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Uma publicação da Academia Brasileira de Neurocirurgia

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4. Patel MA, Kim JE, Theodros D, et al. Agonist anti-GITR monoclonal antibody and stereotactic radiation induce immune-mediated survival

advantage in murine intracranial glioma. J Immunother Cancer. 2016;4:28. http://dx.doi.org/10.1186/s40425-016-0132-2.

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Donald PJ, editor. Surgery of the skull base. Philadelphia: Lippincott-Raven; 1998.

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Instituto Brasileiro de Geografia e Estatística. Estatísticas da saúde: assistência médico-sanitária. Disponível em: http://www.ibge.gov.br. Acessado em: 5/2/2004.

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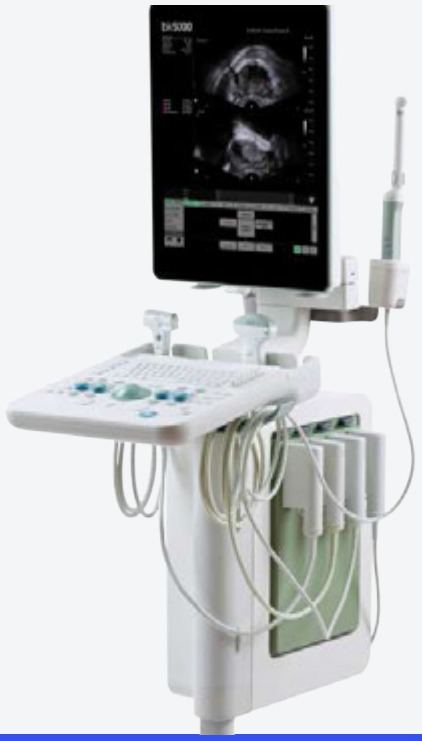

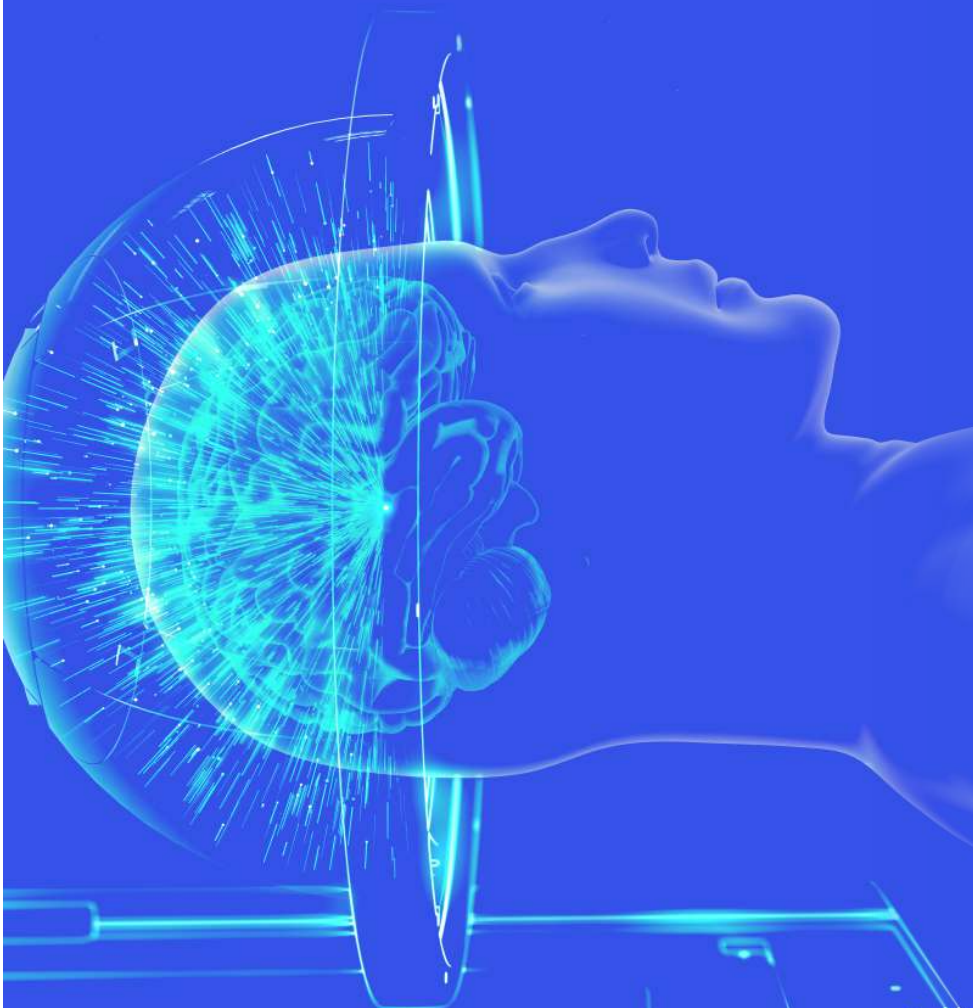

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Intracranial Aneurysms in Elderly Individuals: case series epidemiology

Aneurismas Intracranianos em Idosos: epidemiologia de série de casos

Leandro José Haas[1]
Guilherme Wandall[2]
Wesley Severino[2]
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ABSTRACT

Introduction*: Aneurysmal pathology is becoming increasingly prevalent in the general population, especially as life expectancy increases. Dilation of cerebral arteries in elderly patients tends to be increasingly present in neurosurgeons' routine. Therefore, the investigation of cerebral aneurysms in elderly patients is relevant to their clinical and surgical management.* **Objective***: to establish a relationship between age and propensity to aneurysmal disease, as well as to draw up a clinical-epidemiological profile in this age group.* **Methods***: Descriptive observational study of individuals aged 70 or older diagnosed with cerebral aneurysm who underwent endovascular treatment at the Endovascular Neurosurgery Service of the Santa Isabel Hospital between 2005 and 2023.* **Results***: Females were the most affected (75.81%), saccular aneurysms were the most prevalent (95.81%), and their size was often small (69.76%). Endovascular treatment was the method of choice for this group of patients, with coil therapy being the most prevalent (66.97%).* **Conclusion***: Aneurysms in the elderly had similar general characteristics to those in adult patients; however, the aging process manifested itself in certain nuances in clinical presentation, such as associated comorbidities. This topic requires further investigation in the literature, especially in patients over the age of 80, where the smaller number of individuals makes scientific analysis challenging.*

Keywords: *Intracranial Aneurysm; Elderly; Neurosurgery; Endovascular procedures; Subarachnoid hemorrhage*

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RESUMO

Introdução: *O diagnóstico da patologia aneurismática está ficando cada vez mais prevalente na população geral, em especial com o aumento da expectativa de vida. A dilatação das artérias cerebrais em paciente com idade avançada tende a estar cada vez mais presente na rotina do neurocirurgião. Dessa forma, a investigação de aneurismas cerebrais em pacientes idosos torna-se relevante no manejo clínico-cirúrgico dessas pessoas.* **Objetivo***: Estabelecer relação entre idade e propensão à doença aneurismática, assim como traçar perfil clínico-epidemiológico nessa faixa etária.* **Métodos:** *Estudo observacional descritivo, de indivíduos com idade maior ou igual a 70 anos, com diagnóstico de aneurisma cerebral, submetidos ao tratamento endovascular em serviço de neurocirurgia endovascular do Hospital Santa Isabel, Blumenau, Santa Catarina, no período de 2005 a 2023.* **Resultados:** *O sexo feminino foi o mais acometido (75,81%), o aneurisma sacular foi o mais prevalente (95,81%), e a dimensão pequena (69,76%). O tratamento endovascular foi o método optado nessa gama de pacientes, onde a terapia com a utilização de coils foi a mais prevalente (66,97%).* **Conclusão:** *O quadro aneurismático em idosos apresentou características gerais similares ao paciente adulto. Contudo, o processo de envelhecimento manifestou-se em certas nuances na apresentação clínica como, por exemplo, nas comorbidades associadas. Esse tópico requer maior investigação em literatura, especialmente em pacientes com idade superior a 80 anos, onde o menor número de indivíduos torna desafiante a análise científica.*

Palavras-chave: *Aneurisma intracraniano; Idoso; Neurocirurgia; Procedimentos endovasculares; Hemorragia subaracnoidea*

INTRODUCTION

Cerebral aneurysms are arterial dilations that occur at points of weakening of the tunica vascularis; the most common morphology is saccular, and the most prevalent site of involvement is the anterior cerebral circulation, arising from the carotid arteries. Cerebral aneurysms have been more often diagnosed due to the spread of new examination techniques and the increased accessibility of advanced imaging exams[1-3].

While reports of ruptured cerebral aneurysms have been extensively catalogued, there is no consensus on their correct management, especially in patients over 70 years of age. In addition, epidemiological data on this pathology in this age group is scarce. The few existing studies come predominantly from Japan and the USA, where life expectancies are 83.98 and 78.69, respectively, and a few of them from Nordic countries, where life expectancy is also above the world average[4,5].

In Brazil life expectancy is 75.51 years. In a few states, however, it is above 78 years and an increasingly significant percentage of the population is over 70 years old, making it necessary to review pathologies such as cerebral aneurysms, which are becoming increasingly more important as a cause of morbidity and mortality, as in the above mentioned countries[5].

The scarcity of initial basic national epidemiological information on cerebral aneurysms in this age group interferes with the decision as to the most appropriate management to provide. It should also be noted that the use of epidemiological data from other countries in the Brazilian scenario is not fully adequate, since it does not take into account the variation in population genetic factors, most prevalent comorbidities and different lifestyle habits that can lead to an increase or to a decrease of the incidence of this pathology[1].

With this in mind, this study aims to delve into the characteristics of aneurysms, patient comorbidities and treatments given to the elderly population, in order to gain a better clinical and epidemiological understanding of aneurysms in this population.

METHODOLOGY

This was a concurrent cohort, descriptive, observational study of individuals aged 70 or older diagnosed with ruptured or unruptured intracranial aneurysms who underwent endovascular treatment at the endovascular neurosurgery referral service of the Santa Isabel Hospital, Blumenau, state of Santa Catarina, between October 2005 and July 2023.

