discharge of dopamine in the nucleus accumbens, decreasing neuronal inhibition, thus causing the activation of the reward system. Dopaminergic neurons are projected from the ventral tegmental area to the ventral striatum (including the nucleus accumbens), septal nuclei, amygdala, and prefrontal and cingulate cortices. In addition to activating the reward system, drugs cause an increase in dopamine release in the amygdala, which strengthens the relationship between the rewarding characteristics of the substances and the exteroceptive sensations.[14]

The nucleus accumbens in the limbic system is responsible for the integration involving cognitive and affective information and reward-driven behaviors from the prefrontal cortex. Psychoactive substances stimulate this neurocircuit and the continuous use of the drugs become essential for the survival of the patients.[21]

In the natural history of addiction, the patient goes through three stages that make up a cycle: the first is the "binge/intoxication" phase, the second is the "withdrawal/negative affect" phase, and the third is the "preoccupation/anticipation" (craving) phase.[22] To be considered effective, addiction treatments must ensure successful interventions during all these phases to avoid behavioral responses.

The brain circuitry involved in the long-term chronic effect of drug addiction includes, in addition to the reward effect regulators, circuits involved in learning and memory, as well as those in charge of processing and storing substance-induced rewarding stimuli. Therefore, the hippocampus, amygdala, limbic system, and cerebral cortex play important roles in the neurocircuitry of substance-related disorders.[19]

In the patient of the present case report, the thermocoagulation targets were the nucleus accumbens, anterior limb of the internal capsule, cingulate gyrus, and subgenual area. These targets were chosen after an analysis of the patient's clinical history, self-reported behavior, and psychiatric assessment. However, no consensus has already been reached on the best targets to be chosen for the surgical treatment of OCD associated with drug addiction.

Anterior capsulotomy is based on the disconnection of fibers that connect the orbitofrontal cortex and the limbic

system, located between the caudate nucleus and the putamen. Although this surgical intervention can cause side effects such as weight gain, fatigue, and headache, it generally yields results that are more satisfactory and causes fewer side effects compared with procedures in other brain regions.[23]

The cingulate gyrus has been described as an important point for ablative lesions when aiming to interrupt obsessive thinking connected to substance abuse.[11,14] It is an indicated target for the treatment of affective diseases, chronic anxiety states, OCD, as well as drug addiction.[8] Anterior cingulotomy, first suggested by John Fulton, consists of a bilateral lesion of the anterior cingulate with the objective of interrupting the connection of the cingulate cortex, the orbitofrontal cortex and the limbic system, thus blocking the reward system. The subgenual area is located in the cingulate cortex as a narrow band in the caudal portion of the subcallosal area. It is important in the regulation of emotional responses and, consequently, its ablation especially helps control the emotional state of intense desire for the effects of drugs.[24]

In a clinical study conducted in China,[25] the authors reported that, for the first time, ablation of the nucleus accumbens successfully alleviated drug addiction and simultaneously decreased the relapse rate. The mesolimbic dopaminergic system plays an important role in the reward mechanisms of the brain and the functions of the nucleus accumbens. Therefore, thermocoagulation of the nucleus accumbens leads to the blockade of this circuit, which prevents both the craving for drugs and the relapses.[26]

The possible complications of ablative stereotactic surgeries for the treatment of OCD associated with drug addiction are generally nonspecific, including those not related to the functions of the target area, such as fever, headache, urinary incontinence, and epilepsy. Nevertheless, some specific complications, closely related to the function of the injured targets, such as personality changes, memory complaints, affective disorders, and paraphilias may also occur. The rates of both types of complications do not exceed 5%, and they usually disappear gradually after the appropriate management.[19]

Nowadays, current stereotactic neurosurgery results in less severe adverse events and complications.[17] The patient in the case herein reported presented a mild and transient complication of slow reasoning during the first three months after the neurosurgical procedure, and he remained addicted to nicotine. Interestingly, the patient lost 20 kg in the postoperative period, contradicting the trend of weight gain after NPS.[27]

After the stereotactic surgery, the patient showed sustained improvement and did not have any relapses, corroborating literature data.[1,17,19] The Y-BOCS, used to assess the severity of his OCD symptoms, was applied pre- and postoperatively, and the score of the patient decreased by over 80% postoperatively, evidencing that the stereotactic procedure led to an important improvement in his symptoms.

Despite numerous reports[9,11,14] on the effectiveness and applicability of NPS in psychiatric disorders, certain concerns regarding stereotactic surgery as a treatment for drug addiction remain, especially in relation to its safety and efficacy. One of the concerns is related to the permanent injuries caused by the stereotactic technique,[14] performed in areas of the brain that mediate drug addiction, as well as mood, natural reward, and motivation.[11]

Establishing specific surgical methods for each psychiatric disorder, with more precisely targeted lesions, lower rates of complications, and absence of personality and cognitive adverse effects are the biggest challenges for the future of NPS, and they may be the answers to questions about the safety of the procedure. Ethical issues and the prejudice against psychiatric neurosurgeries date back to the period of lobotomies,[8] raising questions about whether written informed consents were signed by the patients or even if independent reviews were performed before the treatments.[11]

Stereotactic surgery remains a potential treatment for drug addiction, as contemporary pharmacological and behavioral treatments do not cure this condition.[11] Currently, this surgical technique, which has already been proven to be a viable option with excellent results in carefully selected cases, is indicated only for patients who are refractory to the clinical treatment.[28]

Finally, neuromodulation for mental illnesses needs to focus on the approach for the selection of targets and will probably incorporate multiple targeting methods. Patient specificities should not be underrated, and an individualized symptom- and patient-directed approach is necessary.[9]

Conclusion

Given the large biopsychosocial impact of substance-related disorders, their treatment attracts considerable scientific interest. Considering the current lack of evidence that cognitive or pharmacological treatments promote the cure of drug addiction, in addition to their high relapse rates, neurosurgery is a potential therapeutic option for OCD associated with drug addiction. Nowadays, despite its proven efficacy and few side effects, its application is limited to cases refractory to conventional treatments. Therefore, further studies that address stereotactic surgery using multiple targets for the treatment of OCD associated with drug addiction are needed.

Conflict of Interests

The authors have no conflict of interests to declare.

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Multiple Medullary Schwannoma Associated with Lumbar Disc Herniation and Cauda Equina Syndrome: Case Report

Schwannoma medular múltiplo associado a hérnia de disco lombar e síndrome da cauda equina: Relato de caso

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Arq Bras Neurocir 2024;43(2):e117–e120.

Abstract

Introduction Schwannoma is a Schwann cells neoplasm that can occur in various parts of the nervous system, including the medullar region of the cauda equina. Bone involvement is uncommon.

Objective To report a multiple schwannoma case that was initially diagnosed as cauda equina syndrome.

Clinical Case We report the case of a 44-year-old male who presented with pain irradiating to the lower limbs, urinary retention, and saddle paresthesia. Imaging exams revealed tumors in the cervical spine and in the T12/L1, L2/L3, and L3/L4 levels, the last three causing nervous compression. Histopathological analyses confirmed a Schwannoma pattern.

Results The case was solved by surgical resection.

Conclusion The case was solved and, in the end, the patient was stable and with improved pain and waits for a cervical surgery.

Keywords
- schwannoma
- neoplasm
- lumbalgia

Resumo

Introdução Schwannoma é uma neoplasia de células de Schwann que pode ocorrer em diversas partes do sistema nervoso, incluindo a região medular da cauda equina. O acometimento ósseo é incomum.

Objetivo Relatar um caso de schwannoma múltiplo que foi diagnosticado inicialmente como síndrome da cauda equina.

Relato de caso Relatamos o caso de um paciente masculino de 44 anos que apresentou quadro álgico com irradiação para os membros inferiores, retenção urinária

Palavras-chave
- schwannoma
- neoplasia
- lombalgia

received
September 16, 2021
accepted
January 18, 2022
article published online
October 10, 2023

DOI https://doi.org/10.1055/s-0042-1744111.
ISSN 0103-5355.

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

e parestesia em cela. Exames de imagem revelaram tumores na cervical e em níveis de T12/L1, L2/L3 e L3/L4, com os três últimos causando compressão nervosa. A análise histopatológica comprovou padrão de schwannoma.
Resultados A correção do quadro se deu através da ressecção cirúrgica.
Conclusão O quadro foi resolvido com o paciente apresentando-se estável e com melhora do quadro álgico. O paciente aguarda cirurgia a nível cervical.

Introduction

Schwannoma, also known as neurilemoma or neurimoma,[1,2] is a neoplasm that occurs in Schwann cells, which are responsible by the formation of the myelin sheath of the peripheral nerves. In most cases, schwannomas are benign,[3] affect more women than men,[4] and are more frequently seen in the 40th and 50th decades of life. Its incidence is of 0.5 per 100.000 individuals per year.[3] Their most common location is the vestibulocochlear nerve (NC VIII), but they can also affect other nerves.[5] Multiple schwannomas are usually be associated with neurofibromatosis (type I or II) or with schwannomatosis,[3] which are rare conditions. The clinical manifestations are late, due to their slow growth, and occur due to neurological compression.[6]

The aim of the present article is reporting a multiple schwannoma case that was initially diagnosed as cauda equina syndrome.

Material and Methods

Information was collected from medical records, patient interview, the diagnostic methods to which the patient was submitted, surgical findings, and a literature review.

Case Report

Patient, C.L., male, 44 years old, white, bricklayer, presented to the hospital due to a 2-month-long backache.

The backache irradiated to the lower limbs and was associated with urinary retention, saddle paresthesia, reduced sensitivity, and paraparesis. At the first evaluation, a diagnosis of cauda equina syndrome was made. Magnetic Ressonance (MRI) (►**Fig. 1** and ►**Fig. 2**) demonstrated lesions corresponding to C6/C7, T12/L1, L2/L3, and L3/L4 discal herniation. The patient was referred to urgent surgical medullar decompression (L3-L4 laminectomy). During the intraoperative evaluation, the lesion was suggestive of tumoral etiology. The collected tissue was sent to biopsy. The pathological report confirmed an intradural lesion with a suggestive Schwannoma pattern. A subsequent magnetic resonance imaging (MRI) exam showed that the discal herniation was associated with intradural tumoral lesions.

A subsequent surgical approach was made to resect the T12/L1 and L2/L3 lesions and revise the L3/L4. level After the surgery, the patient presented pain improvement.

Currently, the patient is stable, walking normally, without new deficits and with normal neurological examination. The cervical schwannoma is under strict monitoring for the best moment for surgery.

Discussion

Schwannoma is a benign tumor of the nervous sheath[3] that usually appears isolated, but it can also occur more rarely in multiple form with slow growth,[7] with consequent delay to present symptoms,[6] which happens when it reaches 4 cm in size.[8] The classic symptom is pain, which worsens at night,[9] associated with paresthesia due to compression of sensitive roots.[10] Moreover, the patient can also present with other sensitive and motor changes.[7]

Usually, the roots of the back are the most affected location. Generally, the tumors are intradural,[10] extramedullary ($\sim$ 99%), and most are found in the cervical and lumbar regions. In computed tomography (CT), schwannomas are not distinguishable from neurofibromatosis or discal herniation. However, in MRI, schwannoma have characteristic signs, which are hypointensity in T1, intense improvement in T1 + C, and heterogeneous hyperintensity in T2; generally, large tumors appear with hemosiderin areas in T2 sequences.[11] Normally, schwannomas appear as solid, well-defined rounded lesions[10] and are frequently associated with bone remodeling.[11] As they grow, they can extend to several levels of the spine or protude to the neural foramen. Macroscopically, these tumors are encapsulated and arise eccentrically to the nerve, with nerve fibers along their surface.

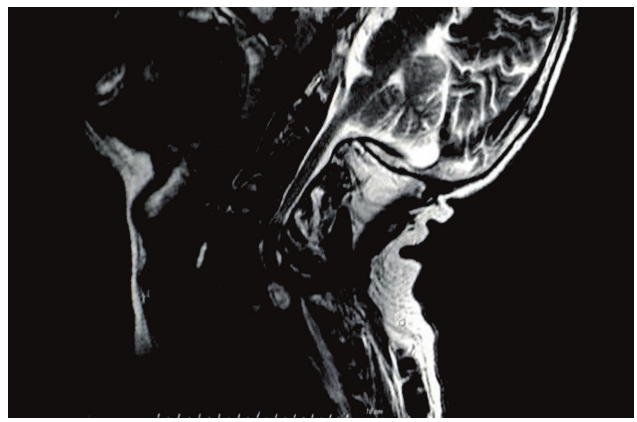

Fig.1 C7 tumor showed in MRI T2-weighted.

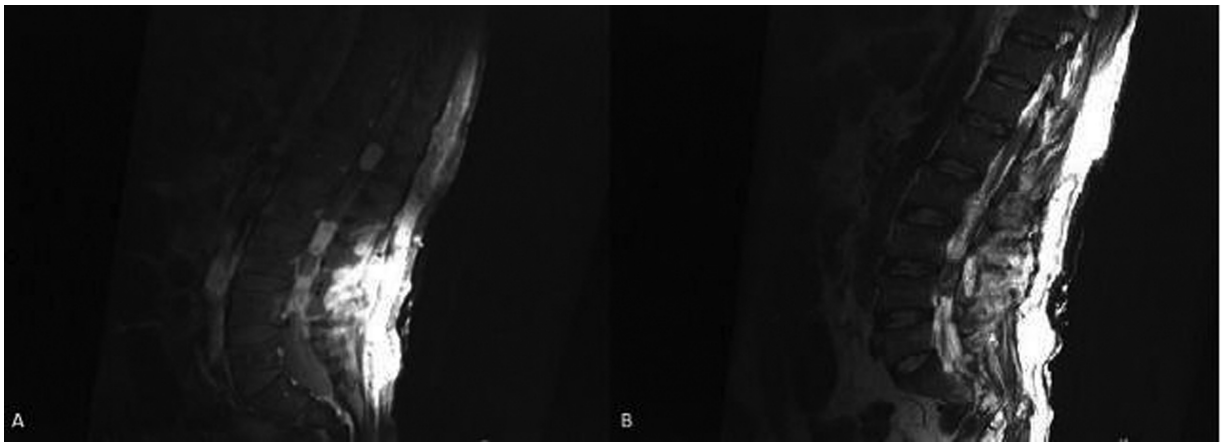

Fig. 2 . Massas em T12/L1, L2/L3 e L3/L4 reveladas por ressonância magnética (A, B).

Histopathological analyses enable confirmation of the diagnosis trough fusiform cells, which can be type Antoni A or Antoni B. The pattern Antoni A consists of elongated cells that are thickly involved and organized into fascicles, and alternating palisades with Verocay bodies can occur. Type Antoni B is less compact and tends to cystic degeneration.[12]

Among the differential diagnoses, the most common are neurofibromatosis type 2 (NF2) and neurofibromatosis type 1 (NF1). Neurofibromatosis type 2 is an autosomal dominant disease, progressive and rare,[13] that usually affects the vestibular nerves and originates cranial and multiple spinal tumors.[14] The schwannoma phenotype is very similar to NF2; nevertheless, the former has a good prognosis and the latter does not. Therefore, differentiation between these tumors is necessary in order to determine the right treatment.[15] Neurofibromatosis type 1 is also an autosomal dominant neurocutaneous disorder linked to the formation of benign and malignant tumors; however, it has a different phenotype from NF2. Neurofibromatosis type 1 can present coffee latte stains, neurofibromas in any type, axillary and inguinal freckles, optical nerve glioma, Lisch nodules (pigmented iris hamartomas), typical bone disease lesions, such as small wing sphenoidal dysplasia, thinning of the cortex of long bones with or without pseudarthrosis, and family history.[14] Neurofibromatosis type 1 is linked to the *NF1* gene, which is located in the long arm of chromosome 17 (17q12).[10]

Schwannoma can also be confused with disc herniation. Both can lead to neurological compression, originating the symptoms.[16] The most common locations for herniation are the C6/C7 level in the cervical spine, the L4/L5, and L5/S1 levels in the lumbar spine.[17] The latter causes cauda equina syndrome,[18] just as a medullary tumor in this region would.[19]

Disc protrusion is more common than schwannomas, being the disease that most leads to spinal surgery today. It occurs more in males in the 40th decade of life.[20]

The first line of treatment for schwannomas is surgical. Since the tumor does not infiltrate the originating nerve, it can be totally separated, without nerve lesion.[12]

Conclusion

Spinal schwannoma is a rare neoplasm with unspecific clinical presentation for which the most used imaging exam is MRI. Confirmation of the diagnosis is obtained by histological and immunohistochemical studies. The treatment is surgical and its aim is complete resection. Incomplete resection can lead to future recurrence.[3] The present case report describes a rare concomitant lumbar and cervical multiple schwannoma associated with symptoms of cauda equina syndrome. Surgical approach for the resection of lumbar schwannoma with arthrodesis leads the patient to improvement of symptoms.

Ethics Statement

In the present case report, neither the patient nor any of his data have been identified.

Conflict of Interests

The authors have no conflict of interests to declare.

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Minimally Invasive Microsurgery for Cerebral Contusions

Microcirurgia minimamente invasiva para tratamento de contusões cerebrais

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Arq Bras Neurocir 2024;43(2):121–126.

Abstract

Introduction Traumatic brain injury (TBI) is among the main causes of death and neurological sequelae worldwide. Injuries are classified as diffuse (diffuse axonal injury and brain swelling) or focal (cerebral contusion [CCo], epidural hematoma, and acute subdural hematoma). Among all TBIs, CCos are the most frequent focal lesion, and treatment modalities are many. Hematoma evacuation using large craniotomies has been well described in the literature. The main goal of the present study is to discuss the advantages of minimally invasive approaches for the treatment of CCos, regarding operative time, blood loss, and postoperative tomographic results.

Methods An integrative literature review was conducted on the SciELO, LILACS, and PubMed databases. Seven case reports were included in the present study. Retrospective data collection was performed, analyzing gender, age, Glasgow coma scale score on hospital admission, surgical approach, and postoperative (tomographic) results.