The variables studied were: aneurysm morphology (saccular, fusiform, mammillary), size, vascular location and integrity of the aneurysm (ruptured or unruptured), comorbidities, age, sex, type of treatment given, as well as Fischer and Hunt-Hess classification of intracerebral hemorrhage.

Patients were analyzed according to their respective imaging findings, thus assigning them a Fisher scale score, as well as according to their respective clinical manifestations, assigning them a Hunt and Hess scale score. Only patients with a score equal to or higher than Fisher scale 2 were considered to have ruptured aneurysms, thus having a Hunt and Hess scale score equal to or higher than grade 1.

Aneurysms can be classified according to their specific dimensions: small aneurysms are characterized by dimensions below 10 millimeters, whereas large aneurysms are equal to or larger than 10 mm and smaller than 20 mm, and giant aneurysms are equal to or larger than 20 millimeters.

All the procedures were carried out by a neurosurgeon specializing in neurointervention with more than 17 years' experience and more than 2,000 angioplasties performed. The choice of the technique and of the stent was left to the discretion of the operating physician.

The project complied with current ethical standards and was approved by the local ethics committee under CAAE 36208720.7.0000.5370. The authors have no conflicts of interest and have received no funding.

RESULTS

Of the 1,903 cases of intracranial aneurysms treated at the endovascular neurosurgery service, Santa Isabel Hospital, between October 2005 and July 2023, 11.29% were aneurysms in the elderly. Of these patients, 52 were male (24.18%), with a mean age of 75.71, and 163 were female (75.81%), with a mean age of 75.39.

The overall average age of the sample of 215 cases was 75.47 (Chart 1).

As for the presence of comorbidities, systemic arterial hypertension (SAH) was the most prevalent, in 164 cases (76.27%), 26.21% (N = 43) of which in male and 73.78% (N = 121) in female patients, followed by dyslipidemia in 50.23% (N = 108), of the patients, 27.77% (N = 30) male and 72.22% (N = 78) female, and diabetes mellitus in 17.20% (N = 37) of the patients, 29.72% (N = 11) male and 70.27% (N = 26) female. A previous or current history of smoking was reported in 21.86% of the patients (N = 47), 40.42% (N = 19) of whom were male and 59.57% (N = 28) were female.

Saccular aneurysms were 95.81% of the cases (N = 206), of which 23.78% (N = 49) in male and 76.21% (N = 157) in female patients. Fusiform aneurysms were 1.86% (N = 04), 25% (N = 01) in male and 75% (N = 03) in female patients. Mammillary aneurysms were 1.39% (N = 03), 33.33% (N = 01) in female and 66.66% (N = 02) in male patients. Dissecting aneurysms were 0.46% (N = 01), 100% (N = 01) in male patients, and infundibular aneurysms were 0.46% (N = 01), 100% (N = 01) in female patients.

As for aneurysm size, 69.76% (N = 150) of the cases were small aneurysms, of which 26% (N = 39) in male and 74% (N = 111) in female patients; 20.46% (N = 44) of the cases were large aneurysms, of which 22.72% (N = 10) in male and 77.27% (N = 34) in female patients; 9.76% (N = 21) of the cases were giant aneurysms, of which 14.28% (N = 03) in male and 85.71% (N = 18) in female patients. (Table 1).

As for aneurysm topography, Table 2 shows the relationship between aneurysm location and involvement by sex, highlighting the highest prevalence – f 25.11% (N = 54) – of posterior communicating artery aneurysms, of which 20.37% (N = 11) in male and 79.62% (N = 43) in female patients (Table 2).

Chart 1. Age distribution of elderly patients with intracranial aneurysms by sex, November 2005-July 2023, Santa Isabel Hospital, Blumenau, 2023.

Age ranges	Male	Female	Total number of individuals
(70 – 80)	44	142	186
(81 – 90)	07	21	28
(91 – 100)	01	0	01
Total	**52**	**163**	**215**

Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

Table 1. Clinical and epidemiological characteristics of elderly individuals with intracranial aneurysms according to sex (n = 215).

Age by age group	Male	Female
70-80 years/n (%)	44/52 (84,6)	142/163 (87,1)
81-90 years/n (%)	7/52 (13,5)	21/163 (12,9)
90 years/n (%)	1/52 (1,9)	0/163 (0)
Comorbidities – total / n (%)		
SAH*	43/52 (82.6)	121/163 (74.2)
Dyslipidemia	30/52 (57.6)	78/163 (47.8)
Diabetes mellitus	11/52 (21.1)	26/163 (15.9)
Smoking	19/52 (36.5)	28/163 (17.1)
Aneurysm morphology – total / n (%)		
Saccular	49/52 (94.2)	157/163 (96.3)
Fusiform	1/52 (0.2)	3/163 (1.8)
Mammillary	1/52 (0.2)	2/163 (1.2)
Dissecting	1/52 (0.2)	0/163 (0)
Infundibular	0/52 (0)	1/163 (0.06)
Aneurysm size – total / n (%)		
Small	39/52 (75)	111/163 (68)
Large	10/52 (19.2)	34/163 (20.8)
Giant	3/52 (0.5)	18/163 (11)

*SAH = Systemic Arterial Hypertension.
Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

Table 2. Aneurysm topography in elderly individuals with intracranial aneurysms according to sex (n = 215).

Artery involved – total / n (%)	Male	Female
BA	4/52 (7.6)	8/163 (4.9)
pACA	2/52 (3.8)	3/163 (1.8)
Cn-ICA	1/52 (1.9)	1/163 (0.6)
Coa-ICA	2/52 (3.8)	3/163 (1.8)
Hps-ICA	0/52 (0)	4/163 (2.4)
Of-ICA	1/52 (1.9)	12/163 (7.3)
Po-ICA	0/52 (0)	2/163 (1.2)
MCA-M1	2/52 (3.8)	2/163 (1.2)
MCA-M2	2/52 (3.8)	2/163 (1.2)
ACoA	15/52 (28.8)	28/163 (17.1)
ACoP	11/52 (21.1)	43/163 (26.3)
PCA	1/52 (1.9)	1/163 (0.6)
SCA	0/52 (0)	1/163 (0.6)
VA	1/52 (1.9)	0/163 (0)
B-ICA	0/52 (0)	3/163 (1.8)
B-MCA	4/52 (7.6)	25/163 (15.3)
Cv-ACI	3/52 (5.7)	13/163 (7.9)
P-ICA	2/52 (3.8)	2/163 (1.2)
PICA	1/52 (1.9)	7/163 (4.2)
T-MCA	0/52 (0)	3/163 (1.8)

Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

The Fisher scale scores point out that 68.83% (N = 148) of these individuals were Fisher scale 1, 25.67%, (N = 38) of whom male and 74.32%, (N = 110) female patients, as reported and complemented in Chart 2.

Based on the Hunt and Hess scale, we found that 68.83% (N = 148) of the individuals were grade 0, 25.67% (N = 38) of whom were male and 74.32% (N = 110) were female patients. The other data can be found in the chart below (Chart 3).

It was thus established that 68.83% (N = 148) were unruptured aneurysms, Fisher scale 1 and Hunt and Hess scale grade 0, 25.67% (N = 38) of which in male and 74.32% (N = 110) in female patients. So, 31.16% of aneurysms (N = 67) were ruptured, Fisher scale 2 or higher and Hunt and Hess scale 1 or higher, 20.89% (N = 14) of which in male and 79.10% (N = 53) in female patients (Chart 4).

Table 3. Therapeutic characteristics and aneurysm integrity in elderly individuals with intracranial aneurysms according to sex (n = 215).

Aneurysm integrity – total / n (%)	Male	Female
Ruptured aneurysms	14/52 (26.7)	53/163 (32.5)
Unruptured aneurysms	38/52 (73)	110/163 (67.4)
Selected therapy – total nº/ n (%)		
Stents	6/52 (11.5)	5/163 (3)
Coils	32/52 (61.5)	112/163 (68.7)
Stents + Coils	14/52 (26.9)	38/163 (23.3)
Flow-diverting stent	0/52 (0)	5/163 (3)
Therapeutic failure – total / n (%)	0/52 (0)	3/163 (1.8)

Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

Regarding to the treatment of intracranial aneurysms in the elderly, 100% of the sample (N = 215) underwent endovascular procedures. A stent-only approach was used in 5.11% (N = 11) of these procedures, of which 54.54% (N = 06) were performed on male and 45.46% (N = 05) on female patients. In 66.97% (N = 144) of the cases, only coils were used, 22.22% (N = 32) of which on male and 77.77% (N = 112) on female patients. In 24.18% (N = 52) of the procedures, the treatment of choice was a combination of coils and stents, 26.92% (N = 14) of which performed on male and 73.07% (N = 38) on female patients. In 2.32% (N = 05) of the cases, only flow-diverting stents were used, 100% (N = 01) on female patients. The procedures failed in 1.39% (N = 03) of the patients, 100% (N = 03) of whom were female, due to unfavorable anatomy and to the unavailability of suitable materials at the beginning of the study (Chart 5 and Table 3).

Chart 2. Fisher scale scores for elderly patients with intracranial aneurysms, according to sex, November 2005-July 2023, at Santa Isabel Hospital, Blumenau, 2023.

Fisher scale	Male	Female	Total
Fisher 1 (no blood detected in the subarachnoid space)	38	110	148
Fisher 2 (diffuse bleeding with vertical layers of blood less than 1 mm thick, no clots)	0	10	10
Fisher 3 (localized clot and/or vertical layers of blood 1 mm or more thick, no intraventricular hemorrhage)	07	10	17
Fisher 4 (intraparenchymal or intraventricular clots with or without diffuse subarachnoid hemorrhage)	07	33	40
Total	**52**	**163**	**215**

Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

Chart 3. Hunt and Hess scores for elderly patients with intracranial aneurysms, according to sex, November 2005-2023, at Santa Isabel Hospital, Blumenau, 2023.

Hunt and Hess scale	Male	Female	Total
Grade 0 (unruptured aneurysm)	38	110	148
Grade 1 (asymptomatic or minimum headache and nuchal rigidity)	01	01	02
Grade 2 (moderate-to-severe headache, nuchal rigidity, no neurological deficits except for cranial nerve palsy)	06	21	27
Grade 3 (drowsiness, confusion, moderate focal deficit)	03	18	21
Grade 4 (stupor, moderate-to-severe hemiparesis, early decerebrate rigidity, vegetative disorders)	02	09	11
Grade 5 (deep coma, decerebrate rigidity, moribund appearance)	02	04	06
Total	**52**	**163**	**215**

Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

Chart 4. Intracranial aneurysm integrity in elderly patients, according to sex, November 2005-July 2023, Santa Isabel Hospital, Blumenau, 2023.

Aneurysm integrity	Male	Female	Total
Unruptured aneurysms (Fisher scale = 1, Hunt and Hess scale = 0)	38	110	148
Ruptured aneurysms (Fisher scale ≥ 2, Hunt and Hess scale ≥ 1)	14	53	67
Total	**52**	**163**	**215**

S**ource:** Santa Isabel Hospital, Neurosurgery Department, 2023.

Chart 5. Endovascular treatments in elderly patients with intracranial aneurysms, according to sex, November 2005-July 2023, at Santa Isabel Hospital, Blumenau, 2023.

Endovascular treatments	Male	Female	Total
Only Stents	06	05	11
Only Coils	32	112	144
Stents with Coils	14	38	52
Only flow-diverting stent	0	05	05
Failure	0	03	03
Total	**52**	**163**	**215**

Source: Santa Isabel Hospital, Neurosurgery Department, 2023.

DISCUSSION

When we look at the entire universe of cerebral aneurysms, it is clear that there is a patient profile that is more predisposed to developing this arterial problem, with females between the ages of 35 and 60 accounting for the largest number of cerebral aneurysms. This consideration leads us to believe that hormonal interference may be associated with the higher number of women with aneurysms[1,3].

Initially, the group of patients aged 70-80 was clearly the largest, making up over 80% of the patients registered in this study, followed by the groups aged 81-90 and then over 90. The two last groups included considerably fewer patients. As for an increase in the incidence of aneurysms with advancing patient age, there is no definitive data on the number of patients in each group. However, an analysis of autopsies conducted in 1999 by the Hisayama study group showed an increase in the incidence of aneurysms with advancing age. However, in a systematic review and meta-analysis carried out by Vlak et al. in 2011, there was no association between age and an increase in the incidence of aneurysms[5-7]. Now, moving on to the main nuances found in aneurysms in patients over 70, we found that just over 75% of all 215 patients registered in this study were female.

The comorbidities most classically associated with cerebral aneurysms as etiological and morbidity and mortality factors are hypertension and smoking/history of smoking, with risk factors which, on their own, can substantially impair the clinical history of patients with cerebral aneurysms. Their association, however, increases the risk of subarachnoid hemorrhage due to aneurysm rupture by up to 15 times. Other factors, such as a family history of aneurysms and collagen diseases, are also known to be associated with aneurysms[1-3]. As expected, systemic arterial hypertension was highly prevalent in all groups, with 76.27% (N=164) of the patients having this previous comorbidity. For smoking, on the other hand, the results were not as we expected, being higher only than that for diabetes mellitus. Smoking patients were a small proportion of the elderly population, 21.86% (N=47). Dyslipidemia had a surprisingly high level of incidence, being the second most common comorbidity in these patients (second only to hypertension), with just over half of all patients having this lipid imbalance.

The average size of cerebral aneurysms ranged from 2 to 7 mm[6], which is 62% of the total sample, followed by aneurysms of 7 to 12 mm with a 23% sample incidence. In a different study, the majority of cerebral aneurysms were between 7 and 12 mm (86.5%)[8], but 71% were between 3 and 4.9 mm. Vlak et al.[7] also showed that most of the sample in their meta-analysis had aneurysms of less than 5 mm. When it comes specifically to the elderly, Hishikawa's study showed that aneurysms smaller than 5 mm were still the most frequently found ones even in this age group, but in a different proportion relative to the younger population, with 37.7% of the aneurysms found being 3-4 mm, 25.4% 5-6 mm and 20.7% 7-9 mm, i.e. there was a significant increase in the incidence of larger aneurysms in this population, but the small ones continued to be the most common ones[5]. The distribution was similar to that in Hishikawa's study in relation to Inagawa's study, which showed an even higher prevalence of larger aneurysms, with 20% for aneurysms measuring 10-14 mm[5]. However, there is controversy, since studies such as Lanzino's and Sedat's, from 1996 and 2005, respectively, found no association between age and aneurysm size[9,10].

During the course of this study, aneurysm sizes were clearly consistent with the findings of the authors cited below, small aneurysms remaining the main size observed in the entire universe of patients; however, with the advancing age of the typical patient, the larger sizes of cerebral aneurysms become more and more prevalent. The most consistent example was that large aneurysms were found in approximately 20% of all patients, which coincides with Hishikawa's data[5].

As for the types of cerebral aneurysm conformation, there is already a consensus regarding the high prevalence of saccular aneurysms over the other conformations, demonstrating that the history of the typical patient tends to be almost dominated by saccular aneurysms[1]. The empirical results based on the elderly population tend to further highlight this claim, since more than 95% of aneurysm patients over 70 are diagnosed with saccular aneurysms; the other conformations, such as fusiform and mammillary, for example, account for only 1.86% (N=4) and 1.39% (N=3) of these cases, respectively. The prevalence of female patients was noticeable in all the other conformations, with an average incidence of 72.62%.

As for the most common locations of aneurysms, in young patients, we have the descending order as follows: middle cerebral artery, internal carotid artery, and posterior communicating artery[3,7,8]. In elderly patients, the vast majority of studies have shown the same sites as in younger patients[5,9,11], with the exception of a study by Sakaki et al.[12], which showed a slightly higher incidence of

aneurysms in the vertebrobasilar territory. In our study, the site with the highest incidence was the posterior communicating artery, accounting for just over ¼ of cases in patients over 70 years old.

Using the Fisher scale, the most common type was Fisher 1, accounting for 68.83% (N=148) of the total range of patients. After a rupture, patients are Fisher 4, the second largest group in this study, but they are still 18.6% (N=40), significantly less than Fisher 1.

Proceeding with the Hunt and Hess scale, 68.83% (N=148) of all patients were grade 0. Curiously enough, grade 1 was the only score with an even distribution of male and female patients. The other grades, from 2 to 5, followed a decreasing sequence of prevalence, with female patients always predominating in all of them.

These aneurysms are currently treated with either microsurgical clipping or endovascular techniques. The nuances regarding the advantages of each technique were highlighted by different studies in order to establish which one is the best. Several studies comparing the treatment routes were already carried out and what has been established so far is that both alternatives are effective and the choice of the type of procedure depends mainly on the area of expertise of the service in question.

According to the results of this study, coil therapy was the dominant treatment, with an overall prevalence of 66.97% (N=144) for ruptured aneurysms, followed by stents in association with coils, with 24.18% (N=52) for unruptured aneurysms. The two major forms of treatment were most commonly used on female patients.

With regard to morbidity and mortality, we found that patients with ruptured cerebral aneurysms, who scored 4 on the Fisher scale and 4 and 5 on the Hunt Hess scale, had a worse outcome. Patients with unruptured aneurysms, on the other hand, had a complication rate of 2%, with embolic effects and hematomas at the puncture site being the main complications.

CONCLUSION

In general, for this type of patient, the epidemiology did not deviate too much from a typical patient affected by cerebral aneurysm. The total scope of the data leads to the conclusion that the most typical patient who develops a cerebral aneurysm in old age would be a woman with a history of systemic arterial hypertension and dyslipidemia. The most common conformation and size was consistent with the typical history of aneurysmal disease, i.e. the most likely aneurysm would be saccular and small. The topography was perhaps the most unique feature in the study, with the posterior communicating artery being the site of most cases of arterial dilation. The most commonly used endovascular treatment in patients over 70 was coil therapy, used in over 60% of all cases.

Inherent in the ageing process, sarcopenia is one of the many aggravating factors of aneurysmal disease, which means that the elderly population requires more attention in terms of their medical care than the general adult patient population. However, epidemiological observation of cerebral aneurysms in patients over the age of 70 is seldom found in the current literature.

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Epidemiological Analysis of Patients Victims of Surgical Thoracic/Lumbar Fractures Treated at a Tertiary Hospital in Brazil

Análise Epidemiológica de Pacientes Vítimas de Fraturas Cirúrgicas Torácicas/Lombares Tratados em um Hospital Terciário no Brasil

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ABSTRACT

Introduction: *Spinal cord injury, one of the most feared sequelae of spinal fractures, is a common cause of permanent functional disability in young individuals, with significant morbidity and mortality rates. According to this perspective, exploring the epidemiological pattern of these lesions is the first step to develop preventive strategies to avoid complications and improve decision-making. Objective: to analyze the epidemiological profile of operated patients who were victims of thoracolumbar fractures.* ***Methods:*** *retrospective cross-sectional descriptive study with sample consisting of 223 thoracolumbar fractures that occurred between 2015 and 2019. Data (gender, age, place of origin, etiology of the injury, Frankel scale for assessing neurological deficit, and affected vertebral segment) were extracted from the records of patients who were victims of trauma to the thoracic and lumbar spine and surgically treated at the institution.* ***Results:*** *A total of 223 patients were analyzed, of whom 164 (73.5%) were men. The mean age was 35.9 ± 14.3 years. Most traumas were caused by motorcycle accidents (36.7%), followed by falls from heights (31.8%) and car accidents (17.0%). The main cause of trauma in men was motorcycle accidents (39.0%), while in women it was falls from height (35.5%). The most affected segment was the thoracolumbar spine in 118 (52.9%) cases, followed by the thoracic segment in 78 (34.9%) cases. A total of 46.1% of the patients were admitted with a Frankel E. Traffic accidents were the main cause of complete motor deficits at hospital admission (Frankel A).* ***Conclusions:*** *Among patients surgically treated for trauma to the thoracic and/or lumbar spine there was a predominance of motorcycle accidents, followed by car accidents, and men were more prone to fractures. In addition, the thoracolumbar transition region was the most affected. However, lesions in the thoracic region exhibited worse Frankel status.*