Results The minimally invasive keyhole approach was used in seven patients with CCos. The supraorbital approach ($n = 5$) was performed for frontal lobe contusions, and the minipterional approach ($n = 2$) was performed for temporal lobe contusions. All cases had adequate hematoma evacuation, confirmed by postoperative computed tomography scans.

Conclusion The minimally invasive approaches were effective for hematoma evacuation, with adequate clinical and radiological postoperative results.

Keywords
- brain contusion
- minimally invasive surgery
- brain trauma
- traumatic brain injuries
- microsurgery
- trauma surgery

received
June 10, 2021
accepted
January 18, 2022
article published online
October 10, 2023

DOI https://doi.org/10.1055/s-0042-1744115.
ISSN 0103-5355.

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

Resumo

Introdução O traumatismo cranioencefálico se encontra entre as principais causas de óbito e sequelas neurológicas na estatística mundial. As lesões são classificadas como difusas (lesão axonal difusa e edema cerebral traumático) ou focais (contusões cerebrais [CoC], hematoma epidural, e hematoma subdural agudo). Dentre todos os tipos de lesões cerebrais traumáticas, as contusões são a lesão focal mais comum, e são reservadas a elas múltiplas modalidades de tratamento. O principal objetivo desse estudo é discutir as vantagens dos acessos minimamente invasivos no tratamento de contusões cerebrais, especialmente no que concerne à duração do procedimento, perda sanguínea e resultados tomográficos pós-operatórios.

Métodos Uma revisão integrativa de literatura foi conduzida nas plataformas Scientific Electronic Library Online (SciELO), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e PubMed. Sete relatos de caso foram incluídos neste estudo. A coleta retrospectiva de dados foi realizada com a análise das seguintes variáveis: gênero, idade, escala de coma de Glasgow à admissão, acesso cirúrgico utilizado e resultados tomográficos pós-operatórios.

Resultados O acesso cirúrgico minimamente invasivo foi utilizado em sete pacientes com CoC. O acesso supraorbital ($n = 5$) foi usado para tratar contusões frontais, enquanto o acesso minipterional ($n = 2$) foi usado para o tratamento de contusões temporais. Em todos os casos, foi obtida drenagem satisfatória do hematoma, confirmada por meio de tomografias pós-operatórias.

Conclusão Os acessos minimamente invasivos foram efetivos para evacuação dos hematomas intraparenquimatosos, com resultados clínicos e tomográficos favoráveis.

Palavras-chave

- contusão cerebral
- cirurgia minimamente invasiva
- trauma cerebral
- lesões cerebrais traumáticas
- microcirurgia
- cirurgia de trauma

Introduction

Traumatic brain injury (TBI) is among the three main causes of death in several developed and developing countries. Worldwide, $\sim$ 5.4 million people die from TBI every year, with 90% of deaths occurring in underdeveloped or developing countries.[1] Neurological sequelae are frequent. In Brazil, it is estimated that $>$ 1 million people live with neurological sequelae resulting from TBI.

There are many intracranial injuries caused by TBI. They may be classified as diffuse (diffuse axonal injury and brain swelling) and focal injuries (cerebral contusion [CCo], epidural hematoma, and acute subdural hematoma).[2,3] Cerebral contusion is the most frequent focal lesion in blunt head trauma ($\sim$ 35%), although $<$ 20% of these are treated with surgery. Due to the great epidemiological relevance of CCo, it is crucial to understand its physiopathology and the most adequate treatment for the special cases that deserve a surgical approach, regarding efficiency of the procedure and good outcomes.

Case Series – Data Collection

The authors present in the present case series results of the surgical treatment of brain contusions, performed through keyhole approaches, in our institution (Hospital Pronto Socorro João XXIII, Belo Horizonte, MG, Brazil), a level I trauma center.

Data was collected regarding gender and age of the patients, as well as Glasgow Outcome Scale during hospital admission, surgical approach, and effectiveness of the procedure. Nine cases of patients with unilateral or bilateral frontal or temporal contusions who underwent evacuation through the supraorbital or minipterional keyhole approach, respectively, were analyzed,. All patients were male, with an average age of 49.2 ± 21.85 years old (range: 7–69 years old). Family members provided informed consent for the present study.

Case Series – Results

As many patients who present with CCos after TBI have concomitant intracranial injuries, which may be other focal injuries (epidural and subdural hematomas) and/or diffuse axonal injury (DAI), neurological outcomes may be heterogeneous for these groups. For this reason, the authors used in this study, as a result of effectiveness of the procedure, adequate evacuation of the intraparenchymal hematoma, confirmed by a postoperative computed tomography (CT) head scan, and the absence of need of a new surgery to treat the CCo (new hematoma evacuation surgery; decompressive craniectomy).

All nine cases submitted to minimally invasive surgical approaches (supraorbital keyhole or minipterional craniotomy) presented with satisfactory tomographic postoperative results, as shown in ►**Table 1**. ►**Figures 1** and **2** are used as examples of adequate postoperative tomographic results, from two patients included in the present study who were submitted to a minimally invasive approach for the treatment of CCo.

Table 1 Effectiveness of surgical drainage of brain contusions

Gender	Age (years old)	Glasgow Coma Scale	Chosen approach	Result
Male	43	10	Supraorbital	Effective
Male	69	8	Supraorbital	Effective
Male	69	10	Supraorbital	Effective
Male	60	9	Supraorbital	Effective
Male	57	13	Minipterional	Effective
Male	40	8	Minipterional	Effective
Male	7	13	Supraorbital	Effective
Male	61	11	Supraorbital	Effective
Male	21	13	Minipterional	Effective

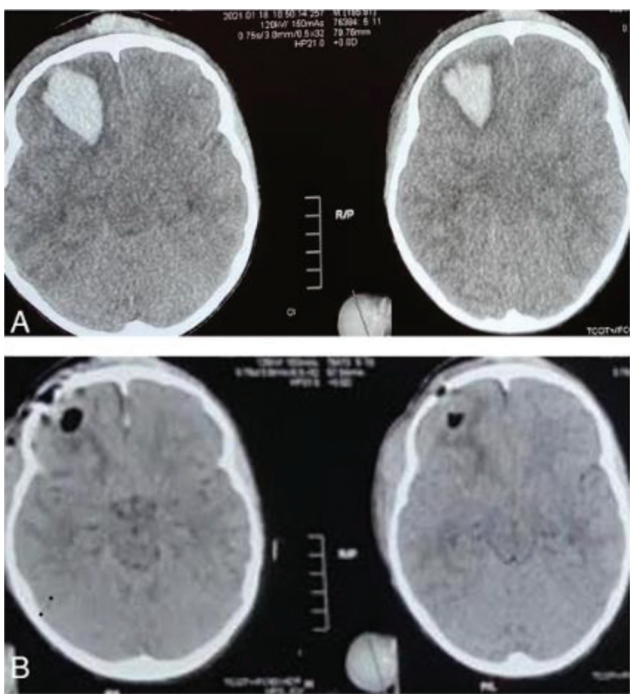

Fig. 1 Pre- (A) and postoperative (B) head computed tomographies of an effective supraorbital approach.

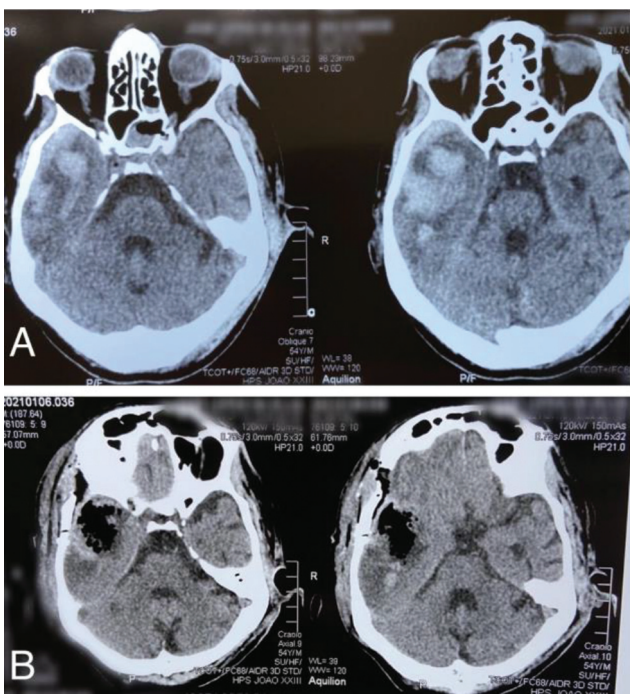

Fig. 2 Pre- (A) and postoperative (B) head computed tomographies of an effective minipterional approach.

Discussion

Cerebral contusions may arise at the direct impact site (coup injury) or at the diametrically opposite location of the impact (contrecoup injury), and they are more common at the temporal and frontal poles. Several studies have demonstrated that the CCo is formed by a "central necrotic core" and by the pericontusional penumbra, which has a lower-than-ischemic-threshold regional cerebral blood flow, and where viable nervous tissue may be saved when the intraparenchymal hematoma is treated properly.[4]

At the center of the injury (central core), organelle destruction occurs, creating a highly osmolar region. This hyperosmolar core promotes water accumulation into the injury, which leads to contusion growth, associated with hemorrhagic progression at the pericontusional penumbra.[4]

Based on the aforementioned concepts, hematoma evacuation surgery is proposed by the authors, not only to decrease local mass effect caused by the lesion, but also in order to avoid hemorrhage progression and increases on hematoma volume.

The main goal of the present study is to propose a new standard method of treating CCos, specifically the ones that require surgical treatment and may be approached using keyhole craniotomies. The authors propose that using smaller craniotomies and less invasive approaches, neurosurgeons will be able to treat properly intraparenchymal hematomas, with satisfactory clinical and radiological outcomes.

The supraorbital and minipterional keyhole approaches, performed using a minimally invasive craniotomy (as shown in ►**Figure 3**, through the schematic drawing, done by one of the authors), were first proposed in trauma surgery by Zhang

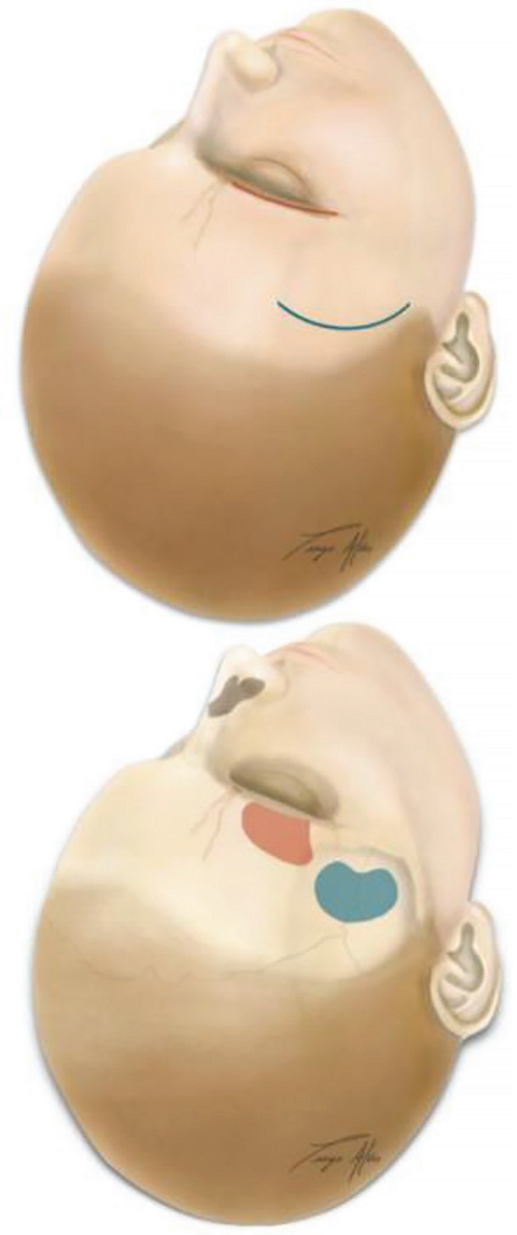

Fig. 3 Schematic drawing illustrating the keyhole approaches – incisions and craniotomies.

et al.,[5] seeking smaller approaches for the treatment of focal brain injuries. The goals of the technique are: avoidance of hemorrhagic progression of CCos, reduction of perilesional edema associated with the process of blood resorption,[6] and the immediate resolution of mass effect on the cerebral parenchyma, along with the advantages of a shorter operating time, reduction of intraoperative blood loss and, consequently, a lesser metabolic response to trauma, as proposed by Figueiredo et al.[7]

Trauma surgery is historically known for large craniotomies for the treatment of intracranial hematomas, not only for epidural and subdural hematomas, but also for CCos. Nonetheless, small areas of corticectomy are needed to approach the central core of intraparenchymal hematomas and to provide adequate hematoma evacuation and hemostasis. Therefore, why not apply the concept of the keyhole approach to directly access the desired location of the corticectomy?

Technical Note

Supraorbital Keyhole Approach

Skin Incision and Soft Tissue Dissection

The skin incision consists of a slightly curvilinear incision, along the superciliary arch, following the outline of the orbital rim, of ~ 3 to 4 cm in length. Care must be taken to avoid injury to the medial superficial neurovascular structures (supraorbital nerves and artery) near the supraorbital foramen. Some authors recommend performing the incision exactly in the haired area, in order to cover the scar and achieve a pleasing cosmetic outcome; however, others associate this technique with a risk of alopecia and worse cosmetic results, which may be avoided with an incision just above the eyebrow.

The subcutaneous tissue is dissected upwards, in a cranial direction, while the skin flap is gently mobilized downwards and retracted with stitches to expose the frontal belly of the occipitofrontal, the orbicular, and the temporal muscles.

The frontal muscles are cut with a scalpel or monopolar cautery, through a linear cut, parallel to the glabella. The temporal muscle is stripped from its bony insertion and mobilized laterally, using blunt dissection just enough to expose the pterion. The two separate frontal muscle bellies are retracted upwards and downwards (along with the orbicular muscle). The temporal muscle is retracted laterally with wound hooks in order to expose the fronto-orbital keyhole. The pericranium is dissected away from the center of the surgical field before proceeding with the craniotomy.

Craniotomy and Dural Opening

A single frontobasal burr hole is made, posterior to the temporal line, using a high-speed drill, at the level of the frontal skull base. Then, a "C" shaped craniotomy is performed with a high-speed drill, with its base parallel to the glabella, creating a bone flap with 2 to 3 cm in its largest diameters. Drilling of the inner table of the bone above the orbital rim may be performed in order to achieve better exposure of the basal surface of the skull and less brain retraction.

Durotomy can be performed through a linear or curvilinear incision, with its base toward the skull base, exposing the underlying brain parenchyma, using dural tenting sutures. ►**Figure 4** illustrates the supraorbital approach regarding the skin incision, the craniotomy, and the dural opening.

Hematoma Evacuation and Surgical Hemostasis

Through a small corticectomy (~ 1 to 2 cm), the core of the CCo is properly assessed, especially when using magnifying tools (surgical microscope). Then, the hematoma is carefully evacuated, using suction and wound irrigation. Hemostasis is performed under magnification, with gentle coagulation of

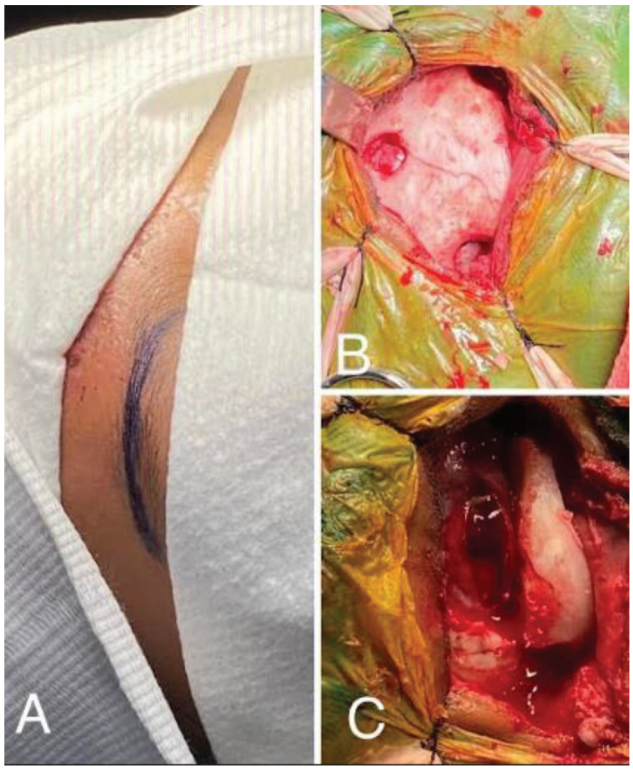

Fig. 4 Skin incision (A); craniotomy (B) and dural opening (C) are illustrated.

the friable brain parenchyma, irrigation, and use of hemostatic agents (when necessary).

Wound Closure

Watertight dural closure is carried after assurance of adequate hemostasis. The bone defect may be covered using the bone flap and titanium plates, or only a titanium mesh.

The muscle and subcutaneous tissue are closed with interrupted sutures, and the skin may be closed with intradermal, running, or interrupted sutures. As there is limited tissue trauma and bleeding using this technique, a surgical drain is not required.[8]

Minipterional Craniotomy

Surgical Incision and Tissue Dissection

This technique consists of performing a curvilinear scalp incision, ~ 1 cm anterior to the auricular tragus, which corresponds to the anterior root of the zygomatic arch, at the anterior edge of the hairline, extending rostrally towards the ipsilateral hemipupillary line, with an extension of ~ 5 cm. After dissection and exposure of the temporal muscle fascia, with preservation of the superficial temporal artery, an arcuate incision of the temporal fascia, in its most posterior extension, is performed, followed by subfascial dissection (as proposed by Spetzler et al.,[9] unlike the original interfascial technique, described by Yasargil[10]), with careful retraction of the skin flap, in order to avoid injuries to the frontal branch of the facial nerve. After subfascial dissection and protection of the deep layer of the temporal muscle fascia, along with the fat pad, a myofascial flap is then retracted with wound hooks, and subperiosteal dissection of the frontotemporal region is performed in order to expose the pterion.