Keywords: *Thoracolumbar; Trauma; Spinal cord injury; Epidemiology; Incidence*

RESUMO

Introdução: *A lesão da medula espinhal, uma das sequelas mais temidas das fraturas da coluna vertebral, é uma causa comum de incapacidade funcional permanente em indivíduos jovens, com taxas significativas de morbidade e mortalidade. De acordo com esta perspectiva, explorar o padrão epidemiológico dessas lesões é o primeiro passo para desenvolver estratégias preventivas visando evitar complicações e melhorar a tomada de decisão. Objetivo: analisar o perfil epidemiológico de pacientes operados que foram vítimas de fraturas toracolombares. Métodos: Estudo descritivo retrospectivo de corte transversal com amostra composta por 223 fraturas*

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toracolombares ocorridas entre 2015 e 2019. Os dados (sexo, idade, local de origem, etiologia da lesão, escala de Frankel para avaliação do déficit neurológico e segmento vertebral afetado) foram extraídos dos registros de pacientes vítimas de trauma na coluna torácica e lombar e tratados cirurgicamente na instituição. Resultados: Foram analisados um total de 223 pacientes, dos quais 164 (73,5%) eram homens. A idade média foi de 35,9 ± 14,3 anos. A maioria dos traumas foi causada por acidentes de motocicleta (36,7%), seguidos por quedas de altura (31,8%) e acidentes de carro (17,0%). A principal causa de trauma em homens foram acidentes de motocicleta (39,0%), enquanto em mulheres foram quedas de altura (35,5%). O segmento mais afetado foi a coluna toracolombar em 118 (52,9%) casos, seguido pelo segmento torácico em 78 (34,9%) casos. Um total de 46,1% dos pacientes foi admitido com escore Frankel E. Acidentes de trânsito foram a principal causa de déficits motores completos na admissão hospitalar (Frankel A). Conclusões: Entre os pacientes tratados cirurgicamente por trauma na coluna torácica e/ou lombar, houve predominância de acidentes de motocicleta, seguidos por acidentes de carro, e os homens apresentaram maior propensão a fraturas. Além disso, a região de transição toracolombar foi a mais afetada, no entanto, as lesões na região torácica exibiram pior status de Frankel.

Palavras-chave: *Toracolombar; Trauma; Lesão da medula espinhal; Epidemiologia; Incidência*

INTRODUCTION

In affluent countries, the incidence of thoracic and lumbar fractures ranges from 12.1 to 57.8 instances per million inhabitants. This figure should be even higher in developing countries owing to a lack of accurately recorded data and societal disorders[1,2]. The incidence of traumatic spine fractures is uncertain in Brazil, not only because there is no statutory reporting requirement but also because there are few nationwide studies. One of the few findings was from the Belo Horizonte metropolitan zone, where there was an incidence of 11.8 traumatic spine injuries per million inhabitants[3]. These fractures affect mostly males in their productive years as a result of road accidents, weapon injuries, falls from great heights, and diving in shallow water[1,3,4].

Spinal cord damage (SCI), one of the most feared sequelae of spinal fractures, is a common cause of permanent functional disability in young individuals, with significant morbidity and mortality rates[2,4,5].

According to this perspective, exploring the epidemiological pattern of these lesions is the first step in developing preventive strategies to avoid complications and improve decision-making in a scenario that typically involves urgency, life-threatening conditions, and limited resource availability[6,7].

Therefore, this study aimed to analyze the epidemiological profile of operated patients who were victims of thoracolumbar fractures, identify risk groups, and support managers in reducing the incidence of this devastating entity.

METHODS

This was a descriptive, cross-sectional, retrospective study. All methods were conducted in accordance with applicable norms and legislation. The study was approved by the joint ethics committee, and all patients provided written informed consent for participation.

The inclusion criteria were as follows: surgical patients who experienced trauma to the thoracic or lumbar spine and were admitted between 2015 and 2019. Those who did not have data (sex, age, Frankel scale, fracture level, and etiology) were excluded.

Data collected from patient medical records included sex, age, etiology of the injury, Frankel scale of neurological deficit, and affected spinal segment classified as the thoracic segment (T1-T10), thoracolumbar transition segment (T11-L2), and lumbosacral segment (L3-S5). Furthermore, the patients' ages were divided into the following age groups: 0-20, 21-40, 41-60, and 61+.

RESULTS

A total of 223 patients (164 men [73%] and 59 women [26%]) were analyzed. The age ranged from 2 to 72 years, with a mean of 35.9 ± 14.5 years, and the highest frequency range was between 21 and 40 years (109 [48.8%]). When comparing ages and considering the sex of the patient, the 20-41 age group was the

most prevalent for the male sex (53.6%), while for women, the majority of trauma occurred in the 41-60 age group (44.0%).

Most traumas were caused by motorcycle accidents (36.7%), followed by falls from heights (31.4%), and car accidents (17%). The main cause in men was motorcycle accidents (about 39%), while in women, it was fall from height (approximately 35.5%). The most affected segment was the level of thoracolumbar transition in 118 (52.9%) cases, followed by the thoracic segment in 78 (34.9%). Furthermore, 46.1% of the patients were admitted to Frankel E, followed by Frankel A (33.6%). Furthermore, most fractures were classified as type A (41%), followed by type C (32%) and type B (26%) (Table 1).

There was a significant difference between the distribution of trauma etiology in the age groups ($p < 0.001$), as all trauma causes had peaked before 40 years, but falls from height had peaked in the 41-60 age group (Figure 1).

For the affected segment, all segments peaked in the 21-40 age group, followed by the 41-60 age group ($p=0.55$) (Figure 2).

According to the neurological and emotional correlation of the traumatic deficit (Figure 3), traffic accidents (motorbikes or cars) were the most common cause of complete motor deficits (Frankel A) when admitted to the hospital, and most victims of motorcycle accidents had Frankel A status ($p = 0.01$).

Regarding the relationship between the cause and the affected spinal column (Figure 4), motorcycle accidents primarily affected the chest spinal column, car accidents and high-rise falls primarily affected the chest spinal column, and weapon injuries affected the lumbar spinal column ($p < 0.001$).

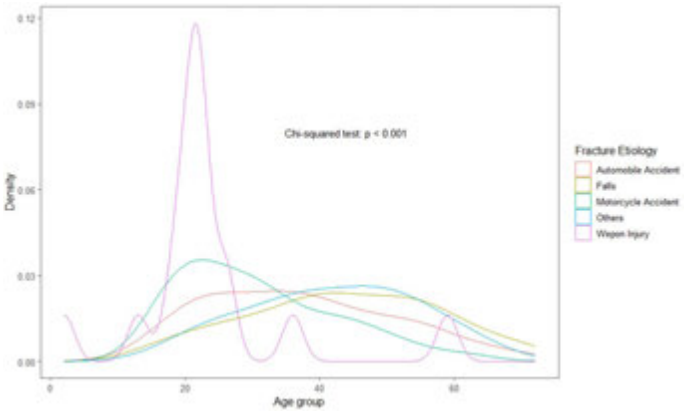

Figure 1. Distribution of trauma etiology by age.

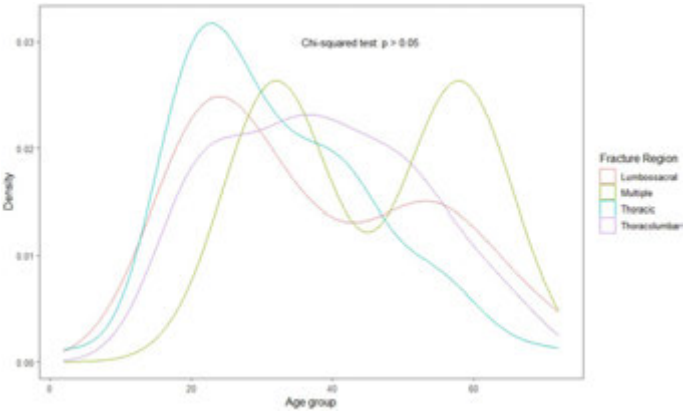

Figure 2. Segment distribution by age.

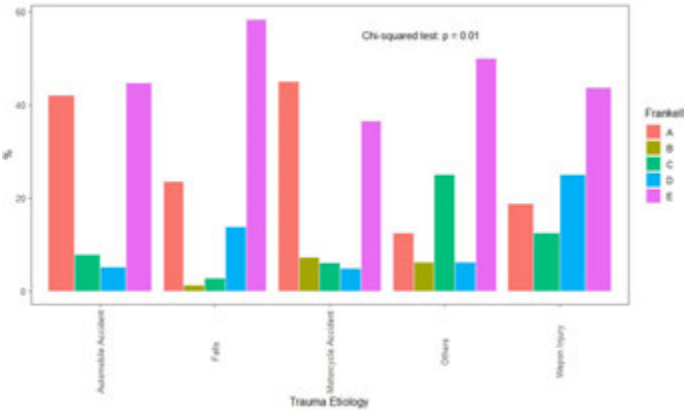

Figure 3. Distribution of fracture etiology according to the Frankel classification.

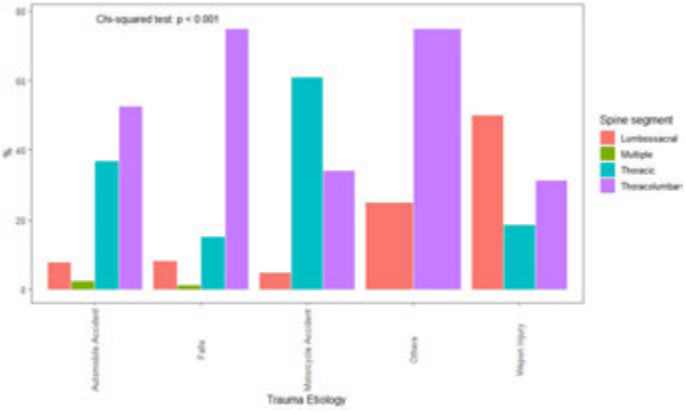

Figure 4. Distribution of the etiology of the fracture by affected segment.

Finally, when analyzing the relationship between the affected segment and Frankel scale at admission, there was a significant difference, with thoracic trauma presenting the majority of Frankel A status (57%) and thoracolumbar and lumbosacral injuries with Frankel E (55% and 56%, respectively).

Table 1. Characteristics of patients with thoracolumbar fractures according to sex, etiology, and neurological deficit.

	Variable	Sex	Total	Row total	Test
		Female	Male		
Trauma etiology	Automobile Accident	16 (42.11%) [27.12%]	22 (57.89%) [13.41%]	38 (17.04%)	p-value: 0.0471 (Chi-squared test)
	Falls	21 (29.58%) [35.59%]	50 (70.42%) [30.49%]	71 (31.84%)	
	Motorcycle Accident	18 (21.95%) [30.51%]	64 (78.05%) [39.02%]	82 (36.77%)	
	Others	1 (6.25%) [1.69%]	15 (93.75%) [9.15%]	16 (7.17%)	
	Wepon Injury	3 (18.75%) [5.08%]	13 (81.25%) [7.93%]	16 (7.17%)	
	Total	59 (26.46%)	164 (73.54%)	223 (100.00%)	
Segment	Lumbossacral	5 (20.00%) [8.47%]	20 (80.00%) [12.20%]	25 (11.21%)	p-value: 0.5611 (Chi-squared test)
	Multiple	1 (50.00%) [1.69%]	1 (50.00%) [0.61%]	2 (0.90%)	
	Thoracic	19 (24.36%) [32.20%]	59 (75.64%) [35.98%]	78 (34.98%)	
	Thoracolumbar	34 (28.81%) [57.63%]	84 (71.19%) [51.22%]	118 (52.91%)	
	Total	59 (26.46%)	164 (73.54%)	223 (100.00%)	
Frankel	A	13 (17.33%) [22.03%]	62 (82.67%) [37.80%]	75 (33.63%)	p-value: 0.0732 (Chi-squared test)
	B	2 (25.00%) [3.39%]	6 (75.00%) [3.66%]	8 (3.59%)	
	C	2 (12.50%) [3.39%]	14 (87.50%) [8.54%]	16 (7.17%)	
	D	7 (33.33%) [11.86%]	14 (66.67%) [8.54%]	21 (9.42%)	
	E	35 (33.98%) [59.32%]	68 (66.02%) [41.46%]	103 (46.19%)	
	Total	59 (26.46%)	164 (73.54%)	223 (100.00%)	
Age group	0-21	7 (23.33%) [11.86%]	23 (76.67%) [14.02%]	30 (13.45%)	p-value: 0.0465 (Chi-squared test))
	21-40	21 (19.27%) [35.59%]	88 (80.73%) [53.66%]	109 (48.88%)	
	41-60	26 (36.62%) [44.07%]	45 (63.38%) [27.44%]	71 (31.84%)	
	61+	5 (38.46%) [8.47%]	8 (61.54%) [4.88%]	13 (5.83%)	
	Total	59 (26.46%)	164 (73.54%)	223 (100.00%)	
	A	15 (30.00%) [48.38%]	35 (70.00%) [38.99%]	50 [41.30%]	
	B	5 (15.62%) [16.12%]	27 (74.38%) [30%]	32 [26.40%]	p-value: 0.3138 (Chi-squared test)
	C	11 (28.20%) [35.50%]	28 (71.80%) [31.11%]	39 [32.30%]	
	Total	31 (25.61%)	90 (74.39%)		

DISCUSSION

According to the World Health Organization (WHO)[8], spinal fractures affect between 250 and 500 thousand individuals globally each year, inflicting significant harm to patients' health, productivity, and quality of life[5,9]. Therefore, understanding its epidemiology is critical for developing public health strategies to prevent or treat it.

Our study found comparable results to prior studies, with males accounting for the majority of trauma patients, traffic accidents topping the population under 40 years old, and falls from height dominating those beyond this age[10,11].

Other significant findings include the prevalence of motorcycle and automotive accidents, with a higher percentage of accidents occurring in the state's heartland. This underscores the importance of public measures in the education, inspection, and re-evaluation of campaigns to stimulate motorcycle purchases[12,13].

The need for additional references in the state for admission of this population should also be emphasized, as early care and treatment might have a direct impact on the prognosis of affected patients[7]. Therefore, specialized care centers should be distributed throughout the capital and interior of the state.

According to research, 15-40% of individuals with thoracic and lumbar spine fractures have neurological impairment[14-16]. Similar to the results presented in this study, 54% of the population had some degree of neurological deficit.

This study had some limitations, including data loss due to its retrospective design. To resolve this issue, we excluded patients with missing data. Another limitation is that the single-centric design may not cover the entire country. However, since the center is one of the city's reference hospitals for traumatic surgery, it is feasible that these findings, while not generalizable nationally, can serve as an important epidemiological dataset to assist in guiding future policymaking on this topic.

CONCLUSION

Motorcycle accidents were the most common cause of thoracic and/or lumbar spine trauma among surgically treated patients, followed by car accidents, and men were more likely to experience fractures. Furthermore, the thoracolumbar transition was the most affected location, however, thoracic injuries exhibited the worst Frankel condition.

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Oberlin Technique for Restoring Elbow Flexion: technical note and functional outcome

Técnica Oberlin para Restauração da Flexão do Cotovelo: nota técnica e resultado funcional

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ABSTRACT

Introduction: *the Oberlin technique, developed by Philippe Oberlin, involves the transfer of ulnar nerve motor fascicles to the musculocutaneous nerve to restore forearm flexion in patients with high brachial plexus injuries. This paper provides a detailed description of the surgical procedure, accompanied by step-by-step illustrations, aiming to assist in the training of neurosurgeons.* **Objective:** *the primary aim is to present a detailed procedural guide and assess its effectiveness by evaluating the functional outcomes of a patient cohort.* **Methods:** *to conduct this study, a retrospective analysis was performed with 10 patients who underwent the Oberlin technique between 2020 and 2022. The patients' ages ranged from 18 to 40 years, and their progress was tracked for an average period of 14.8 months. Elbow flexion strength was assessed using the Medical Research Council (MRC) power grading system, and pain levels were evaluated using the Visual Analogue Scale (VAS). Additionally, injury cause, injury level, time gap between injury and surgery, and pre- and post-operative physical therapy were also analyzed.* **Results:** *among the 10 patients, 4 achieved excellent elbow flexion strength (M4), 4 achieved moderate strength (M2), and 1 patient demonstrated weak strength (M1). Encouragingly, all patients experienced an improvement in paresthesia, and reduction in pain levels was observed post-surgery. On average, the interval between injury and surgery was approximately 7.4 months, and all patients received pre- and post-operative physical therapy.* **Conclusion:** *in conclusion, the findings of this study demonstrate the effectiveness of the Oberlin technique in restoring elbow flexion strength and reducing pain for patients with brachial plexus injuries. The sample size was limited, therefore, no statistical analysis was performed, the results strongly indicate that early surgical intervention within a few months of the injury yields superior functional outcomes. The detailed procedural description provided in this article serves as a valuable resource for the training of young neurosurgeons during their medical residency.*

Keywords: *Oberlin technique; Peripheral nerve; Brachial plexus injuries*

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RESUMO

Introdução: *a técnica de Oberlin, desenvolvida por Philippe Oberlin, envolve a transferência de fascículos motores do nervo ulnar para o nervo musculocutâneo para restaurar a flexão do antebraço em pacientes com lesões altas do plexo braquial. Este artigo fornece uma descrição detalhada do procedimento cirúrgico, acompanhada de ilustrações passo-a-passo, com o objetivo de auxiliar na formação de neurocirurgiões.* **Objetivo:** *o objetivo principal é apresentar um guia com procedimentos detalhados e avaliar sua eficácia avaliando os resultados funcionais de uma coorte de pacientes.* **Métodos:** *para a realização deste estudo, foi realizada uma análise retrospectiva com 10 pacientes submetidos à técnica de Oberlin entre 2020 e 2022. A idade dos pacientes variou de 18 a 40 anos, e sua evolução foi acompanhada por um período médio de 14,8 meses. A força de flexão do cotovelo foi avaliada usando o sistema de classificação de potência do Medical Research Council (MRC) e os níveis de dor foram avaliados usando a Escala Visual Analógica (EVA). Além disso, a causa da lesão, o nível de lesão, o intervalo de tempo entre a lesão e a cirurgia e a fisioterapia pré e pós-operatória também foram analisados.* **Resultados:** *dos 10 pacientes, 4 alcançaram excelente recuperação de força de flexão do cotovelo (M4), 4 alcançaram força moderada (M2) e 1 paciente demonstrou força fraca (M1). De forma encorajadora, todos os pacientes apresentaram uma melhora na parestesia e a redução nos níveis de dor foi observada após a cirurgia. Em média, o intervalo entre a lesão e a cirurgia foi de aproximadamente 7,4 meses, e todos os pacientes receberam fisioterapia pré e pós-operatória.* **Conclusão:** *os achados deste estudo demonstram a eficácia da técnica de Oberlin na restauração da força de flexão do cotovelo e na redução da dor em pacientes com lesões do plexo braquial. O tamanho da amostra foi limitado, portanto, nenhuma análise estatística foi realizada, os resultados indicam fortemente que a intervenção cirúrgica precoce dentro de alguns meses após a lesão produz resultados funcionais superiores. A descrição detalhada do procedimento fornecida neste artigo serve como um recurso valioso para a formação de jovens neurocirurgiões durante sua residência médica.*

Palavras-chave: *Técnica de Oberlin; Nervo periférico; Trauma do plexo braquial*

INTRODUCTION

The surgical technique of transferring motor fascicles of the ulnar nerve for innervation of the biceps muscle was described in the 1990s by the French surgeon, Philippe Oberlin, and this procedure is known as Oberlin Surgery[1]. Initially the technique was tested in animals, consisting of a direct end-to-end transfer of motor branches from the ulnar nerve to the musculocutaneous nerve[2]. Due to the good results, Oberlin started to apply the technique in humans, and observed great results[3]. Since then, it has been widely used around the world as a treatment option for patients with high brachial plexus injuries.