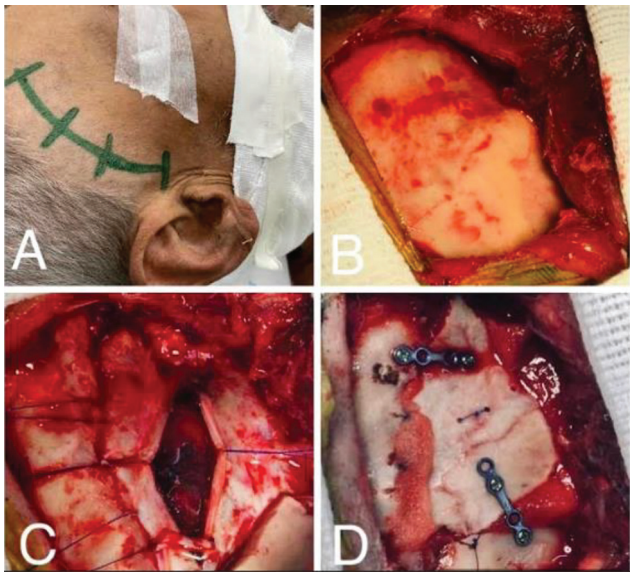

Fig. 5 Skin incision (A); craniotomy (B), dural opening (C), and wound closure (D) are illustrated, from the minipterional approach.

Craniotomy and Dural Opening

A burr-hole is placed at the upper limit of the frontozygomatic suture, below the temporal line; another burr-hole is placed at the pterion, and a third burr-hole is made at the basal region of the temporal bone. The craniotomy is completed after connecting the three burr-holes with a high-speed drill. The bone flap consists of the lateral part of the sphenoid bone, of the lower part of the frontal bone, and of a small part of the temporal bone (squamous part).

Durotomy may be performed using a curvilinear or a linear incision in order to expose the cerebral cortex and the underlying contusion. Dural tack-up sutures may be of help in order to expose the brain parenchyma. ►**Figure 5** illustrates the minipterional approach, regarding the skin incision, the planning of the craniotomy, the dural opening, and the cranioplasty.

Hematoma Evacuation and Surgical Hemostasis

After adequate exposure of the brain parenchyma, corticectomy is performed at the contusional area, with delicate dissection, in order to gain access to the core of the contusion. After evacuation of the hematoma, hemostasis is performed with bipolar cautery, irrigation, and use of hemostatic substances (if necessary).

Wound Closure

Dura mater closure is performed in a watertight fashion. Pericranial grafts may be used if duraplasty is necessary. The bone flap may be reimplanted with titanium implants or with suture threads. The temporal muscle and fascia are attached together, with interrupted sutures, just like the subcutaneous tissue. Skin closure may be performed with interrupted or running sutures.[7,11]

Conclusion

As analyzed by the effectiveness of minimally invasive approaches for the treatment of CCo, using microscopic magnification, the authors offer, through the present study, a promising guideline for the surgical treatment of traumatic intraparenchymal hematomas. With impelling results on the efficacy of hematoma evacuation, shorter operating times, and minor intraoperative blood losses, this new approach may be used as a standard protocol in the future of trauma surgery.

Conflict of Interests

The authors have no conflict of interests to declare.

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Giant Quadrigeminal Cistern Lipoma: A Case Report and Literature Review

Lipoma gigante de cisterna quadrigeminal: Relato de caso e revisão da literatura

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Arq Bras Neurocir 2024;43(2):127–130.

Abstract

We report the case of a giant lipoma of the quadrigeminal cistern in a 30-year-old female patient with headache, nausea, vomiting, and phono and photophobia. Despite the large size of the tumor, conservative treatment was chosen. Intracranial lipomas are rare benign tumors commonly associated with congenital anomalies, and their origin is related to an incorrect embryonic development. The diagnosis is made mainly by cranial computed tomographyand magnetic resonance imaging. The treatment of lipoma can be surgical or conservative, and there is no single treatment for the different patients' cases.

Keywords
- lipoma
- tectum mesencephali
- resonance imaging

Resumo

Relatamos o caso de um lipoma gigante de cisterna quadrigeminal em uma paciente de 30 anos, do sexo feminino, com cefaleia, náusea, fono e fotofobia, no qual se optou pelo tratamento conservador. Os lipomas intracranianos são tumores benignos raros comumente associados a anomalias congênitas, e sua origem relaciona-se ao mau desenvolvimento embrionário. A investigação diagnóstica é feita predominantemente através da tomografia computadorizada e ressonância nuclear magnética do crânio, e não existe um tratamento único para os diferentes quadros dos pacientes.

Palavras-chave
- lipoma
- teto do mesencéfalo
- imageamento por ressonância magnética

Introduction

Intracranial lipomas are rare, corresponding to about 0.1 to 0.5% of brain tumors[1–7] and are found, mainly, in the pericallosal and quadrigeminal cisterns, which represent, respectively, about 45 to 64% and 13 to 25% of intracranial lipomas.[1,2,8–11] Its origin is related to inadequate embryonic development, due to the involution of the primitive

received
December 1, 2020
accepted after revision
July 30, 2021
article published online
October 13, 2023

DOI https://doi.org/10.1055/s-0041-1739274.
ISSN 0103-5355.

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

meninge[1–4,6–8,10–12] commonly associated with other congenital malformations.[1,3–12] These lesions are generally asymptomatic, due to slow growth,[1,4–6,8–12] so that differentiation to a malignant character has never been reported.[1] The fact that the majority of those who have intracranial lipomas do not present symptoms makes the diagnosis difficult, causing it to occur accidentally, often among patients who have other pathologies.[1,4–6,8–12] The asymptomatic course, associated to the microscopic constitution of lipomas, composed of adipose tissue surrounded by vascular elements,[1] leads many doctors to opt for conservative treatment instead of surgery, although there are cases in which surgery is necessary, such as in patients with severe symptoms.[1,2,4,6,8,10–12] However, there is no universally accepted approach to treat intracranial lipomas, since a disease has a variable course; therefore, a choice of management must be made individually. The present case report concerns a patient with a giant quadrigeminal cisternal lipoma, who received conservative treatment, due to the absence of serious symptoms, despite the size of the lesion.

Case Report

A 30-year-old woman presented with a complaint of moderate hemicranial headache, usually in the afternoon, associated with nausea, vomiting, and phono and photophobia. These symptoms worsened with physical activity, and there were no alterations at bedtime. There was also a long-standing visual aura report. Two months earlier, she developed a change in the headache pattern, now stronger in the occipital region, without nausea, vomiting, or aura; thus, it was necessary to seek the emergency room to receive intravenous medications. The patient denied diplopia, visual cloudiness, or other signs. In the diagnostic investigation, the skull computed tomography (CT) showed a median nodular formation, with fat density and dense material measuring $2.2 \times 2.0 \times 2.5$ cm, located in the topography of the perimesencephalic cistern, which may correspond to a lipoma or dermoid cyst. The skull magnetic resonance imaging (MRI) (►**Fig. 1**) showed an extra-axial oval formation measuring $2.2 \times 1.9 \times 1.9$ cm, with a fat-like signal in all sequences located in the cistern of the quadrigeminal plate, without uptake of contrast or diffusion restriction, also suggesting as diagnostic possibilities a lipoma or a dermoid cyst. A proton spectroscopy study was performed to better elucidate the diagnosis, which revealed an extra-axial lesion in the quadrigeminal/pineal cistern, measuring $2.5 \times 2.0 \times 1.7$ cm, according to the images of the usual protocol, without evidence of brain metabolites in this topography. These characteristics strongly suggested the possibility of a lipoma. Conservative treatment was the option adopted by the team.

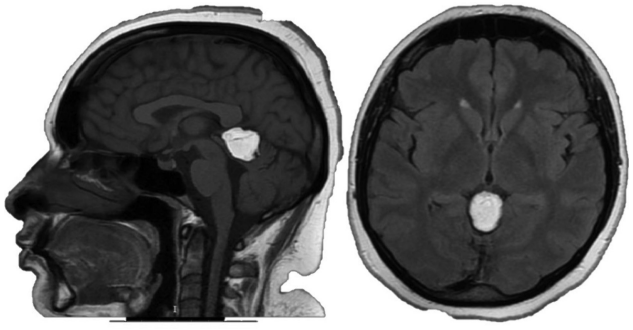

Fig. 1 Brain MRI FLAIR weighted image.

Literature Review and Discussion

Intracranial lipomas correspond to rare benign tumors, whose etiology is not fully elucidated.[1–7] There are a lot of theories about the origin of these lesions, and the prevalent hypothesis suggests that its etiology is related to inadequate development of the primitive meninges.[1–4,6–8,10–12] In addition, there is an inadequate development of the subarachnoid spaces.[7] This condition allows that nerves and vessels pass through the tumors.[7] When lipomas are located in the quadrigeminal cistern, they are generally asymptomatic or associated with mild symptoms, such as headache.[1,4–6,8–12] However, patients may manifest diplopia and hydrocephalus, due to possible compression in the cerebral aqueduct, causing signs of increased intracranial pressure.[1,2,6–13] In addition, in cases of extensive quadrigeminal lipomas, brainstem and cerebellum compression may occur, causing Parinaud syndrome and cerebellar symptoms.[1] The patient in question presented headache, nausea, vomiting, as well as phono and photophobia. Often, patients with lipoma may present associated congenital malformations, which are responsible for the appearance of some symptons.[1,3,7,9,10] Lipomas of the quadrigeminal cistern, however, are not frequently related to embryological abnormalities, as opposed to lipomas of the corpus callosum.[2,3,7–10,12] The diagnosis of lipomas is commonly accomplished through CT and MRI of the skull.[1,4–12] Confirmation made by histopathological analysis is not generally used, since the findings of these imaging tests, associated with the patient's clinical condition and the differential diagnosis are tools that show characteristics strongly suggestive of lipomas.[12] On CT, these lesions appear with marked homogeneous hypodensity and with fat density (-40 to -100 Hounsfield).[1,2,4,5,7–9,11] In MRI, in T1-weighted sequence, lipomas appear in hypersignal, whereas in T2, they present isohypointensity.[1,2,4–12] In a fat-sat T2 sequence, there is a homogeneous decrease in the lipoma region, due to its abundant adipose content.

These imaging methods are essential for the differential diagnosis, which includes other adipose lesions, such as a dermoid tumor. On the CT, both have similar characteristics, showing an aspect of hypodensity, with variation in the values acquired on the Hounsfield scale, since dermoid tumors show rates between 20 and 40 HU. On the MRI, these two lesions are also similar, as they produce high signal intensity in T1-weighted images and low signal intensity in T2. Dermoid tumors, however, unlike lipomas, may not be homogeneous on resonance, due to the presence of skin and hair.[1,2,4,5,7,9,12]

The treatment of intracranial lipomas differs according to the patient's condition and clinical manifestation, and there is no single and universal management for the resolution of these tumors. In this context, surgery to remove the tumor is

Table 1 Quadrigeminal Cistern Lipoma Reports

Article (author; year)	Gender	Age	Symptomatology	Measure	Treatment
Ammor and Ajjal; 2015[13]	M	55	Headache and complex partial seizures	3 × 2.7 cm	Conservative
Mashiko and Shibata 2014[14]	M	51	No symptoms related to lipoma**	–	Conservative
Ono et al.; 1998[15]	M	7	Seizures	–	Conservative
Baeesa et al.; 1996[16]	F	15	Headache associated with nausea and vomit	1.5 × 1.5 × 2.0 cm	Surgery - partial excision
Baeesa et al.; 1996[16]	F	Neonate	Asymptomatic	1.4 × 1.0 × 1.0 cm	Conservative
Nikaido et al.; 1995[17]	M	65	Involvement of abducent nerve	3.3 × 3.0 × 3.0 cm	Surgery – total excision
Kawamata et al.; 1995[5]	M	Neonate	Hydrocephalus	1.2 × 1.0 × 9.0 cm	Surgery*
Kapoor et al.; 2015[11]	M	31	Asymptomatic	–	Conservative
Kapoor et al.; 2015[11]	M	36	Headache e dizziness	–	Conservative
Kapoor et al.; 2015[11]	M	42	Headache	–	Conservative
Majumdar et al.; 2013[2]	M	10	Headache. vomiting associated with eyelid fall	2.5 × 2 × 1.5 cm	Surgery*
Chaurasia et al.; 2017[12]	M	19	Headache. visual disorders. hydrocephalus	2.1 × 1.9 cm	Surgery*
Rahman e Arshad.; 2014[18]	F	3	Headache	–	Conservative
Yilmaziar et al.; 2005[1]	M	37	Nausea. vomiting and headache	3 × 3 cm	Surgery–total excision
Ogbole et al.; 2019[19]	M	70	Headache and transient loss of consciousness	1.3 × 0.9 cm	Conservative

*Surgery performed for symptom relief without tumor excision.
**The patient had symptoms, but these were not caused by the lipoma.
Note: Only papers with case reports were included in the table.

usually performed in severely symptomatic patients, in order to prevent neurological deterioration.[1,2,4,6,8,10–12] In individuals with severe hydrocephalus secondary to lipoma obstruction, for example, it is possible to perform a bypass surgery in order to relieve symptoms,[2] while in those who have a marked mass effect, a resection of the tumor[1] can be chosen.[2,4,6,8,10–12]

Thus, when a surgical treatment is chosen, great caution and detail is necessary, since the tendency of the lipoma to adhere neural tissue and the presence of adjacent vascular elements makes this technique risky, so partial resection is recommended by many authors.[1–3,6]

In cases of asymptomatic individuals or those presenting mild symptoms, it is necessary to consider conservative treatment in the first instance, due to risks and difficulties of surgery, related to the fact that lipomas have a slow growth, which makes surgical management to be, many times, an unnecessary and dangerous approach.[1,2,4,6,8,10–12] Thus, as the patient in the case has an extensive lipoma, measuring 2.5 × 2.0 × 1.7 cm, but did not present very severe symptoms or signs of neurological deterioration, conservative treatment was chosen.

Several cases of patients with lipoma in the quadrigeminal cistern were selected for this literature review, following a search in the Pubmed, Cochrane Library, Scielo, and Scopus databases. Only papers with case reports were included, which are shown in ►**Table 1**. In the analysis of articles, it was observed that the manifestation of symptoms in individuals who have lipoma in this location is variable, but a large number of subjects presented headache. Moreover, due to the presented difficulties of surgical treatment, this approach was not applied to all the patients. It was observed that the excision of the tumor mostly occurred when there were alarming signals, such as those with a mass effect. However, the choice of treatment is not unique either, and the most frequently observed treatment choice in this analysis was conservative, so that surgery was an effective alternative, especially for symptom relief.

Conclusion

Intracranial lipomas are tumors characterized by slow growth and strong adherence to vascular structures and neural tissue, leading the neurosurgeon to reflect and be cautious to indicate the most appropriate conduct for the individual. Our case report concerns an extensive quadrigeminal cistern lipoma in which conservative treatment was chosen due to mild symptoms presented by the patient. In conclusion, the size of lipoma is not a determinant factor for the choice of treatment. It is necessary to analyze the patient

clinical presentation to elect the most pertinent approach for each situation.

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

Acknowledgments
The authors would like to thank the patient for her cooperation, and the hospital staff.

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Intranasal Glioma with Post-Endoscopic Resection in 1 Year Old Infant: Case Report and Literature Review*

Glioma intranasal com ressecção pós-endoscópica em bebê de 1 ano: Relato de caso e revisão da literatura

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Arq Bras Neurocir 2024;43(2):e131–e137.

Abstract

Introduction Nasal gliomas - or nasal glial heterotopias - are rare congenital malformations, which correspond to 5% of the congenital nasal masses. It is a mass composed of mature glial tissue that can be located outside, inside or near the nasal region, and may or may not be connected to the brain by a fibrous pedicle. This report addresses a case of nasal glioma that suffered recurrence after endoscopic treatment.

Case Report A 1-year-old boy has, since birth, a mass inside the left nostril, which obstructs and widens the bridge of the nose. Upon physical examination, it is observed that the mass does not increase in size with crying and presents negative transluminescence and Furstenberg test. Upon being biopsied, the lesion reveals malignancy and the presence of inflammatory cells. MRI ruled out communication with intracranial structures. The endoscopic resection of the heterotopia removed a mass of 3,0 × 2,5 × 1,7 cm, whose histological and immunohistochemical analysis revealed glial pattern cell proliferation in the nasal mucosa.

Conclusion Considering that nasal glial heterotopy is frequently present at birth, and that newborns breathe predominantly through this route, early diagnosis of the lesion is of great importance, as it can cause signs and symptoms of respiratory distress. In addition, it is worth noting that the early approach also prevents bone deformities.

Keywords
- nasal glioma
- congenital malformations
- endoscopic resection
- respiratory stress
- bone deformities

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received
January 25, 2021
accepted
June 16, 2021
article published online
April 26, 2024

DOI https://doi.org/10.1055/s-0043-1776285.
ISSN 0103-5355.

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

Resumo

Introdução Os gliomas nasais – ou heterotopias gliais nasais – são malformações congênitas raras, que correspondem a 5% das massas nasais congênitas. Trata-se de uma massa composta por tecido glial maduro que pode se localizar no exterior, no interior ou nas proximidades da região nasal, podendo ou não estar conectado ao cérebro por um pedículo fibroso. Este relato aborda um caso de glioma nasal que sofreu recidiva após tratamento por via endoscópica.

Relato do caso Um menino de 1 ano de idade apresenta, desde o nascimento, massa no interior da narina esquerda, a qual obstrui e alarga a ponte do nariz. Ao exame físico, observa-se que a massa não aumenta de tamanho com o choro e apresenta transluminescência e teste de Furstenberg negativos. Ao ser biopsiada, a lesão revela malignidade e presença de células inflamatórias. A ressonância magnética descartou comunicação com estruturas intracranianas. A ressecção endoscópica da heterotopia removeu uma massa de 3,0 × 2,5 × 1,7 cm, cujas análise histológica e imuno-histoquímica revelaram proliferação celular de padrão glial em mucosa nasal.