The ulnar nerve is one of the main nerves of the arm and forearm, responsible for providing sensory and motor innervation to the hand and some muscles of the forearm. It originates from the brachial plexus, formed by the C8 and T1 nerve roots. After passing through the elbow, the ulnar nerve goes to the hand, where it divides into several nerve branches that innervate the intrinsic muscles of the hand, as well as the medial portion of the hand sensation[4,5,6]. The musculocutaneous nerve, on the other hand, innervates the anterior compartment of the arm, providing motor innervation for the coracobrachialis, biceps brachii, and much of the brachialis muscles. It also provides sensory innervation for a small region of skin on the lateral surface of the forearm[4,5,7].

Nerve transfers involve the transfer of an expendable, healthy nerve to a distal denervated nerve with a higher functional priority. The donor nerves must provide redundant function to avoid functional deficits and be synergistic to the recipient nerve to facilitate motor rehabilitation[8,9].

Currently, Oberlin's technique consists of transferring ulnar nerve motor fascicles, intended for the ulnar flexor carpi muscle, to the musculocutaneous nerve in order to recover forearm flexion.

It can be indicated in cases of severe musculocutaneous nerve damage in the arm and in upper brachial plexus injuries and can help to restore muscle function in the affected limb. Among the advantages of the technique are short distance to the denervated motor plates, anatomical proximity between donor and recipient, as well as size compatibility between the anastomosed segments[10].

Although there are many papers in the literature about Oberlin's technique, with numerous case series, there is a lack of detailed descriptions of the procedure, with well illustrated images and step-

by-step techniques, especially to help in the training of neurosurgeons during medical residency. This paper aims to discuss the technique in detail, as well as to illustrate the procedure step-by-step, and finally to analyze the results of a series of cases operated with this procedure.

METHODS

A retrospective study was made with patients who suffered brachial plexus trauma, resulting in loss of forearm flexion, and underwent surgery in which the Oberlin technique was used in an attempt to recover the movement.

Patients who were victims of obstetric trauma, patients who did not return for follow-up care, and patients in whom a nerve other than the ulnar was used as a donor for the musculocutaneous nerve were excluded from the study. In total, the study included 10 patients who underwent surgery between 2020 and 2022 and were followed-up, however, one was excluded as he did not return for follow-up appointments. On average, the follow-up time was 14.8 months.

For strength analysis, the Medical Research Council (MRC) power grading system was used in which M0 corresponds to the absence of muscle contraction, M1 flicker or trace of contraction, M2 movement exists but is not able to overcome gravity, M3 movement is able to overcome gravity, M4 movement is able to overcome submaximal resistance imposed by the examiner, and M5 when the movement is able to overcome the maximum resistance imposed by the examiner. To examine flexion strength, patients were asked to remain seated, with the trunk straight and stable.

The strength gain of M3 was considered good and M4 and M5 excellent, as classified by Terzis et al.[11].

To determine preoperative and postoperative pain, the Visual analogue scale (VAS) was used, in which pain is reported by the patient on a scale from 0 to 10, with 0 being no pain at all and 10 being the worst pain imaginable.

Besides strength, other variables analyzed were trauma mechanism, level of injury, pain and paresthesia before and after surgery, time between injury and surgery, and pre- and postoperative physical therapy.

The study was approved by the hospital's ethics committee, and all patients agreed to provide their data for the study.

Surgical procedure

Positioning and incision

The patient is positioned in dorsal decubitus with the upper limb to be operated on positioned in abduction, exposure of the medial aspect of the arm. The incision should be 10-15 cm, between the middle and upper third of the medial side of the arm, below the pectoralis major muscle tendon (Figure 1).

Soft-tissue dissection

After dissection, identification and incision of the brachial fascia (Figures 2 and 3), we proceeded to dissect the deep planes in a blunt fashion, identifying the ulnar and median nerves, the basilic vein, and eventually the lateral cutaneous nerve of the forearm, which follows through to the forearm (Figure 4).

Identifying the musculocutaneous nerve

After separation of these structures, we proceed to the inferior displacement of them, to identify the medial intermuscular septum (Figure 5), incision and opening of it, and then to identify the biceps brachii muscle (Figure 6). Dissection of the biceps muscle fibers was performed for identification of the musculocutaneous nerve motor branch destined to this muscle, and then proceeded the dissection in retrograde until we identified

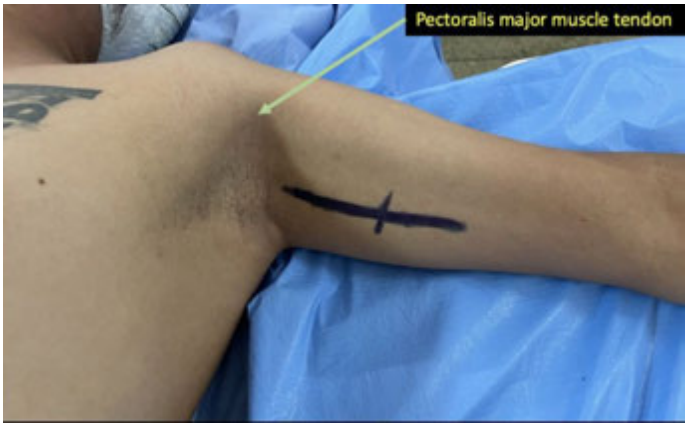

Figure 1. Marking the surgical incision, patient in dorsal decubitus with the upper limb abducted.

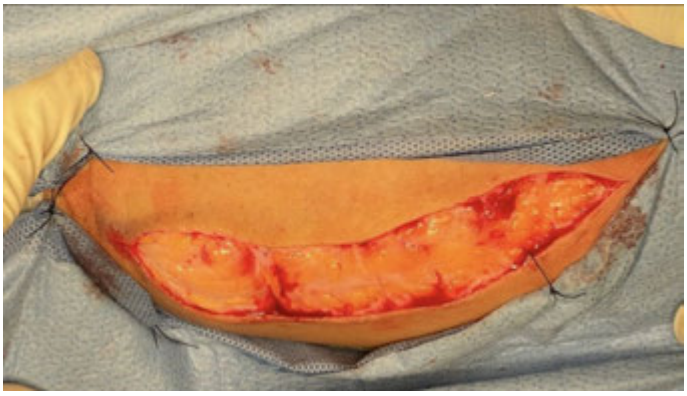

Figure 2. Incision of the skin, identified subcutaneous fat.

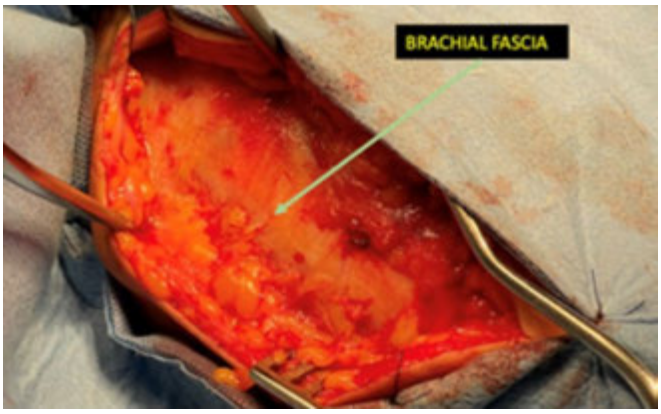

Figure 3. Brachial fascia identification.

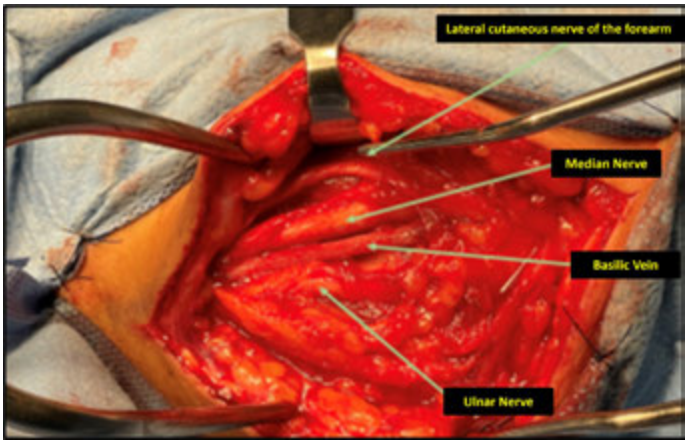

Figure 4. After opening the fascia and dissection, the median, ulnar, and lateral cutaneous forearm nerve, as well as the basilic vein, are identified and separated.

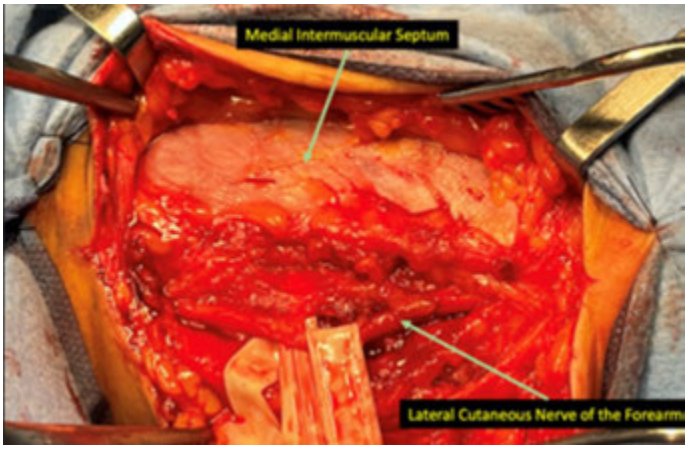

Figure 5. Inferior folding of the previously identified structures, and highlighting the medial intermuscular septum.

the musculocutaneous nerve trunk, where it is divided into the motor branch for the brachial biceps muscle and a larger branch containing fibers for the brachial muscle and the sensitive portion of the nerve (Figure 7).

Preparation of the donor segment

After isolating the motor branch of the musculocutaneous nerve destined to the biceps, the ulnar nerve was dissected, the closest to the receptor, opening the epineurium and identifying the motor fascicles destined to the flexor carpi ulnaris muscle, tested with the help of nerve stimulation (Figure 8).

Preparing the segments for anastomosis

Then it was proceeded to section the ulnar donor segment as distally as possible, and then the Musculocutaneous muscle recipient segment as proximally as possible, ideally near its bifurcation, thus allowing a suture with tension-free approximation (Figure 9).

End-to-end neurorrhaphy

A neurorrhaphy (end-to-end) was performed between the fascicles of the ulnar nerve and the motor branch of the musculocutaneous muscle for the biceps with 9-0 nylon and fibrin glue. After the suture, the subcutaneous and skin was closed by layers (Figure 11).

Postoperative follow-up

After the procedure, the patient must remain with the upper limb immobilized for two weeks, starting motor physiotherapy after this period. Some degree of mild motor or sensory deficit in wrist flexion and forearm region is expected.

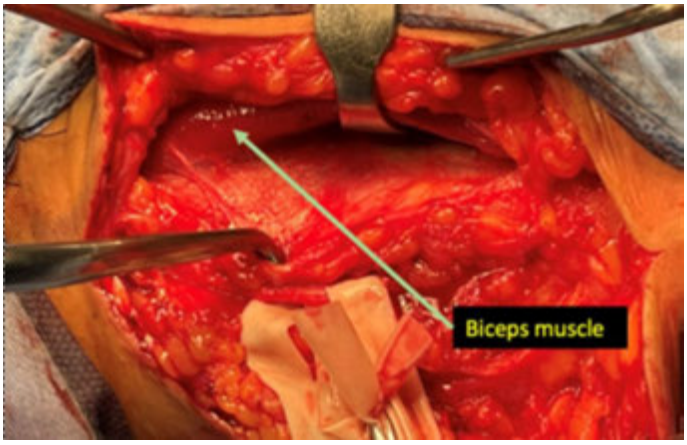

Figure 6. After opening the medial intermuscular septum, the biceps muscle is identified.

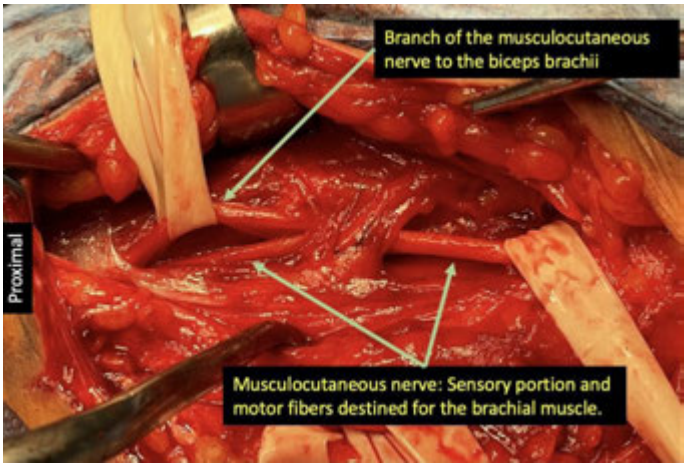

Figure 7. Identification of the Musculocutaneous nerve, and retrograde dissection to the pre-bifurcation segment of the nerve.

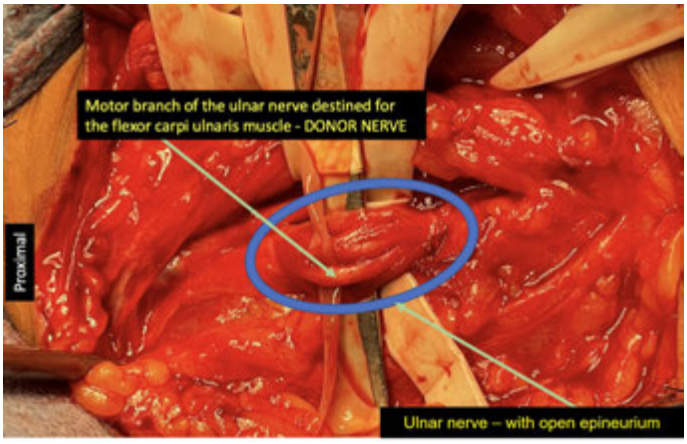

Figure 8. Opening of the ulnar nerve epineurium and identification of the motor fascicles, and separating the donor segment.

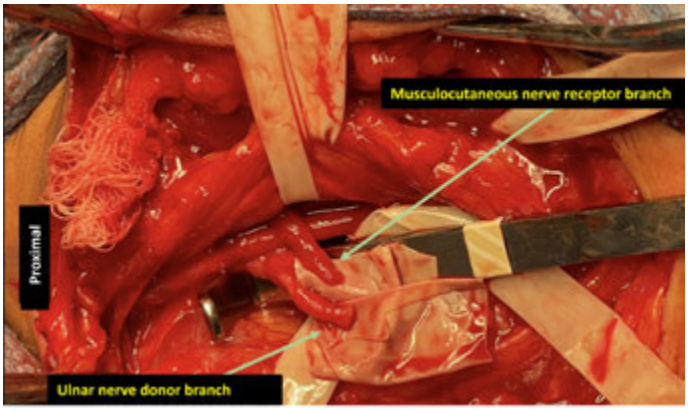

Figure 9. Cross-section of donor and recipient segments, and preparation for end-to-end anastomosis.

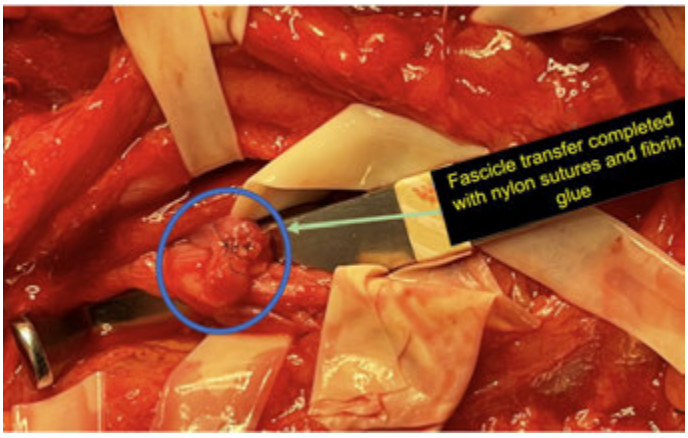

Figure 10. End-to-end suture between donor and recipient.

RESULTS

A total of 9 patients, operated between 2020 and 2022 were included in the study, all were male and the mean age was 30.7 years. Only two trauma mechanisms were identified, the main one being motorcycle accidents, corresponding to 88.8%, and physical aggression, 11.2%.

As for the level of the injuries, 7 of them occurred in the upper trunk, 1 in the lateral cord, and 1 in the roots of C5-C6. All patients had M0 strength after the accident. After surgery four were able to achieve M4 strength, four M2 and one M1.

Eight patients reported paresthesia after the accident, but all had improvement after surgery, and there was also improvement in

the pain level, with the mean value before surgery being 9 and after surgery decreasing to 4.

The average time between injury and surgery was 231 days (7.4 months), and all patients reported that they had performed physiotherapy before and after surgery.

DISCUSSION

In several studies, including this one, traffic accidents were the main cause of brachial plexus injuries, with the frequency varying among different countries, reaching 91% in the study conducted in Thailand by Songcharoen, 88% in this one done in Brazil, and 60% in the one done in Belgium by Dubuisson and Kline[12,13].

The relationship between strength recovery and age is still discussed in the literature, once some studies, like the ones conducted by Samardzic et al.[14] did not find a statistically significant correlation between these two variables. Despite the fact that statistical analysis was not performed due to the limited number of patients, this relation was also observed in the present study, in which it was noted that the mean age of patients who had excellent strength recovery was higher than that of those who had not (39.5 x 26.2 years)[14,15,16].

In Sharma et al.[17] study, in which 18 people were divided into group A, formed by 10 patients between 18 and 40 years of age, and group B, formed by 7 patients over 40 years of age, a statistically significant difference in strength gain between the 2 groups was observed, with group A having a better result[17]. Moreover, it is known that the reinnervation speed ranges from 1-2.5 mm per day, being lower the older the patient is[18].

Due to the limited number of patients, it was not possible to perform a statistical analysis of the data, however, we noticed strength gain in all patients, with 4 (44%) having significant gain (strength M4 or more).

The outcome found for strength gain, although the mean age of the patients (30.7 x 39.2 years) and the time between the accident and surgery (7.4 x 11.7 months) shorter in this study, was below the one found in the 10-case series done by Verdins and Kapickis[19], in which 90% of the patients achieved a strength gain of M4 or more[19].

Although the value was lower than in the series by Verdins and Kapickis[19], it was similar to that found in the series published by de Azevedo et al.[10], in which 9 (50%) of 18 patients had M4 strength regain, and it was higher than the one found in the series with 49 patients published by Cho et al.[20], in which 16 (41%) had M4 strength gain[10,20].

A possible reason for this difference is that the mean follow-up time in Verdins and Kapickis[19] series was 43.6 months, significantly longer than the 14.8 months in this series and the 22.5 months in the Cho et al.[20] series.

A variable that influences strength recovery is the time between the accident and the surgery, as shown by Liu et al.[21], who found a statistically significant difference in strength gain between the group operated on before 4 months and after 4 months, with 96% of the first group having strength gain M3 or more, while in the second group this number was 43%[21]. Some studies, such as the one by Jivan et al.[22], suggested that surgery should be performed at an even shorter interval of 2 months[22,23].

These results were also seen in the systematic review made by Martin et al.[24], which showed that approximately 90% of the patients operated on within 3 months had strength gains of M3 or higher, while in the group operated on after 12 months this number decreased to 35.7%. In addition, the group that was treated earlier had shorter recovery time[24].

The reason for earlier operated patients achieving better functional results is related to less fibrosis at the site of injury and the importance of neurotrophins produced by target tissues and Schwann cells, which are essential for neuron survival, as concluded by Carlstedt who showed in their study that up to half of the lower motor neurons die within 2 weeks after nerve root avulsions[25].