Conclusão Considerando que a heterotopia glial nasal frequentemente se encontra presente ao nascimento, e que os recém-natos respiram predominantemente por essa via, é de grande importância o diagnóstico precoce da lesão, já que ela pode causar sinais e sintomas de desconforto respiratório. Além disso, vale destacar que a abordagem precoce também previne deformidades ósseas.

Palavras-chave

- glioma nasal
- malformações congênitas
- ressecção endoscópica
- estresse respiratório
- deformidades ósseas

Introduction

Nasal gliomas are rare congenital malformations, which correspond to 5% of the congenital nasal masses, first described by Reid in 1852 and called "glioma" by Schmidt in 1900. Black and Smith, in 1950, defined nasal glioma as a congenital extracranial mass of mature glial tissue that can be located outside, inside the nasal cavity, in both, or near the root of the nose. The glioma may or may not be connected to the brain by a pedicle of glial tissue, it does not contain a fluid-filled space connecting it to the cerebral ventricles or the subarachnoid space. Thus, these tumors consist of remnants of neuroglial tissue that are among the differential diagnoses of congenital midline nasal masses.[1–7]

Congenital malformations are often present at birth, even if diagnosed later. Encephalocele is the most frequent midline congenital nasal mass, followed by dermoid cysts, epidermoid cysts, gliomas, teratoma and hemangiomas.[7,8] The differentiation of glioma in relation to encephalocele is of great importance, since the extracranial management of encephaloceles can increase the risk of meningitis.[6] Nasal gliomas are, therefore, of neurogenic origin and are part of the spectrum of anomalies in the development of the central nervous system, particularly neural crest cells.[1,9]

The most accepted theory regarding the emergence of nasal glioma is that of herniation of the tissue through the *fonticulus frontalis* of the *foramen cecum* displaced by the closure of the anterior neuropore, during the development of the skull base.[10] Some researchers define nasal glioma as an encephalocele that has lost its connection with intracranial contents. Thus, the encephalocele would be a protrusion of the cerebral content connected to the rest of the brain by a pedicle, associated with a bone defect, while the nasal glial heterotopia has no communication with the subarachnoid space or with the central nervous system.[4,11,12]

Bearing in mind that the heterotopic tissue represents a histologically normal tissue in an atypical location, many authors argue that the name "glioma" is not appropriate, as it is given to a neoplasm of the same constitution. For this reason, it can also be called nasal glial heterotopy.[13]

Heterotopy has an approximate incidence of one case for every 20.000 to 40.000 live births and is considered benign but can cause deformities due to its slow growth.[3,7,9,11,14,15] Some authors report that there is no gender predominance, while others believe that the anomaly is more common in boys (3:2). There is no family predisposition.[3,10]

On clinical examination, the consistency of the glioma is usually firm and can be seen as a polypoid structure in the nasal cavity. It is a mass with negative transluminescence and that does not increase with compression of the jugular vein - negative Furstenberg sign.[3,13] As for their location, 60% of the gliomas are extranasal, 20% are intranasal and 10%, mixed. Extranasals are typically lateral to the midline and can result in visual and tear changes on the affected side. There may be hypertelorism. Intranasal gliomas are firm, pale masses that can obstruct and lead to breathing difficulties, deviated septum, epistaxis or nasal congestion. They are most commonly from the lateral nasal wall. The septum and nasal bones are often displaced. Because of the obstruction due to the presence of the mass, there may be symptoms of respiratory stress.[3,6,11] Unlike gliomas, encephaloceles are deformable and pulsatile, increase with effort and crying and have a positive Furstenberg signal.[3]

Magnetic resonance imaging (MRI) is considered the exam of choice for the evaluation. The diagnosis can be

made in the pre- or post-natal period, with 60% of cases being diagnosed in the neonatal period. Although most commonly found in children, they can also be present in adults. Mass biopsy and aspiration are contraindicated due to the risk of meningitis or loss of functional brain tissue in an encephalocele. Its treatment is complete surgical resection, which can prevent complications such as meningitis, intracranial abscess and facial deformities.[4,6,7,10,15] Histologically, the tumor is characterized by the presence of nerve fibers intertwined with fibrous and vascular connective tissue. Neurons and astrocytes can be identified in some lesions. The arrangement is usually lobular and cystic structures may be present.[4]

Case Report

A 1-year-old male patient was referred to the service for a cyst in the nasal region. The mother says that the change was already present at birth. The patient was born by cesarean delivery, of a twin pregnancy, with a gestational age of 27 weeks, having remained in the neonatal intensive care unit (ICU) for ~2 months. His corrected chronological age was 9 months and two days. The mother reports breastfeeding up to five months of age, supplemented with NAN without lactose. She also reports an updated vaccination schedule. Two months before the appointment, he had been admitted for bacterial meningitis. On physical examination, an expansive nasal cavity mass, which was not enlarged with crying or exertion, with negative transluminescence and with a negative Furstenberg test, was noticed. The lesion was benign in appearance, but the possibility of esthesioneuroblastoma was considered.

A computed tomography (CT) scan of the sinus of the face (►**Fig. 1**) showed an expansive lesion with a density of soft tissues widening and obliterating the left nasal cavity, measuring 20 mm, of undetermined nature, without associated bone destruction or communication with the central nervous system. An incisional endoscopic biopsy of the lesion was then proposed. The histological study was negative for malignancy and indicated the presence of inflammatory tissue, raising the hypothesis of angiofibroma. The patient presented bronchospasm after extubation, requiring inhalation of adrenaline and dexamethasone.

Two months after the biopsy, the mother reports an increase in the tumor, followed by spontaneous reduction. She reports an episode of epistaxis after surgery. Then, it was proposed to perform an MRI examination of the face, to better assess the presence or absence of mass communication with intracranial content. MRI revealed an expansive heterogeneous solid nodular lesion in the left lateral wall and back of the nose, which protrudes and obliterates the left nasal cavity and measures ~3,0 × 2,5 × 1,7 cm, with nonspecific characteristics that differed from the hemangioma. The lesion has no intracranial connection. On physical examination, there was an increase in volume in the nasal bridge and obstruction of the left nostril with mass.

Nine months after MRI, microsurgery was performed to resect the nasal cavity / skull base tumor by endoscopy, without complications. The expansive lesion originated in the lateral nasal wall and extended to the floor of the orbit. The histological diagnosis was of cell proliferation of the glial pattern in the nasal mucosa. Immunohistochemistry (►**Fig. 2**) demonstrated the positivity of glial fibrillary acid protein (GFAP), S-100 positive protein and K_i-67 positive in 1% of the neoplastic cell nuclei. The pattern of markers corroborated for the diagnosis of glial heterotopia (nasal glioma).

After two years of follow-up of the case, a CT scan of the face (►**Fig. 3**) revealed a soft tissue lesion measuring 15 × 16 mm, located in the anterior portion of the left nasal fossa (middle / upper third) with infiltrate and thickening of the septum nasal, determining adjacent bone erosion, in addition to the presence of soft part components in the associated nasal dorsal subcutaneous. The images indicated a recurrence of the lesion, which had been resected by nasal endoscopy about a year ago. Skull CT performed in the same circumstances did not reveal any abnormalities. Another MRI scan (►**Fig. 4**) made one year after the last one, during the

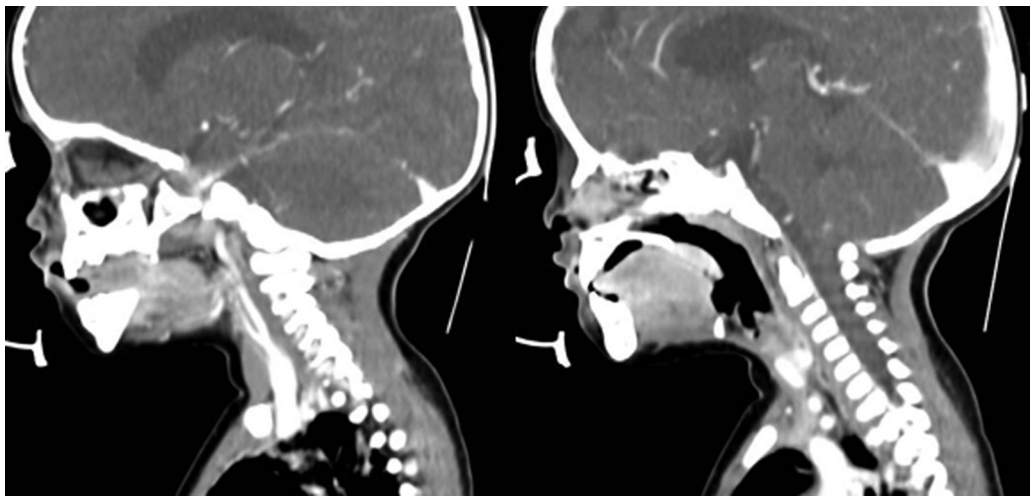

Fig. 1 Sequence of CT sections of the sinus of the face expansive lesion with a density of soft tissues widening and obliterating the left nasal cavity, measuring 20 mm.

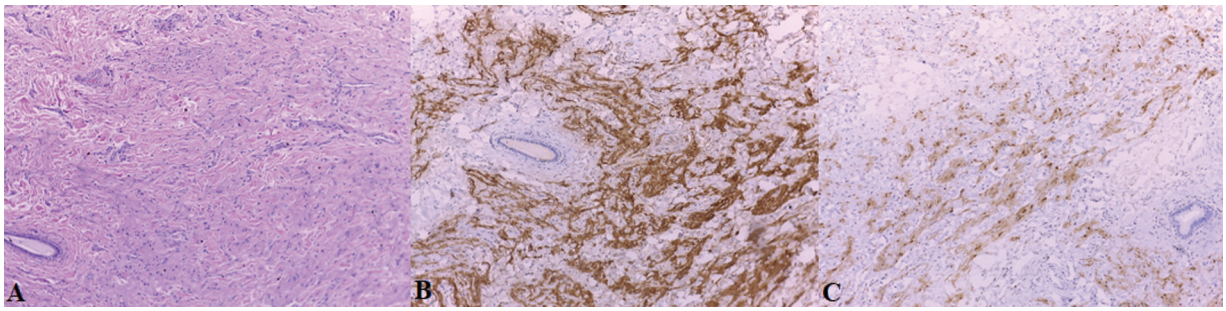

Fig. 2 (**A**) Histological section of the nasal mucosa with astrocytes and gliosis permeating the lamina propria (staining in hematoxylin and eosin, original magnification 100x). (**B**) Immunohistochemical reaction with the GFAP antibody revealed by the staining of the diamino benzidine chromogen (DAB) showing the glial tissue stained in brown and counterstained with hematoxylin (original magnification 100x). (**C**) Immunohistochemical reaction with the S100 antibody, revealed by the staining of the diamino benzidine chromogen (DAB) showing the glial tissue stained in brown and counterstained with hematoxylin (original magnification 100x).

follow-up, showed persistence of the lesion and led to the indication of a surgical procedure for removal. The removal was successful, and the patient did not experience new relapses since then.

Discussion

Nasal glioma is an anomaly of neurogenic origin with no potential for malignancy with ~300 cases reported in the literature, corresponding to ~5% of congenital nasal masses. The lesion consists of normal brain tissue and fibrous bands that can connect to the internal part of the skull in 15 to 20% of cases, which develop with a bone defect at the base of the skull.[1–3,6,8,10,16] Their growth rate is usually the same as that of adjacent tissues, but they have the potential to produce bone deformities.[1]

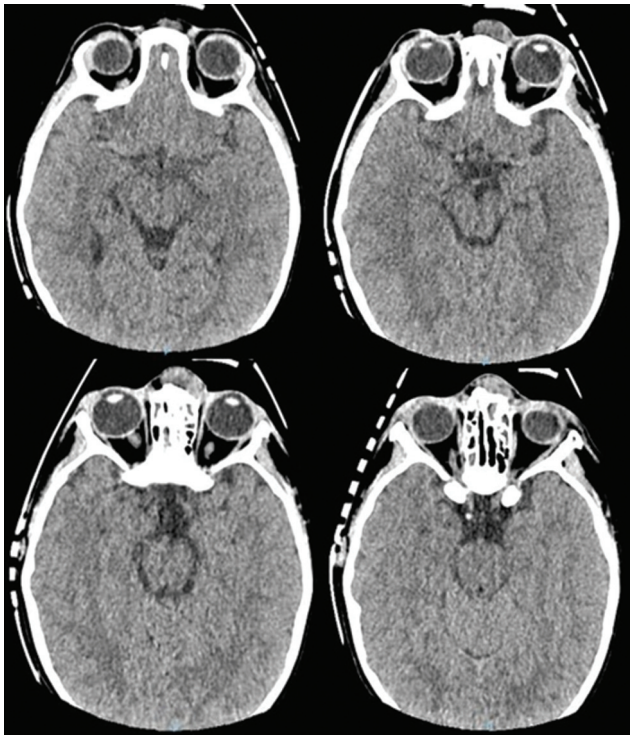

Fig. 3 Sequence of CT sections of the face showing residual lesion in the left nasal cavity (middle and upper third), measuring 15 × 16 mm, infiltrating and thickening the nasal septum and determining adjunctive bone erosion.

Intranasal gliomas are less frequent and come from the middle turbinate or the lateral nasal wall, which is common to nasal polyps. The latter are the ones with the most intracranial connection, which occurs in 35% of cases.[2,5,7,10,15–17]

Also called glial nasal heterotopy, due to the non-neoplastic nature of the lesion, gliomas are not considered hereditary. Some authors believe there is a predilection for the tumor in males, in a ratio of 3:2.[2,3,7,13]

The etiology of nasal gliomas is not well defined. There are four theories that could explain its appearance: sequestration of glial tissue from the olfactory bulb during fusion of the cribiform plaque - which would not explain the emergence of the encephalocele -, ectopic cells of neural tissue, encephaloceles with lost intracranial connection and meningeal continuity and inappropriate closure of the anterior neuropore (the *fonticulus frontalis*), however, the most accepted theory is that the glioma represents an encephalocele sequestered from intracranial brain content at the beginning of pregnancy.[2,6,8] This latter theory is called the pre-nasal space theory, and was first described by Grumwald in 1910.[11]

At the end of the 2nd month of embryogenesis, a small fontanelle - the *fonticulus frontalis* - appears, located between the nasal and frontal bones. There is also the pre-nasal space, located between the nasal bones and the nasal cartilage capsule, which extends from the base of the skull to the nasal apex. In the same period, a dura mater diverticulum (with or without arachnoid or neural tissue) protrudes anteriorly through the *fonticulus frontalis* and / or inferiorly through the pre-nasal space. This diverticulum can contact and adhere to the skin. Normally, this diverticulum regresses over time and the bone then closes, creating the nasofrontal suture and *foramen cecum* (a small channel that passes through the base of the skull before the galli crest). A defect in the regression of this diverticulum can leave ectodermal tissue in this path, preventing complete bone closure at this location, keeping the *foramen cecum* enlarged and distorting the crista galli. Depending on the patency of this

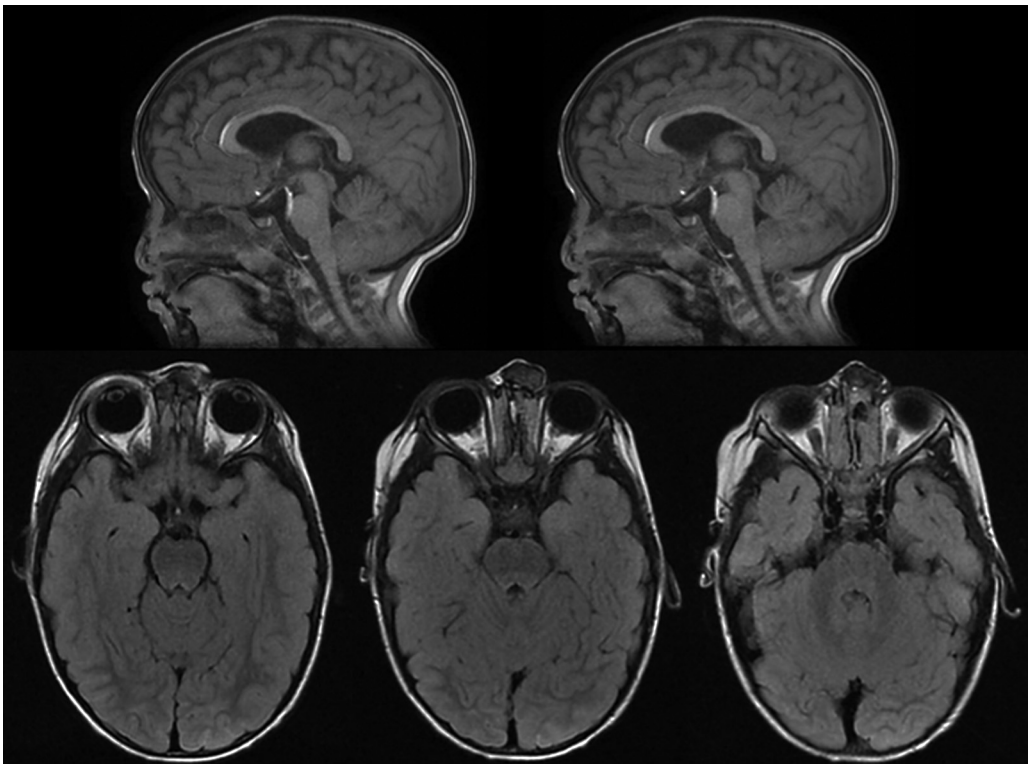

Fig. 4 Sequence of MRI sections of the face showing persistence of the residual lesion in the left nasal cavity.

diverticulum and its content, the resulting lesion may be a dermoid cyst, a glioma or an encephalocele, which are the nasal masses with the potential to link with the central nervous system.[1,5,7–9,14,15,17]

Encephalocele has the same embryological origin as nasal glioma and is an important differential diagnosis between nasal masses.[2] Encephaloceles have an incidence of one in 3.000 live births and are caused by herniation of neural tissue through defects in the skull, which may contain brain tissue and meninges or just meninges. They can communicate with the ventricular system and are always associated with a significant defect at the base of the skull. In 40% of cases, patients have other associated abnormalities. Most encephaloceles are located later, but 15 to 20% are anterior. The clinical characteristics of encephaloceles are of a soft and flexible mass, which increases with effort or crying and with a positive Furstenberg sign, with positive transluminescence. Encephaloceles can develop with CSF rhinorrhea and meningitis. Gliomas are considered encephaloceles that have lost their connection with the meninges of the intracranial space sarcomas.[9,12,13,15–18]

Dermoid cysts are also a relevant differential diagnosis. They are connected to intracranial content in 26 to 30% of cases, with an incidence of one in 6.000 live births. These are sinus tracts or cavities that have an epithelial lining and a variable number of cutaneous appendages, including hair follicles and glands. Cysts are usually solid and have no pulse. The negative transillumination test can differentiate you from meningocele. It is important to note that ~4 to 45% of the cysts contain intracranial content.[10]

Capillary hemangiomas, another differential diagnosis to be considered, present themselves as reddish masses with a surface with telangectasis - differentiation must be made through Doppler ultrasonography, since hemangiomas have a higher systolic blood peak than gliomas. Other differential diagnoses include sebaceous cysts, epidermoid cysts, papillomas, inflammatory nasal polyps - extremely rare in children -, carcinomas, lipomas, fibromas, meningiomas, lymphomas and sarcomas.[6,8,9,13–18]

Gliomas are more commonly identified at birth, but their diagnosis can also be made during a later stage of childhood or even in adulthood.[2,16] This type of congenital nasal mass is not associated with other anomalies, in most cases, but it can develop with cleft lip and palate, choanal atresia, hydrocephalus, urethral duplication and supernumerary finger.[1,5,15,16]

The form of presentation of the lesion depends on its location. Clinically, the masses are of firm consistency, non-compressible, non-pulsatile, with negative transluminescence and of a gray or purple color. The Furstenberg sign must be negative. The patient with intranasal glioma may present nasal obstruction, epistaxis, cerebrospinal fluid rhinorrhea, nasolacrimal duct obstruction, hypertelorism and bone deformities. When they produce protrusion through the nostril, they can be confused with nasal polyps.[1,4,8,15,16]

Bearing in mind that newborns are mandatory nasal breathers and that upper airway obstruction at delivery has been described among patients with nasal and nasopharyngeal gliomas, prenatal MRI imaging in the presence of suspicion is paramount for that the appropriate intervention is made at the time of birth.[7,11]

In cases of extranasal gliomas, the masses appear between the tip of the nose and the eyebrow and there may be bone deformities, hypertelorism, visual or lacrimal changes and the growth of a mass somewhere on the face.[1,2,7,16] In 5% of cases, glioma can occupy other locations, such as scalp, cheek, soft palate, tonsil, medical ear, nasopharynx, oropharynx, submandibular region and orbit.[7,15]

Surgical resection of the mass is the treatment of choice, since gliomas are not sensitive to radiation therapy. When incomplete, it results in recurrence in ~4 to 10% of cases, which may justify the use of intraoperative freezing, to define surgical margins. Therefore, in order for the excision to be the best possible, an adequate evaluation is essential to define the site, extent and content of the tumor.[1–3,7–9,15,16,18]

Prenatal ultrasound can raise the diagnostic suspicion by revealing a solid frontonasal mass, with a final diastolic characteristic of low arterial flow velocity on Doppler.[3,6,10,14] MRI is considered the best exam for the analysis of nasal glioma, as it shows in detail the soft tissues and the possibility of intracranial connection, in addition to not using radiation. Sometimes, herniation of meninges alone (meningocele) or brain and meninges (encephalocele) is evident. Contrast images should be obtained to assist in the differential diagnosis of solid masses or when infection is suspected. Computed tomography (CT) is useful in checking bone defects and in assessing the nasal roof.[1–3,5–9,11,15,16,18] When viewed through CT, the tumor mass is the same density as brain tissue. Through MRI, the lesion is isointense to hypointense in relation to the gray matter in T1-weighted images and hyperintense and heterogeneous in T2-weighted images and proton density sequence.[7,10,16] Some imaging findings that should be investigated among patients with a midline nasal mass are: enlargement of the nasal bones, enlargement of the nasal septum, nasal septum, bifid perpendicular plaque, galli bifida crest, interorbital enlargement, cribiform lamina defects and extension of the mass intracranially.[15] Since ~10 to 20% of nasal gliomas connect to intracranial structures through a fibrous band, it is unlikely that the size of the *foramen cecum* is likely to be useful to differentiate nasal gliomas from dermoid and encephalocele cysts.[1,4]

In view of the possibility of mass communication with brain tissue, any preoperative biopsy should be avoided, as it may cause spillage of cerebrospinal fluid, formation of fistula and meningitis. If there is no evidence of an intracranial glioma, a conservative extracranial approach should be performed early - preferably in the first year of life, due to the risk of developing bone deformities or secondary infection. In general, the surgical approach should be based on the location and size of the mass, bone or associated cartilage deformity and, most importantly, the surgeon's experience. Transnasal endoscopic resection is widely used for this purpose, since it allows precise excision with minimal trauma to adjacent tissues. The endoscopic examination can also be easily used for follow-up. In the presence of intracranial extension, frontal craniotomy is indicated, in addition to the multidisciplinary approach, involving otolaryngology, neurosurgery and neuroradiology.[1–3,7–9,14–17] Macroscopically, differentiating the glioma from brain tissue is difficult in the presence of a mass filament. In these cases, broad resection and repair of the bone defect with dural graft, bone wax or methacrylate are considered1. For extranasal gliomas, an external incision must be performed (lateral rhinotomy, open rhinoplasty, midline incision or bicoronal incision). A conservative and aesthetic incision is recommended, since the glioma is benign and recurrence is rare.[7,8]

The largest series of cases of nasal glioma ever reported was published by Rahbar et al, who described 9 cases in infants during 32 years of study. Five patients underwent intra or transnasal excision. Among the four patients with extranasal gliomas, two external rhinoplasties, a lateral rhinotomy and a median rhinotomy were performed.[17]

The diagnosis is confirmed by histological evaluation, through which a mass without capsule is identified, with mature astrocytic cells of eosinophilic cytoplasm with varying proportion of fibrous and vascular connective tissue, which can be covered by skin or nasal respiratory mucosa. Mitoses are often absent. There may be malignant histological features similar to those of astrocytoma, but there is no potential for malignancy. The presence of leptomeninges, ependyma and choroid plexus are compatible with the diagnosis of encephalocele. In 40% of cases, some degree of inflammation and calcifications and ependymal cystic degeneration can also be seen occasionally. Immunohistochemistry has an important role in the analysis of tumors. The glial and neuronal nature of cells is demonstrated by the presence of the S100 protein, GFAP, NSE (neuron specific enolase) and vimetida.[3–7,10,15–17] Neuronal cells, when present, are sparse and not prominent. The Ki67 and p53 markers are negative among gliomas.[15]

Conclusion

Nasal gliomas are rare congenital anomalies that must be considered among the differential diagnoses of nasal masses in newborns, as well as dermoid cysts and encephaloceles. Diagnostic suspicion can be made in the prenatal period, first through Doppler ultrasonography and, later, by MRI. Imaging exams are mandatory to exclude the intracranial extension of the mass. In the case of intranasal glioma, the treatment of choice is endoscopic resection. The approach to extranasal gliomas may vary according to their location. In the presence of intracranial communication, craniotomy is indicated. Early intervention favors the prevention of facial deformities and secondary infections. Diagnostic difficulty can be found in children older than 1 year, in view of the atypical presentation of the condition.

Ethics statement

Este estudo está em conformidade com todas as diretrizes institucionais relativas a seres humanos. O consentimento informado foi obtido do responsável pelo paciente.

Disclosure statement

Os autores declaram não haver conflitos de interesse.

Funding
Nenhum financiamento direcionado foi relatado.

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A Rare Case of Clival Hemangioma Simulating Chordoma

Um caso raro de hemangioma clival simulando cordoma

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Arq Bras Neurocir 2024;43(2):e138–e141.

Abstract

Primary intraosseous hemangiomas are rare, benign, vascular malformations that account for ∼1% of all primary bone neoplasias. A 59-year-old female patient with unknown comorbidities had a history of headache, visual impairment and dizziness that led to the diagnosis of a clivus tumor. Two resections were attempted through transcranial and transnasal transsphenoidal approach in the last two years in another hospital. The initial MRI scan showed an expansive lesion with T2 hyperintense signal and diffuse, heterogenic contrast enhancement. Clival chordoma was the main diagnostic hypothesis done. A CT scan was performed to evaluate the extent of clival invasion, the sinus anatomy, and the clival destruction - all simulating clival chordoma. The interdisciplinary tumor board decided to proceed with endoscopic endonasal tumor resection. There were no postoperative complications and the histopathological analysis revealed a primary intraosseous haemangioma. Skull base intraosseous hemangiomas are rare entities, with a limited number of case reports found after literature reviews, especially in the clival region. The clinical pattern and imaging characteristics can vary widely according to the tumor extension and development, simulating some other common tumors found at this topography. We present a case report of a clival intraosseous hemangioma presenting as an isolated abducens paresis with a positive outcome after intranasal endoscopic resection after two years of follow-up.

Keywords
- chordoma
- hemangioma
- neurosurgery
- tumor

Resumo

Os hemangiomas intraósseos primários são malformações vasculares benignas raras que representam cerca de ∼1% de todas as neoplasias ósseas primárias. Uma paciente de 59 anos do sexo feminino com comorbidades desconhecidas história de cefaleia deficiência visual e tontura que levou ao diagnóstico de tumor de clivus. Duas ressecç ões foram tentadas por via transcraniana e transesfenoidal transnasal nos dois anos anteriores ao presente estudo em outro hospital. A ressonância magnética inicial

Palavras-chave
- cordoma
- hemangioma
- neurocirurgia
- tumor

received
October 9, 2020
accepted
March 9, 2021
article published online
May 2, 2024

DOI https://doi.org/10.1055/s-0041-1731061.
ISSN 0103-5355.

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

mostrou lesão expansiva com sinal hiperintenso em T2 e realce difuso e heterogêneo pelo contraste. Cordoma clival foi a principal hipótese diagnóstica. Uma tomografia computadorizada foi realizada para avaliar a extensão da invasão clival a anatomia do seio e a destruiç ão clival - todas simulando cordoma clival. A comissão interdisciplinar do tumor decidiu prosseguir coma ressecç ão endoscópica do tumor endonasal. Não houve complicaç ões pós-operatórias e a análise histopatológica revelou hemangioma intraósseo primário. Os hemangiomas intraósseos da base do crânio são entidades raras com número limitado de relatos de casos encontrados após revisões da literatura principalmente na região clival. O padrão clínico e as características de imagem podem variar amplamente de acordo com a extensão e desenvolvimento do tumor simulando alguns outros tumores comuns encontrados nesta topografia. Apresentamos um relato de caso de hemangioma clival intraósseo apresentando-se como uma paresia isolada do abducente com evoluç ão positive após ressecç ão endoscópica intranasal e dois anos de acompanhamento.

Introduction

Primary intraosseous hemangiomas are benign, vascular malformations that account for ~1% of all primary bone neoplasias. These tumors are commonly found in the calvarium and vertebral bones but are distinctly unusual in the skull base, where they represent 0.2% of bony neoplasias and 10% of benign skull tumors.[1] We present a case of primary intraosseous hemangioma of the clivus simulating a chordoma and a review of the pertinent literature.

Case Report

A 59-year-old female patient with unknown comorbidities had a history of headache, visual impairment and dizziness that led to the diagnosis of a clivus tumor. Two resections were attempted through transcranial and transnasal transsphenoidal approach in the last two years in another hospital. She reported no neurological symptoms after those interventions. Months later presented with a new isolated right abducens paresis at the emergency service of a tertiary hospital. The patient was awake, fully oriented and pupils were equal, reactive to light and accommodation. There were no signs of meningeal irritation, no other cranial nerves affected. The remaining examination showed no abnormalities except for right abducens paresis.

The initial MRI scan (►**Fig. 1**) showed a $3.6 \times 3.4 \times 3.4$ cm expansive lesion with T2 hyperintense signal and diffuse, heterogenic contrast enhancement. The geometric center was sitting at the basal portion of the sphenoidal bone (clivus), with no cavernous sinus invasion. The mass expanded within the clivus infiltrating the sphenoidal sinus anteriorly and the pre-pontine cistern and clinoid processes posteriorly, where it touched the ventral portion of the pons and basilar artery. Cranially, the lesion expanded through the pituitary gland and anteriorly to the clinoid process. The cavernous sinus, internal carotid and petrous apex were involved, including the optic canal.

Clival chordoma was the main diagnostic hypothesis done. A CT scan was performed to evaluate the extent of clival invasion, the sinus anatomy, and the clival destruction - all simulating clival chordoma. The interdisciplinary tumor board decided to proceed with endoscopic endonasal tumor resection. There were no postoperative complications and the histopathological analysis revealed a primary intraosseous haemangioma (►**Fig. 2**).

The right abducens paresis regressed after the first year of follow up. A new MRI scan performed 6 months after surgery showed near-total resection. The patient is currently in the second year of follow up with no neurological symptoms and the small enhancement at the lower clivus remains stable.

Discussion

Primary intraosseous hemangiomas (PIH) of the skull base are extremely rare tumors. They appear typically in the parietal and frontal bones of the calvarium, whereas location in the craniofacial bones is less common (zygoma, maxilla, mandible, and vomer).[2] The particular clinical evolution and especially the risks inherent to the surgical approach make the management of skull base intraosseous hemangiomas significantly different from those arising in cranial vault bones. Furthermore, an additional challenge in preoperative diagnosis is due to the lack of cases reported in the literature and to the fact that this type of lesion can simulate other

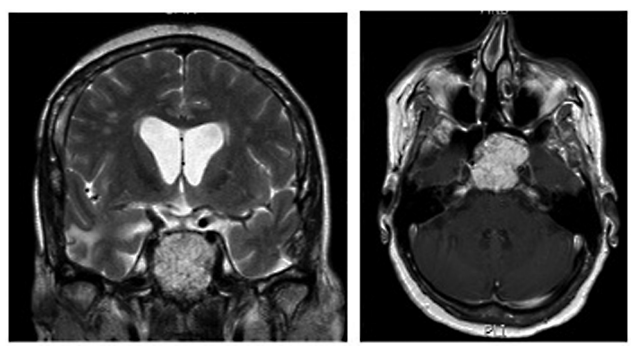

Fig. 1 T2 coronal and T1-weigthed axial images revealing a hyperintense lesion with diffuse enhancement after gadolinium injection.

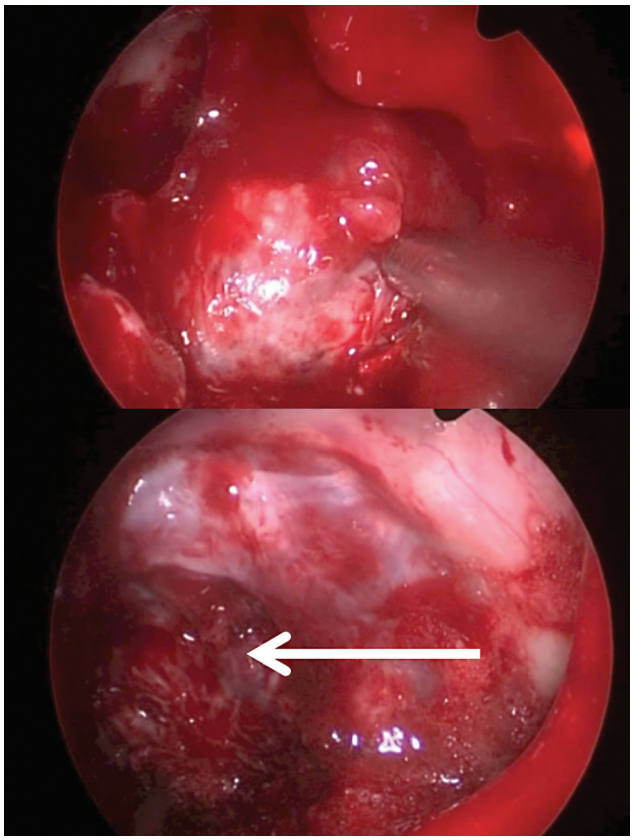

Fig. 2 Intraoperative endoscopic view before (above) and after (below) tumor resection.

common lesions of the skull base (i. e., clival chordoma, pituitary adenoma).[3]

The few published cases of clival PIH tell us that while these tumors can present with progressive cranial nerve deficits, they usually expand extracranially with minimal symptomatic manifestations. Neurological deficits are unusual. However, when intracranial extension is present, they tend to grow very slowly, leading to headaches, visual impairment or other cranial nerve deficits. Additionally, skull base intraosseous hemangiomas may involve neighboring structures, including cavernous sinus and carotid artery.[4] Interestingly, our patient presented with an isolated right abducens paresis - the same pattern of presentation that was recently described by Serrano et al.[5] In their case, the paresis remitted during the early postoperative follow-up, suggesting that opening the tumor cavity relieved the intratumoral pressure and, therefore, improved its compressive effect on the abducens nerve. In our case, however, the paresis improved after almost one year of postoperative follow-up, an outcome reported in no other case throughout the literature.

PIH are usually solitary tumors most commonly found in women between the second and fifth decades. Histologically, they can be classified as cavernous or capillary hemangiomas. Cavernous ones are composed of large dilated blood vessels separated by fibrous tissue, whereas capillary ones lack fibrous septa and have smaller vascular lumens. Calvarial hemangiomas are usually of the cavernous type, whereas vertebral hemangiomas are most frequently of the capillary type.[6]

Concerning the radiological features, there is little difference between the vertebral, commonly found hemangiomas and the skull base ones. The imaging study of choice is the MRI scan, but the characteristics can change in both T1 and T2-weighted sequences according to the amount of venous flow and fatty transformation within the tumor. Lesions with more significant fat content present high signal intensity on T1-weighted images, whereas larger lesions tend to have lower signal intensity. On T2-weighted images, high signal intensity may be caused by the pooling of blood or slow-flowing blood.[2] Cavernous hemangiomas typically enhance after administrations of gadolinium contrast.[7] As in our case, the radiographic findings are nonspecific and can mimic various common lesions of the skull base. Consequently, the diagnosis is most often made after surgical resection and histopathological analysis. In terms of surgical planning, the CT scan is more helpful than the MRI, for the first can evaluate more accurately where the extent of the lesion, the nasal and sinus endoscopic possibility approach on the bone windows.

Reports of PIH show they have a slow growth tendency, but they do not seem to show involution. Therefore, symptomatic tumors should be removed “en bloc” when possible, because the recurrence after this approach is uncommon.[8,9] In our case, the tumor was resected progressively through transnasal and extradural approaches and had no identified adherence to the meninges. Macroscopically, the gross tumor removal was achieved, even though the MRI after surgery may suggest some residual tumor. Once the transnasal approach was selected, a pedicled nasoseptal vascularized flap was used over the dura mater due to the risk of cerebrospinal fluid (CSF) fistula, even though this event was not observed during surgery. The patient remained with no signs or symptoms of CSF leak in the postoperative period.

Relevant differential diagnoses of clivus lesions include chordoma, chondroma, chondrosarcoma, osteosarcoma, osteoblastoma and metastasis. These lesions have differential imaging features and also more aggressive clinical presentations - particularly chondrosarcomas, osteosarcomas and metastases. (2). Finally, the definitive diagnosis is often obtained after biopsy and histological examination of the resection specimen by an experienced pathologist aware of the histopathological features found in PIH tumors. The choice of the surgical technique is of particular importance – in our case, conventional pterional approaches that had been attempted in two institutions were unsuccessful in removing the macroscopic lesion.

In terms of adjuvant therapy for PIH, some authors have suggested that fractionated radiotherapy can be offered as an alternative in patients with partial resection, as well as in high-risk elderly patients.[3] However, as these tumors usually grow slowly, a conservative follow-up of residual lesions is often more reasonable than to submit a patient to radiation and its well-known side effects.[10,11] Moreover, the proximity of the lesions to the cavernous sinus - of which the present case is an excellent example - increases the risk of radiation-

induced cranial nerve deficit and hypopituitarism. Once we obtained complete resection in our patient, no adjuvant treatment was prescribed and no neurological symptoms or deficits have been related during the post-operative period.

Conclusion

Skull base intraosseous hemangiomas are rare entities, with a limited number of case reports found after literature reviews, especially in the clival region. The clinical pattern and imaging characteristics can vary widely according to the tumor extension and development, simulating some other common tumors found at this topography. We present a case report of a clival intraosseous hemangioma presenting as an isolated abducens paresis with a positive outcome after intranasal endoscopic resection after two years of follow-up. Additionally, we discuss key imaging and clinical particularities of this rare type of tumor.

Note

This article was developed in collaboration between the departments of Neurosurgery from the Federal University of Rio Grande do Sul (Porto Alegre, RS, Brazil), and the University of Sao Paulo (São Paulo, SP, Brazil).

Disclosure

The authors have no disclosures.

Funding

There was no funding for this article.

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Modified Technique to Protect the Superior Sagittal Sinus in Cranial Vault Reconstruction for Scaphocephaly

Técnica modificada para proteger o seio sagital superior em reconstrução da calota craniana por escafocefalia

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Arq Bras Neurocir 2024;43(2):e142–e147.

Abstract

Scaphocephaly remains the most prevalent form of isolated single-suture synostosis. In most Pediatric Neurosurgery Centers, the treatment consists of extensive calvarial reshaping operations which are performed in relatively late ages. We described a modified open technique of cranial vault reconstruction for scaphocephaly and we report the anesthetic approach and how it influences our results and enables the performance of this surgery at earlier ages. A total of 47 patients with an average age of 11 ± 2.72 months underwent to the same surgical technique. Blood transfusion during the surgical intervention was needed in 25 patients (53%), and 22 patients (46.8%) did not need blood transfusion. None of the 14 patients who used tranexamic acid (TXA) needed blood transfusions. We reported a statistically significant association between the use of TXA and blood transfusion ($p < 0.0001$), with a decreased need for blood transfusion with the use of TXA. Besides sagittal suturectomy, we create new parasagittal sutures by replacing the prematurely fused one, and 1.5 cm of the anterior segment of bone of those 2 rectangular structures are cut before fixation, to enable the immediate shortening of the anteroposterior (AP) diameter of the skull. Finally, we put a mesh plate (SonicWeld Rx, KLS Martin Group, Tuttlingen, Baden-Wuerttemberg, Germany) over the superior sagittal sinus (SSS), which is fixed anteriorly and posteriorly with pins (SonicPins Rx, KLS Martin Group). This procedure enables an immediate reduction of the AP diameter of the skull, with no further therapies needed, and promotes a wide decompression and remodeling of the skull. With an experienced

Keywords
- scaphocephaly
- superior sagittal sinus

received
July 2, 2023
accepted
February 21, 2024
article published online
April 26, 2024

DOI https://doi.org/10.1055/s-0044-1786049.
ISSN 0103-5355.

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

surgical team and an anesthesiologic protocol, we were able to perform this surgery at early ages, requiring no blood transfusions.

Resumo

A escafocefalia continua sendo a forma mais prevalente de sinostose isolada de sutura única. Na maioria dos Centros de Neurocirurgia Pediátrica, o tratamento consiste em extensas operações de remodelação calvária, realizadas em idades relativamente tardias. Descrevemos uma técnica aberta modificada de reconstrução da calota craniana para escafocefalia e relatamos a abordagem anestésica e como ela influencia nossos resultados e permite a realização desta cirurgia em idades mais precoces. Um total de 47 pacientes com idade média de 11 $\pm$ 2,72 meses foram submetidos à mesma técnica cirúrgica. A transfusão sanguínea durante a intervenção cirúrgica foi necessária em 25 pacientes (53%) e 22 pacientes (46,8%) não necessitaram de transfusão sanguínea. Nenhum dos 14 pacientes que usaram ácido tranexâmico (TXA) precisou de transfusões de sangue. Relatamos uma associação estatisticamente significativa entre o uso de TXA e transfusão de sangue ($p < 0,0001$), com diminuição da necessidade de transfusão de sangue com o uso de TXA. Além da suturectomia sagital, criamos novas suturas parassagitais substituindo a fundida prematuramente, e 1,5 cm do segmento anterior do osso dessas duas estruturas retangulares são cortados antes da fixação, para permitir o encurtamento imediato do diâmetro ântero-posterior (AP) do crânio. Por fim, colocamos uma placa de tela (SonicWeld Rx, KLS Martin Group, Tuttlingen, Baden-Wuerttemberg, Alemanha) sobre o seio sagital superior (SSS), a qual é fixada anterior e posteriormente com pinos (SonicPins Rx, KLS Martin Group). Este procedimento permite uma redução imediata do diâmetro AP do crânio, sem necessidade de terapias adicionais, e promove ampla descompressão e remodelação do crânio. Com uma equipe cirúrgica experiente e um protocolo anestesiológico, conseguimos realizar esta cirurgia em idades precoces, sem necessidade de transfusões sanguíneas.

Palavras-chave
- escafocefalia
- seio sagital superior

Introduction

The premature fusion of the sagittal suture, known as scaphocephaly, remains the most prevalent form of isolated single-suture synostosis, accounting for 40% to 60% of all cases of craniosynostosis.[1,2] The cranium acquires an elongated form with an enhancement of anteroposterior (AP) distance, which is typically accompanied by a bulging forehead and/or a prominent occiput, due to the shape of the coronal and lambdoid sutures. The aim of surgery is to oppose the abnormal longitudinal growth of the skull favoring its latero-lateral enlargement.[3]

The first surgical treatment for sagittal craniosynostosis was performed by Lannelongue in 1892, which consisted in a simple linear sagittal suture craniectomy.[1] Between 1969 and 1990, inadequacies in the results secondary to early reossification led to modifications in this technique to more extensive calvarial reshaping operations, such as the *Renier H* technique and *Pi* procedure.[2,4,5]

More recently, after 1990, there has been a renewed interest in simple linear sagittal suturectomy with spring-assisted surgery or with minimally-invasive endoscopic procedures. However, with the spring-assisted procedure, a second surgery is necessary to remove the metal springs, and with the endoscopic approach, a molding helmet therapy is required to obtain a good long-term cosmetic outcome.[6,7] The esthetic results are not immediately visible in the postoperative period with both of these techniques.

There are many surgical options and opinions about the best operative treatment, but no definitive guidelines have been established, and there is a lack of studies to support or favor a particular surgical technique.[8]

The purpose of the present paper is to describe a modified technique of cranial vault reconstruction, an open approach, that we have used at Centro Hospitalar Universitário São João (CHUSJ) for scaphocephaly. Clinical observation and physical examination with head measurements were the main parameters to propose surgery – elongated head, manual palpation of a bony prominence over the sagittal suture, and biparietal and bitemporal narrowing are the main criteria for early surgery.

With the present technical note, the surgery immediately enables the reduction of the AP diameter of the skull, and does not require the use of a helmet.

Extensive blood loss is common in pediatric craniosynostosis reconstruction surgery. Tranexamic acid (TXA) is increasingly used to reduce perioperative blood loss in various settings, but data on its efficacy in children are limited.[9] Here, we also aimed to report the anesthetic approach with the use of TXA, and how it has influenced our results,

as far as blood loss is concerned, enabling the performance of this surgery at earlier ages.

Materials and Methods

We designed a retrospective study to analyze the children with scaphocephaly who were surgically treated by an individual team and with a modified technique of cranial vault reconstruction, from January 2010 to December 2021 at CHUSJ.

Only children with isolated sagittal synostosis were included in the study, while those diagnosed with closing of other cranial sutures in addition to the sagittal and patients with syndromic or complex craniosynostosis were excluded.

All patients underwent a preoperative physical examination and three-dimensional computed tomography (CT). The following determinants were evaluated: age at the time of the surgery, gender, need for blood transfusion, use or not of TXA, and surgery complications.

Statistical Analysis

The continuous variables were expressed as mean, median, standard deviation, minimum, and maximum values, whereas the categorical variables were reported as frequencies and percentages. For the correlation analysis regarding the continuous variables, with normal distribution or not, the Pearson coefficient and Spearman correlation were used respectively. For the correlation analysis involving the categorical variables, the Chi-squared test was used. Values of $p < 0.05$ were considered statistically significant. The IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, United States) software, version 23.0, was used for the statistical analyses.

Surgical Technique

The operation is performed with the patient in the prone position with the head positioned on a horseshoe headrest to protect the eyes. The head is slightly elevated, retroflexed, and we use antidecubitus gel cushion to protect the shoulders and hip. An air-warming blanket is placed over the patient's body. The head is shaved in the operating theater and the skin is thoroughly prepared with antiseptic-colored tincture.

We perform a skin scalp incision in the retrocoronal plane from one ear to the other. A unique subgaleal and pericranium flap is elevated to visualize the calvarium from the anterior fontanel region and coronal suture to the lambdoid suture. This *one-layer flap* helps to preserve the pericranium, which is important to further promote osteosynthesis. Meticulous hemostasis of the soft tissue and bone is performed using bipolar cautery and bone wax.

The modified technique of cranial vault reconstruction started with a classic sagittal suturectomy by removing all the sagittal strip craniectomy of bone from the superior sagittal sinus (SSS). With the present technical note, we additionally create 2 AP rectangular structures by performing a strip craniotomy with 1.5 cm in width, parallel and 1.5 cm next to the SSS, stuck by a posterior pedicle of bone to the lambdoid suture but free of the coronal suture. With this maneuver, we create new parasagittal sutures replacing the prematurely fused sagittal suture.

Before fixation, 1.5 cm of the anterior segment of bone of those 2 rectangular structures parallel to the SSS are cut, to enable the immediate shortening of the AP diameter of the skull (►**Fig. 1**).

Laterally, on the parietal bones, toward the squamosal sutures, parallel barrel stave osteotomies with 0.5 to 1 cm in width are performed, as well as removal of the most anterior precoronal bone barrel on each side.

Then, a force-compressing maneuver shortens the AP skull distance and the 2 rectangular structures, parallel to the SSS, advance toward the frontal bone and are fixed with absorbable 2/0 stitches in this new position (►**Fig. 2**).

With the 1.5-cm osteotomy and fixation, we immediately reduce the AP diameter. The extent of calvary shortening in the AP diameter is notorious since then, with correspondent widening in latero-lateral cranial diameter.

Finally, we put a mesh plate (SonicWeld Rx, KLS Martin Group, Tuttlingen, Baden-Wuerttemberg, Germany) over the SSS, which is fixed anteriorly and posteriorly with pins (SonicPins Rx, KLS Martin Group). These mesh and pins are made from *poly-D, L-Lactic Acid* (PDLLA), which is a synthetic total absorbable and osteoinductive material (►**Fig. 3**). The mesh can be easily and flexibly adapted to the bone surface after softening in a water bath heated to 60° C, and once cooled down, the material reliably retains its new shape, turning rigid again.

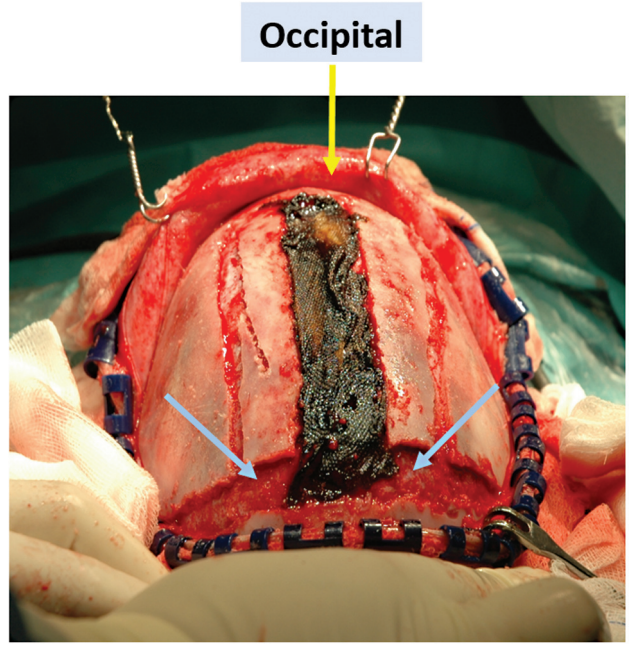

Fig. 1 Sagittal suturectomy and creation of two anteroposterior (AP) rectangular structures with 1.5 cm in width, parallel to the superior sagittal sinus (SSS), stuck by a posterior pedicle of bone and free of the coronal suture. Cut of 1.5 cm of the anterior segment of bone of the two rectangular structures parallel to the SSS (blue arrow).

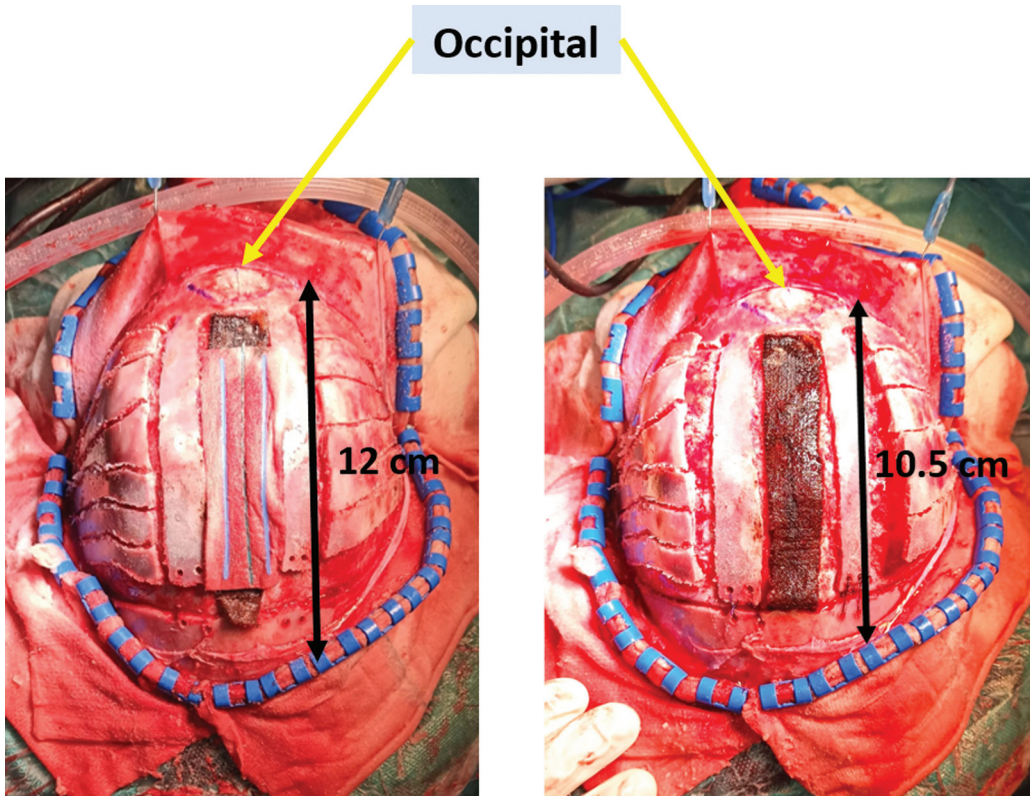

Fig. 2 Left side: cranial vault before the fixation and reduction of the AP cranial diameter; right side: after the force-compressing maneuver and fixation with immediate reduction of the AP cranial diameter.

The periosteal and subcutaneous flap and skin incision are then closed; a subgaleal drain is not used.

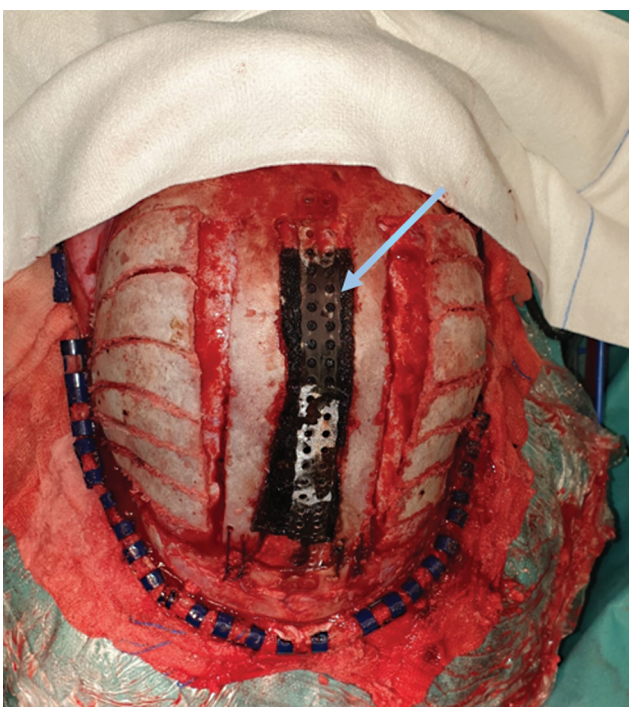

Fig. 3 Mesh plate (SonicWeld Rx, KLS Martin Group) over the SSS (blue arrow).

Results

In total, 47 (42 male and 5 female) patients underwent to the same surgical technique performed by the same surgical team. All patients underwent preoperative CT scans, but, as a matter of routine, postoperative CT scans were not performed, unless the patient showed signs of complications.

In the whole sample, the surgical procedure was performed at an average age of 11 ± 2.72 months. Before the use of TXA (before 2019), the mean age of the children at the time of the surgery was of 12 ± 2.93 months. After 2019, the mean age of the children was of 10 ± 2.31 months.

Blood transfusion during the surgical intervention was needed in 25 patients (53%), and 22 patients (46.8%) did not need blood transfusion. Regarding TXA, it was used in 14 patients (30%). and 33 patients (70.2%) did not receive it. None of the 14 patients who received TXA needed blood transfusions. Of the 33 patients who did not receive TXA, 8 did not need a blood transfusion, but 25 did (►**Table 1**). With the Chi-Square test, we reported a statistically significant association between the use of TXA and blood transfusion ($p < 0.0001$), with a decreased need for blood transfusion with the use of TXA.

No intraoperative complication for the proposed operative technique was identified. We reported 2 postoperative complications (4.26%): 1 wound infection with no need of revision surgery and 1 case of cervical cellulitis which was resolved with antibiotic therapy. The average postoperative follow-up was of 11 ± 3.7 (minimum: 6; maximum: 16) months.

Table 1 Crosstabulation of blood transfusion and administration of tranexamic acid

		Tranexamic acid		Total
		No	Yes	
Blood transfusion	No	8	14	22
	Yes	25	0	25
	Total	33	14	47

Discussion

The one intraoperative advantage of an open cranial vault reconstruction is related to the large exposition of the skull, which enables the safe removal of the sagittal strip craniectomy of bone from the SSS. This enables a safer control of the SSS and the possibility of controlling any dural tears that might occur.

With our modified technique, first we create 2 rectangular bone pillars parallel to the SSS and remove 1.5 cm of the anterior segment of bone of those rectangular structures for frontal fixation. With this technical note, we immediately reduce the AP diameter of the skull, with cosmetic correction visible at the end of the surgery. The location and the number of the parietal barrel stave osteotomies can be easily tailored on the deformed cranium, enabling a targeted enlargement in the regions where the narrowing is greater. The surgical planning can be made in a digital workstation or even manufacturing some cutting guides (KLS Martin Group).

Despite the minimally-invasive nature of endoscopic surgery, it also carries some surgical risks and difficulties during the procedure. The detachment of the dura mater from the inner surface of bones in the craniotomy area can be difficult due to the small opening, increasing the risk of durotomies. Hemostasis is another important problem in this kind of procedure, and it should be performed at each stage during the surgery. There is a high risk of damage to the SSS and its repair can be complex in a minimally-invasive approach. It is important to note that a successful long-term outcome with endoscopic repair is critically dependent on postoperative molding with helmet (orthotic) therapy to augment the cranial index, which increases the costs associated with the procedure as well as its complications, such as alopecia.[7]

Spring-assisted cranioplasty has been proposed as an alternative to total calvarial remodeling. However, some of the major drawbacks include the need for a second procedure for removal, the lack of published long-term follow-up, and the fact that, in groups of older patients, further remodeling surgery is required.[10]

With the type of technique herein described, there is no need for any postoperative or preoperative molding therapy or later surgeries; therefore, further treatment is not required.

Comparing our modified technique of cranial vault reconstruction with other extensive calvarial reshaping operations, such as the *Renier H* technique and the *Pi* procedure, we create new parasagittal sutures replacing the prematurely fused one and we immediately reduce the AP diameter of the skull. With the unique application of the mesh plate over the SSS, we can protect it from traumatic brain injury, which is so common at these ages. Additionally, it is a reinforcement of the bone suture performed to obtain the shortening of the AP diameter of the skull. This technique with this type of mesh and pins has never been described before, and the patients do not need further surgeries to remove the material incorporated.

Reducing blood loss and transfusion requirements has been an endless question in this type of cranial vault reconstruction.[11,12] Tranexamic acid is an antifibrinolytic drug which has demonstrated a significant reduction in perioperative blood loss in many pediatric surgical procedures. Interest in using TXA in craniosynostosis surgery has risen since the publication of randomized controlled studies in 2011.[9] Goobie et al.[9] stated that TXA is effective in reducing blood loss and transfusion requirements in children undergoing craniosynostosis surgery; they reported a mean blood loss of 65 mL in the group that received TXA, and a mean blood loss of 119 mL among the patients who did not received TXA ($p < 0.001$).

In the sample of the present study, we observed a statistically significant association between the use of TXA and blood transfusion, with a decreased of need for blood transfusion with the use of TXA ($p < 0.0001$). According to Martin et al.,[13] TXA administration decreased blood loss both during and after surgery, reduced the volume of red-blood-cell transfusions, and resulted in complete elimination of the transfusion of other blood products, such as platelets and fresh frozen plasma. In most of the articles reviewed, all patients, even those who were administered TXA,[1,3–5,9,13–15] received some type of transfusion, even if in smaller amounts than the group that did not receive TXA. In the sample of the present study, none of the patients who received TXA ($N = 14$) underwent any type of blood product transfusion (►**Table 1**).

In the present study, with the administration of TXA, we reduced the mean age of the child at the time of surgery to 10 ± 2.31 months, and, according to the literature,[16] we know that we can achieve better cognitive and cosmetic results with earlier surgery. Therefore, the use of TXA may help to reduce the need for blood transfusion during and after the surgery and promote earlier surgery.

It is important to underline the importance of an experienced surgical team. The morbidity of the procedure, in the present study, was very low (of 4.26%), and there were no cases of mortality. According to Kajdic et al.,[17] the mortality and morbidity rate is of 0.1%, and it may reach up to 50% in the case of severe blood loss.

Conclusion

The modified technique of cranial vault reconstruction for scaphocephaly herein described is a safe procedure, which enables the immediate reduction of the AP diameter of the skull, and no further therapies are needed. It also results in a

head with a normal appearance right after the procedure. The wide decompression of the brain and remodeling of the skull that can be obtained with the procedure are the most rewarding surgical results. With the combination of a careful anesthesiologic protocol, we were able to perform this surgery at early ages, requiring no blood transfusions.

Institution Where the Work Was Conducted

The Neurosurgery Service at Centro Hospitalar Universitário do São João.

Conflict of Interests

The authors have no conflict of interests to declare.

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The Hoffmann-Tinel Sign: Historical Background and Clinical Significance

Sinal de Hoffmann-Tinel: Contexto histórico e significado clínico

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Arq Bras Neurocir 2024;43(2):e148–e156.

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Abstract

The Hoffmann-Tinel sign is well-known to professionals dealing with nerve lesions and is widely used as a provocative test. It was described by Paul Hoffman and Jules Tinel in the same year (1915), independently. In the present article, a biographical sketch of both authors is presented and the method for eliciting the sign and the sometimes controversial information of its results are discussed.

Keywords
- hoffman-tinel sign
- tinel sign
- tingling sensation
- paul hoffmann
- jules tinel
- nerve regeneration

Resumo

O sinal de Hoffmann-Tinel é bem conhecido pelos profissionais que lidam com lesões de nervos, sendo amplamente utilizado como um teste provocativo. Foi descrito por Paul Hoffmann e por Jules Tinel no mesmo ano (1915), de forma independente. No presente artigo, é apresentado um esboço biográfico de ambos autores e são discutidas a forma de obter o sinal e as informações, por vezes controversas, fornecidas por seus resultados.

Palavras-chaves
- sinal de Hoffmann-Tinel
- sinal de Tinel
- sensação de formigamento
- paul hoffmann
- jules tinel
- regeneração de nervos

Introduction

The Hoffman-Tinel sign (HTS) is a well-known and widely used provocative test in the clinical evaluation of regeneration of an injured nerve and to localize the level of nerve injury. This simple test does not require any instrument and can be easily performed by an examiner using only his finger.[1] A positive HTS is interpreted as paresthesia elicited across the area that corresponds to the location of the most distal sprouts of regenerating axons. Several years after it

received
January 31, 2023
accepted
June 21, 2023
article published online
October 27, 2023

DOI https://doi.org/10.1055/s-0043-1776273.
ISSN 0103-5355.

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

was described, the HTS is also useful for the diagnosis of nerve compression. Although this sign was described much earlier, it was merely considered a phenomenon; its usefulness was acknowledged only after its clinical application in 1915.[2–4]

Definition of the Hoffmann-Tinel Sign

A "positive" HTS refers to paresthesia (tingling sensation) elicited along the distal sensory distribution of an injured nerve or at the site of the injury, provoked by a mechanical stimulus (percussion or pressure). The sensation, which is comparable with that produced by weak electrical stimulation, radiates peripherally from the point where it is triggered to the cutaneous distribution of the nerve. Individuals experience a brief unpleasant sensation but not pain.[5] The peripheral reference of the sensation differs from that elicited by striking a healthy nerve. It is stimulated more easily and persists longer (10 to 15 seconds) after cessation of the stimulus.[6]

The HTS indicates the level of compression or regeneration of peripheral nerve fibers and is also useful to trace the path of recovery or peripheral nerve regeneration along the course of a nerve and across the site of injury from proximal to distal. The most peripheral point at which the tingling sensation is experienced is considered the site to which the fibers have regenerated.

The HTS first becomes evident $\sim$ 4 to 6 weeks after suture or injury.[7] Typically, only $\sim$ 30 centimeters of a nerve is sensitive to percussion at a particular time, which indicates advancement of regenerating axons over the distance and myelination of the proximal part, although these may not necessarily be functionally mature axons.[6]

The neurophysiological or pathophysiological processes underlying a positive HTS is unknown. Demyelination and partial remyelination, accompanied by axonal degeneration and regeneration in chronic nerve entrapment, render the peripheral nerve mechanosensitive.[8]

The HTS undergoes alterations during the course of nerve compression, probably associated with the degree of pathological changes present at the time of evaluation. The HTS tends to be positive during the course of chronic nerve compression and may subsequently show a negative result with further progression of compression.[9]

Overall, a strongly positive HTS elicited immediately postinjury indicates nerve rupture or severance. A centrifugally moving HTS is persistently stronger than that elicited at the suture line suggests the possibility of successful nerve repair, and an HTS that remains stronger than the suture line than that at the growing point suggests the possibility of failure of nerve repair.[10] Failure of distal progression of HTS in a closed lesion indicates rupture or other lesions that may interfere with successful regeneration.[11]

History of the Hoffmann-Tinel sign

Many descriptions of the currently recognized HTS are available in the literature before the classical 1915 publications. However, these early descriptions were purely physiologic in nature, and practical application and clinical interest in the HTS were highlighted only after 1915.

Ibn Sina, one of the most eminent Persian physicians, best known to the West as Avicenna (980–1037 AD), is credited with the first description of compression neuropathy and its clinical examination. In *The Canon of Medicine* (al-Qanun-fi al-Tibb), one of the oldest and most influential historical texts of medicine, Avicenna states '…manual compressing of the hardened nerves produces numbness'.[12]

In his essay (1819) titled *A Dissertation on the Treatment of Morbid Local Affections of the Nerves*, Joseph Swan wrote that '…when a nerve is pressed against a bone for a short time, an uneasy sensation is produced and the parts to which it is distributed feel benumbed'.[13]

Jean Joseph Emile Létiévant, a French surgeon and professor of physiology described a similar sign in many cases of median nerve lesions in his book *Traité des Sections Nerveuses* [Treatise on Nervous Sections], published in 1873.[14]

In 1905, Henry Head observed 'a curious widespread formication' produced by a von Frey hair aesthesiometer, '…that radiates widely over the affected area'.[15]

Wilfred Trotter and Hugh Morriston Davies mentioned '… a large number of sensations elicited from a recovering area referred to distant parts of the area or to the point of the nerve section' in two publications (1909 and 1913).[16,17]

Paul Hoffmann (1884–1962) (►**Fig. 1**) was a German neurophysiologist who performed significant research in human reflexes. He was born in Dorpat (presently in Estonia), which previously belonged to Russia but was inhabited by many German families after the 13th century.[18] Following medical education in Berlin, Marburg and Leipzig, Hoffman graduated from Leipzig University in 1908. After graduation, he worked as a research assistant at the Physiological Institute in Berlin. In 1911, he assisted Professor Max von Frey at the Institute for Physiology of the University of Würsburg. He was primarily involved with research on the action potentials of muscles and the electrophysiology of reflexes and was

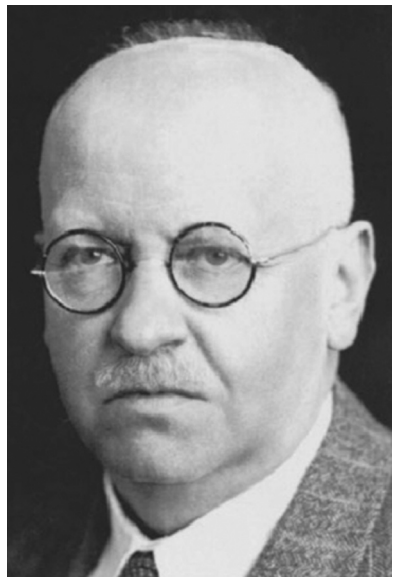

Fig. 1 Paul Hoffman (1884–1962).

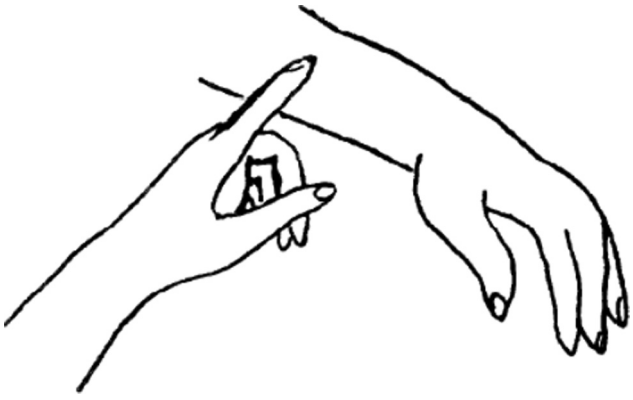

Fig. 2 Illustration from Hoffmann's paper[3] demonstrating the position of the hand during percussion over the radial nerve. Public domain.

recognized as a prolific researcher and writer. Hoffmann published 32 articles before the outbreak of the First World War.[1]

Hoffmann served in the German Army at several field hospitals in France and later at a military hospital in Würzburg during the First World War. He observed that percutaneous percussion of injured and regenerating peripheral nerves elicited a tingling sensation that radiated along the sensory distribution of that nerve in wounded soldiers. He wrote two articles about this sign; the first article published in *Medizinische Klinik* (28 March 1915) described the phenomenon,[2] and the second article in the same journal (1 August 1915) described details of the percussion method used to elicit this sign (►**Fig. 2**).[3] He interpreted the sign as evidence of newly formed, extremely sensitive regenerating nerve fibers.

Between 1912 and 1924, Hoffman rose through the academic ranks from Privatdozent (private lecturer) to Professor at the medical school in Würzburg. In 1924 he joined the faculty of the Physiology Institute at the University of Freiberg-im-Breisgau Medical School as Chair of Physiology.[19] In 1924, he was appointed Director of the Institute for Physiology, where he worked until his retirement in 1954.[1]

At the end of the First World War, Germany was expelled from all international scientific forums. Faced with the boycott of the winners, Germany collaborated with countries that remained neutral in the contest, such as Spain. Paul Hoffmann delivered lectures in Physiology at the School of Medicine, University of Santiago de Compostela, Spain, in 1923 (3 months) and in 1924 (one and a half month) (►**Fig. 3**).[20]

In 1932, Hoffman protested against the Nazi government that restricted him from teaching Jewish students. He nearly lost his position as Chief of Physiology. In November 1944, the Physiology Institute was demolished by errant Allied Forces' aerial bombs,[19] and Hoffman was compelled to relocate to other buildings until the construction of a new institute, where he remained until retirement. According to some historians, Hoffmann had an ambivalent relationship with the Nazi regime.[21] He died in 1962, at the age of 77 years old.[1]

Fig. 3 Paul Hoffmann (1), the Dean of the Faculty (4) and members of the Department of Physiology at the School of Medicine, University of Santiago de Compostela, Spain in 1941. (Reproduced from reference [20] by permission of Cuadernos de Estudios Gallegos).

Fig. 4 Jules Tinel (1879–1952).

Initially, Paul Hoffmann was not widely recognized. It was only through retrospective accounts by medical historians that Hoffmann has begun to receive credit for introducing the sign that he first described in detail.[1]

Jules Tinel (1879–1952) (►**Fig. 4**) was born in Rouen, France, into a family that included five generations of surgeons and physicians. He completed his medical studies in 1906 in Paris and, influenced by Joseph Jules Dejerine, a prominent clinical neurologist and one of his tutors, Tinel began to specialize in neurology and neuropathology.[22,23] In 1911, Tinel became "Chef de Clinique" [Clinic Director] and in 1913 he worked as Chief of the Laboratory at the Neurological Department at the Pitié-Salpetrière Hospital in Paris (►**Fig. 5**). By the end of 1913, Tinel had authored more than 40 publications that, for the most part, were associated with neurological issues.[24] However, these activities were suddenly interrupted by the war.

Following the outbreak of the First World War, Tinel served as an auxiliary physician for an infantry regiment. In March 1915, he was appointed second class assistant physician and was entrusted the responsibility for the Neurology Centre of the 4th military region in Le Mans, France.[25] The numerous traumatic lesions of the peripheral nerves captured his attention, and he was interested in gaining deeper insight into the consequences of ballistic trauma-induced peripheral nerve injuries,[26] which he extensively studied for 3 years. Tinel's exhaustive research led to the understanding of an effect in which compression of an injured nerve led to paresthesias similar to a tingling sensation ['sign du fourmillement'].[4] Tinel also discovered that following progressive regeneration of an injured nerve, the HTS tended to shift to a more peripheral location.

During the Second World War, when he worked at the Boucicaut Hospital, Tinel was actively involved in the French

Fig. 5 Members of the Neurological Department at the Pitié-Salpetrière Hospital in Paris (1912). 1. Jules Tinel; 2. Joseph Jules Dejerine; 3. Augusta Dejerine- Klumpke. Public domain.

Resistance Movement. He belonged to a network referred to as Comete that provided shelter in his home to allied wounded pilots whose planes were shot down over occupied Europe until his son, Jacques Tinel, could drive these men to Spain.[25,27] His son was arrested and transferred to the concentration camp in Mittelbau-Dora, where he died.[26] Tinel spent 3 months in prison in Bordeaux, and his wife and another son spent a year in prison in Fresnes, in the southern suburbs of Paris. The Comete network was completely disabled in 1944.[27]

Following his retirement in 1945, Tinel continued to work in Paris at the Boucicaut Hospital. In 1947, he developed cerebral ischemia and aphasia. He recovered within some weeks and maintained an active research laboratory until his health declined, and he died of heart failure in 1952 at the age of 73 years old.[26,28]

Description of the Hoffman-Tinel sign

In his first paper (March 1915), Hoffman described the phenomenon in two cases of radial nerve lesions during the war and in the second (August 1915) he discussed details regarding the method of percussion to elicit the sign.[2,3,25] In his first paper, Hoffman described the case of a 22-year-old officer who sustained a gunshot wound to the right humerus accompanied by radial nerve transection and sensory loss along distribution of the radial nerve in the hand. The nerve was repaired 2 months later, and moderate finger pressure on the area of the lesion/site of surgery produced a tingling sensation in the indicated area of sensory loss in the hand corresponding to the radial nerve distribution, 3 months postoperatively. More distal stimulation produced no sensation. The patient demonstrated weak extension of the hand, 4 months postoperatively.

Hoffman designated this test 'klopfversuch' [a tapping trial].[2] He emphasized the importance of gentle percussion to avoid an inaccurate result considering that paresthesia may be elicited even in healthy nerves. Hoffmann proposed that a single tap on a ruptured nerve is usually sufficient to provoke paresthesia that could continue for minutes in the innervated area.

In an article titled 'Le signe du fourmillement dans les lesions des nerfs périphériques' [The tingling sign in peripheral nerve damage], published in *Presse Médicale* (October 1915), Jules Tinel reported the conclusions of his clinical experience of war as follows: 'The pressure of a wounded nerve trunk produces very often an impression of tingling, exteriorized by the subject at the periphery of his nerve, and localized by him to a precise territory. It is important to differentiate this tingling from the pain that sometimes also occurs in traumatic nerve lesions. Pain is a sign of neuritic irritation; tingling is a sign of regeneration or, more accurately, tingling reflects the presence of young, growing axons'. Tinel called it "le signe du fourmillement" [the tingling sign].[4]

Tinel carefully distinguished between "formication" generated by pressure over a nerve and referred distally and "sensibility of nerve on pressure" observed in cases of neural irritation, which is invariably experienced as a local sensation.[29] Based on his observations, Tinel stated that the sign is usually seen 4 to 6 weeks after trauma and that the formication sign may disappear over 8 to 10 months or may require an even longer interval following the process of regeneration.[4,30] He was of the opinion that the total absence of the sign below the lesion was pathognomonic of a complete interruption (rupture) if sufficient time had elapsed since injury for the onset of regeneration.[4] Owing to the wartime information blockade, neither author was aware of the other's scientific work.[31]

Method to Elicit the Hoffman-Tinel Sign

Many different descriptions of stimuli to trigger the HTS in an injured nerve have been described, including a 'gentle stroking touch with the finger', 'tapping', 'tapping with a straight finger', 'gentle tapping with a finger', a 'von Frey hair tapping repeatedly', 'pressure', 'percussion', 'pressure with a foam instrument 2–3 mm in width', or even 'gentle percussion with a reflex hammer', or 'a home-made instrument of a rubber eraser fixed at the end of a pencil'.[5]

Tinel originally mentioned that pressure should be applied to the injured nerve to elicit the sign,[4] whereas Hoffman proposed that light percussion was more accurate,[3] and Hoffman's maneuver is more frequently used in clinical practice. Stronger percussion or firmer pressure is necessary to test deeper nerves.

Light percussion by the examiner's finger over a small area along the course of the injured nerve elicits the HTS. A tingling sensation experienced by a patient along the cutaneous distribution of the nerve is interpreted as a positive HTS. Depending on the clinical scenario, the point at which symptoms are provoked indicates nerve compression or regeneration. The nerve is usually stimulated using the examiner's fingertip or the finger in extension (►**Fig. 2**). Subsequent examination may indicate centrifugal progression of the HTS, which becomes progressively stronger at the distal compared with the proximal level of the HTS and indicates nerve regeneration.[11]

Tinel versus the Hoffman-Tinel sign

Ideally, the sign should be referred to as the eponymous 'Hoffman-Tinel Sign'; however, it is currently more commonly known as the Tinel sign in clinical practice, which is perhaps attributable to the fact that Hoffman and Tinel belonged to opposite sides of the war frontline, and neither author was aware of the other's work owing to the wartime blockade of international communication.[31] Although both described an equivalent sign in the same year, Hoffmann belonged to the losing side, and consequently his work was not valued within the scientific community.[18] Furthermore, the lower rank of the German periodical and censorship that affected German publications perhaps contributed to the wider popularity of the Tinel sign.[26] Notably, Tinel's closer ties to the western world, better writing skills, and a keen sense of observation favored rapid translation of his work into English.[1] Tinel's work

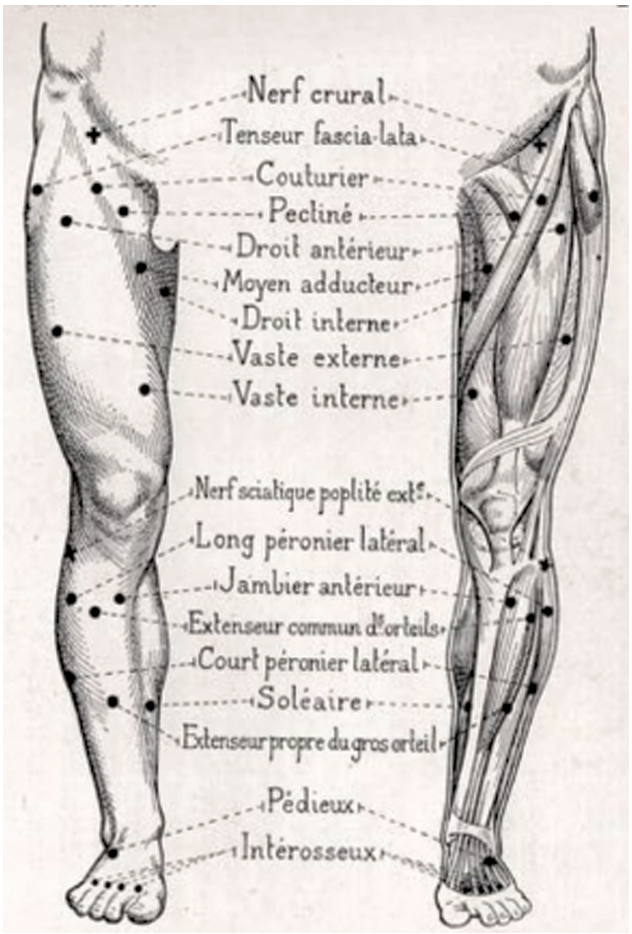

Fig. 6 High-quality illustrations from Tinel's book (1916).[30] Public domain.

includes more comprehensive descriptions, and he pursued research on nerve injuries and published an extensive and renowned reference book titled *'Les Blessures des Nerfs. Sémiologie des Lesions Nerveuses Périphériques par Blessures de Guerre'* [Nerve Injuries. Semiology of Peripheral Nerve Lesions by War Injuries] (1916)[30] based on his personal experience (►**Fig. 6**). The book was translated into English in 1918 and was instrumental in contributing to the wider fame achieved by Tinel and the widespread use of 'Tinel sign' in non-German-speaking medical communities. The 'Hoffmann sign' remained popular in Germanic countries.

Both authors hypothesized that a positive HTS indicated the development of young axons during the process of regeneration[2–4,30]; however, fundamental differences between their observations include the following: Hoffmann observed that the percussion test indicates regeneration of sensory fibers and not motor fibers; however, Tinel did not address this limitation. A positive sign could indicate the possibility of restoration of motor function, but it is not a guarantee of motor regeneration.[1] Hoffmann proposed that regenerating nerve fibers have an extremely low stimulation threshold compared with healthy nerves and therefore recommended the use of light pressure to perform the test because an intact nerve can be stimulated with much higher pressure intensity. However, Tinel virtually did not comment on the method used to elicit the tingling sign. Similarly, Tinel presented his own original ideas. Although Hoffmann described the use of the sign in a more cursory manner, Tinel discussed the application of the sign in greater detail in his book.[30] Tinel has extensively described the syndromes of complete nerve interruption, compression, irritation, and regeneration. In all these cases, he outlined when to expect the formication sign and used the sign to evaluate a patient's condition and to determine the indication for surgical intervention. Tinel addressed the difference between pain and tingling, both of which may be observed upon stimulation of the injured nerve trunk. Tinel explained that pain implies nerve irritation, whereas tingling suggests nerve regeneration. Based on his observations, Tinel was of the view that the sign is usually observed 4 to 6 weeks postinjury; when the nerve is in the process of regeneration, the formication sign may disappear in 8 to 10 months or in an even longer period, to disappear.[4,30]

Clinical Significance of the Hoffman-Tinel sign

The clinical value of the HTS remains controversial. Initially, Hoffman and Tinel's research received negative feedbacks and reactions, and the clinical information obtained from application of the HTS was frequently misunderstood, particularly by clinicians who observed that a positive HTS did not ensure a favorable outcome. Although Tinel emphasized that a positive sign predicted future nerve recovery, some patients recovered full neurologic function without showing a positive HTS. Therefore, many physicians questioned this finding, and the sign was virtually neglected for nearly 30 years.[27] It was only by the end of the Second World War that the significance and usefulness of the HTS was fully appreciated.

In 1948, Henderson,[32] a British neurosurgeon and prisoner-of-war, published his observations based on repeated attempts to elicit HTS in over 400 patients with nerve injuries in field hospitals across Germany, at locations in which surgical treatment was not possible. Henderson observed that the HTS is clinically important $\sim$ 4 months after injury; he was of the view that a strongly positive sign at the level of the lesion with gradual weakening with peripheral movement of the response and a stronger sign in the distal part of the nerve indicated satisfactory progress of regeneration.

Researchers have emphasized that paresthesia phenomenon alone does not predict nerve regeneration. It is important to confirm gradual distal progress of the tingling elicited in a patient for accurate prediction of nerve regeneration. However, if the HTS remains static for several consecutive weeks or months, it is indicative of a likely obstacle to the growth of the nerve fibers[4] or may indicate nerve rupture,[11] and surgical exploration is usually warranted in such cases.[29,33] Nerve regeneration is never associated with a painful sensation[34]; patients invariably compare the vague disagreeable sensation with that caused secondary to an electric current.

Clinicians should be mindful of the following points when interpreting the results of nerve percussion[11]:

(1) The HTS is elicited over a site of nerve fiber regeneration, even in areas where these fibers may grow aimlessly.
(2) The nerve fibers that enter endoneural tubes do not necessarily enter the tubes in which they were originally present or in tubes that lead to the former areas of distribution of the fibers.
(3) The HTS does not accurately indicate the number of regenerating nerve fibers.[35]
(4) The HTS may be elicited even without apparent nerve recovery.
(5) The HTS was shown to be absent throughout the period of regeneration in areas with deep-seated nerves; however, good recovery of nerve function was observed even in such cases.[36]

In light of the current knowledge, Birch interpreted a positive HTS as follows[11]:

1. A strongly positive HTS over a lesion soon after injury indicates ruptured axons or a severed nerve;
2. Centrifugal movement of the HTS that is persistently stronger than that at the suture line suggests a strong likelihood of successful repair.
3. The HTS at the suture line that remains stronger than that shifting distally suggests a strong likelihood of failure of repair.
4. Failure of distal progression of the HTS in a closed lesion indicates rupture or some other injury that is not likely to show natural recovery;
5. A positive HTS indicates a degenerative lesion (not a conduction block) because the injured nerve contains a significant number of axons.
6. A positive HTS result should not be confused with hypersensitivity observed in some cases of neuralgia.

Accurate interpretation of the HTS in brachial plexus lesions is challenging. Landi et al. observed the following responses after tapping in the posterior triangle of the neck[37]: (1) A complete lack of response implies preganglionic injury to the nerve root; (2) Local pain implies a recovery of an underlying cervical plexus lesion; (3) A pure HTS indicates a lesion in anatomic continuity with progressive recovery documented on sequential recordings and sequential recordings can demonstrate progression of recovery. The C5 and C6 nerve roots are most superficial, and the HTS can easily be elicited at this level. C7, C8 and T1 are deep-seated and therefore difficult to evaluate; (4) The neuroma sign is positive in patients in whom pain is elicited along the distribution of the nerve when tapped. This sign indicates disruption of continuity of the nerve.

Birch reported that radiation up to the level of the elbow following percussion in the posterior triangle of the neck suggests rupture of C5 nerve root, radiation that extends to the lateral forearm and thumb suggests C6 nerve root rupture, and radiation that extends to the entire hand, particularly over the dorsum, suggests C7 nerve root rupture.[11]

At the annual meeting of the American Society for the Peripheral Nerve in 2004, Millesi reported the results of HTS testing in 42 consecutive patients with brachial plexus lesions and compared these with surgical findings.[38] He concluded that an absence of HTS supports root avulsion, and an HTS that radiates into the territory of a spinal nerve strongly suggests that at least one root remains intact.

True HTS is experienced as a tingling sensation elicited by stimulation of nerve branches that contain growing touch fibers. In a mixed nerve, touch fibers account for only $\sim$ 10% of all of the fibers; therefore, only a few touch fibers need to remain intact to produce a positive HTS, and the sign provides information regarding regeneration of touch and not of other fibers.[34]

The HTS is consequent to an increased mechanoreceptor sensitization and seems to indicate the presence of young axis cylinders in the process of regeneration; however, the significance appears questionable because this sign is often absent and only sometimes positive even in those with complete nerve division.[39] The absence of the HTS is perhaps of no diagnostic value; however, a positive HTS that advances peripherally from a nerve lesion suggests a strong likelihood of regeneration.[39] However, this sign represents only sensory nerve fiber regeneration; therefore, a positive test provides physiological evidence of nerve fascicle regeneration but does not predict restoration of voluntary movement. Furthermore, some of the regenerating axons are not on their way to any target.

The HTS is often utilized for diagnosis of entrapment neuropathies, particularly median nerve compression within the carpal tunnel or the ulnar nerve compression in the postcondylar groove. Changes during nerve compression are associated with the degree of pathology present at the time of evaluation; a positive HTS elicited during the course of nerve compression changes to a negative sign with further progression of the pathology.[9] The popularity of the HTS for the diagnosis of carpal tunnel syndrome is largely attributable to Phalen, who reported that the Tinel sign showed sensitivity of 73% in 452 patients in whom the clinical presentation was used as the diagnostic standard.[40,41]

The HTS-like elicited by percussion over schwannoma or over nerves in the early stages of entrapment neuropathy does not indicate ruptured axons and suggests sensitization of nerve fibers secondary to focal demyelination and changes in the expression of voltage-gated ion channels at the level of lesion.[11]

Studies have reported a wide range in the sensitivity of the HTS (23–62% [mean 42.4%]), although, usually, it is observed to be highly specific (64–93% [mean 76.4%]).[42–48] Absence of the HTS does not necessarily rule out the diagnosis.[49]

Conclusion

Increased mechanoreceptor sensitization is considered the mechanism underlying the HTS, which suggests the presence of young axis cylinders in the process of regeneration within an injured nerve. However, the significance of this sign appears questionable; it is often absent and only occasionally positive

even in patients with complete division of a nerve. An absent HTS is perhaps of no diagnostic value; however, a positive HTS that advances peripherally from a nerve lesion is strongly suggestive of a regenerative process. However, this sign is associated only with sensory nerve fibers; therefore, a positive test provides physiological evidence for regeneration of nerve fascicles and does not predict restoration of voluntary movement. Furthermore, some regenerating axons are not on their way to any target. If a nerve repair is going to be successful centrifugal moving of the HTS that is persistently stronger than that at the suture line suggests a strong possibility of successful nerve repair, and a HTS that remains stronger at the suture line than that at the growing point is highly suggestive of failure of repair. Failure of distal progression of the HTS in a closed lesion indicates rupture or other lesions that interfere with regeneration. Currently, the HTS is widely used clinically; however, there is lack of standardization, its grading is rarely used, and its reliability or validity is scarcely mentioned in the literature. We recommend that too much should not be expected of the sign, which must be interpreted only in conjunction with other clinical findings.

Conflict of Interests

The authors have no conflict of interests to declare.

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ISSN 0103-5355

Instruções aos Autores

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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

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ISSN 0103-5355

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4. Main text: introduction; casuistry or material and methods; results; discussion; conclusion; acknowledgments.

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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

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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.

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