Although the best results are obtained in patients treated before 6 months, there are studies that show it is possible to recover strength even in patients operated on after this period. Of the 18 patients operated on 12 months after the accident by

Khalifa et al., 10 managed to score M4 or higher[26]. Verdins and Kapickis[19] also had good results operating on 3 patients after 12 months, with 2 scoring M4 and 1 scoring M5[19].

The known contraindications for Oberlin surgery are: (1) patients with complete axonal injury, surgery is not recommended for patients with complete axonal injuries of the musculocutaneous nerve because in these cases, there are no nerve connections available for the ulnar nerve to connect to; (2) low brachial plexus lesions (involving the C7-C8-T1 roots); (3) advanced age, since in elderly patients, nerve regeneration may be slower and less effective, which may affect recovery after surgery; (4) concomitant neurological diseases when patients with concomitant neurological diseases, such as multiple sclerosis or diabetic neuropathy, may have less satisfactory results after Oberlin surgery; (5) circulatory problems, when patients with circulatory problems or impaired vascularization in the arm or hand area may have an increased risk of complications after Oberlin surgery[10,27,28].

CONCLUSION

The Oberlin technique is efficient in the recovery of forearm flexion, with the functional results of the surgery being associated with variables such as patient age and time between the injury and the surgery. Moreover, the surgery is also able to promote improvement in pain perception.

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Intracranial Aneurysms in Patients with Atrial Myxoma: a systematic review of the literature

Aneurismas Intracranianos em Pacientes com Mixoma Atrial: uma revisão sistemática da literatura

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ABSTRACT

Introduction: *more than half of primary cardiac tumors are atrial myxomas (AM) and they may cause neurological complications. However, intracranial aneurysms (IAs) related to these tumors are rare. The pathogenesis of IAs associated with AM is not well established. IA diagnosis can occur before or after myxoma resection. There are no well-defined management guidelines for these patients.* **Objective:** *this study aims to assess the occurrence of IAs in patients with AMs, as well as their clinical characteristics and outcomes.* **Methods:** *this is a systematic review, performed in the databases PubMed, LILACS, Scielo, DOAJ and Cochrane, using different combinations of the keywords, atrial myxoma, neurological complications, myxoma, aneurysm, intracranial aneurysm in both AND and OR combinations.* **Results:** *a total of 62 case reports were analyzed, and 72.6% of patients were women, mean age of 46.31 years. A total of 64.5% of aneurysms were diagnosed after myxoma resection. Fusiform aneurysms affecting the middle cerebral artery predominated (66.1%). Headache, visual changes, and speech disturbances were the main symptoms. Neurological examination was normal in 17.7%. From these patients 40.3% presented with some neurological event and 35.4% received conservative treatment. Deaths were infrequent.* **Conclusion:** *IAs in patients with AM are rare. Women are more affected than men, especially around the age of 50, men were more affected at age of 60. Middle cerebral artery aneurysms were more prevalent. Headache was the main symptom. Management is controversial, and less than a third received a surgical approach. Overall, there is neurological improvement and hospital discharge.*

Keywords: *Atrial myxoma; Neurological complications; Myxoma; Aneurysm; Intracranial aneurysm*

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RESUMO

Introdução: *mais da metade dos tumores cardíacos primários são mixomas atriais (MA), que podem causar complicações neurológicas. Porém, os aneurismas intracranianos (AIs) relacionados a esses tumores são raros. A patogênese de AIs relacionados a MA não está bem estabelecida. O diagnóstico dos AIs pode ocorrer antes ou após a ressecção do MA. Não há diretrizes sobre o manejo desses pacientes.* **Objetivo:** *avaliar a ocorrência de aneurismas intracranianos em pacientes com mixoma atrial, bem como suas características clínicas e desfechos.* **Métodos:** *este estudo é uma revisão sistemática, realizada nas bases de dados PubMed, LILACS, Scielo, DOAJ e Cochrane, utilizando diferentes combinações das palavras-chave: mixoma atrial, complicações neurológicas, mixoma, aneurisma, aneurisma intracraniano, em combinações AND e OR.* **Resultados:** *foram analisados 62 relatos de casos, sendo 72,6% dos acometidos mulheres, com idade média de 46,31 anos. Um total de 64,5% dos aneurismas foram diagnosticados após a ressecção do mixoma. Predominam AIs fusiformes na artéria cerebral média (66,1%). Cefaleia, alterações visuais e distúrbios da fala foram os sintomas principais. O exame neurológico estava normal em 17,7%. Dentre os pacientes, 40,3% já apresentaram algum evento neurológico e 35,4% receberam tratamento conservador. Óbitos foram infrequentes.* **Conclusão:** *AIs em pacientes com MA são raros. Mulheres são mais acometidas que os homens, principalmente aos 50 anos; homens são mais acometidos aos 60 anos. Os AIs predominam na artéria cerebral média. Cefaleia é o principal sintoma. Manejo é controverso, menos de um terço recebe abordagem cirúrgica. No geral, há melhora neurológica e alta hospitalar.*

Palavras-chave: *Mixoma atrial; Complicações neurológicas; Mixoma; Aneurisma; Aneurisma intracraniano*

INTRODUCTION

Atrial Myxoma (AM) corresponds to more than a half of primary cardiac tumors (50-80% of cases)[1]. Despite being benign tumors, they can cause embolic phenomena, which affect the vascular system and provoke infarctions[2]. The true incidence of intracranial aneurysms (IAs) formation after an embolic phenomenon is not known, but the association between these events has already been evidenced[2]. Commonly, myxomas occur in the left atrium, creating symptoms by obstruction of the mitral valve, systemic embolization, and constitutional symptoms[3]. Nevertheless, 10% of patients can be asymptomatic[3].

More than 50% of cases can course with neurological complications[1]. Headache, nausea/vomiting, limbs/body weakness, numbness and seizure are some manifestations of central nervous system involvement[4]. Cerebral embolism is the main neurological complication, intracerebral hemorrhage (parenchymal and subarachnoid hemorrhage) has a lower incidence and is associated with aneurysm formation[1]. Myxomatous metastasis and cerebral cavernous formation are also described as complications of cardiac myxoma[5].

Cerebral artery aneurysms related to atrial myxoma are rare[2]. The pathogenesis of myxomatous aneurysms formation is not well established[6]. It can be associated with embolic myxoma cells invasion of vessel walls, which damage the vessel and create a subintimal growth[1]. Myxoma cells have also been detected in the wall of aneurysm at the same region of a cerebral infarction[2]. It was once theorized that tumor cells could keep spreading after invading the vessel wall, which causes a fibroblastic proliferation and weakens the vessel creating aneurysmal dilatation, but some patients developed aneurysms without embolic signs and some others after the tumor resection[2]. Interleukin-6 (Il-6) may also have a role in aneurysm formation[5]. Myxoma cells produce Il-6, and high levels of these in the cerebrospinal fluid has been reported[5]. It is theorized that IL-6 up-regulates the expression and activity of metalloproteinases and promotes invasion of myxomatous cells into cerebral arteries[5]. Most studies in patients with atrial myxoma describe fusiform aneurysms, but a few others found saccular aneurysms[2].

These associations can occur before or many years after myxoma's diagnosis or resection[1]. Currently, there are few studies about the risk of cerebral myxomatous aneurysm rupture, and there is no established management guidelines for patients with intracranial aneurysms and atrial myxoma[6].

This systematic literature review has the objective of assessing the occurrence of intracranial aneurysms in patients with atrial myxoma, as well as describing their clinical characteristics and outcomes.

METHODS

This study corresponds to a broad systematic review performed in the databases PubMed, LILACS, Scielo, DOAJ (Directory of Open Access Journals) and Cochrane, using different combined keywords of atrial myxoma, neurological complications and the mesh terms myxoma, aneurysm, intracranial aneurysm (and its entry terms brain aneurysm, cerebral aneurysm), hemorrhage stroke, subarachnoid hemorrhage, embolism, metastasis in both AND and OR combinations. Pubmed search strategy: ((“atrialisation”[All Fields] OR “atrialization”[All Fields] OR “atrialized”[All Fields] OR “atrially”[All Fields] OR “heart atria”[MeSH Terms] OR (“heart”[All Fields] AND “atria”[All Fields]) OR “heart atria”[All Fields] OR “atrial”[All Fields]) AND (“myxoma”[MeSH Terms] OR “myxoma”[All Fields] OR “myxomas”[All Fields]) AND (“intracranial aneurysm”[MeSH Terms] OR (“intracranial”[All Fields] AND “aneurysm”[All Fields]) OR “intracranial aneurysm”[All Fields])) AND ((y_5[Filter]) AND (english[Filter] OR portuguese[Filter] OR spanish[Filter])). The correspondents in Portuguese language of the terms were also used. We search for articles in Portuguese, English or Spanish.

Articles were included if they focused on patients with intracranial aneurysm and atrial myxoma, regardless of the study design. Articles were excluded if they were about patients with other neurological diseases rather than aneurysms. Articles which were not completely available online, not available in English, Portuguese or Spanish languages, book chapters and other reviews were also excluded.

RESULTS

The research strategy yielded 243 results, 28 of these were duplicated, and 144 did not satisfy the selection criteria or matched the exclusion criteria, resulting in 71 articles analyzed. There were 62 case reports from these 71 studies.

The majority of patients were women, nearly 72.6% of the total. Male patients were described in 25.8% reports and two studies (about 3.2%) did not report the biological gender of the patient.

Ages of occurrence were diverse: the youngest woman was 14-year-old and the older one was 73 years; men’s ages varied from 11 to 58-year-old. Patients’ age from one of the reports that didn’t mention their sex was 68-year-old, and the other one is a patient who had been followed since she was 17-year-old with aneurysm detection 12 years after that. As a result, the mean age of occurrence was 46.31 years for women (population standard deviation: 16.23) and 36.1 years for men (population standard deviation: 16.28). Table 1 shows the distribution of cases according to age.

Most of the aneurysms were diagnosed after the myxoma’s resection (about 64.5%). The time gap between myxoma resection and aneurysm diagnosis was 25 years. Table 2 shows the percentage of patients with aneurysm diagnosis after myxoma´s resection, according to the period between these events. One study did not report the time gap between myxoma resection and aneurysm diagnosis.

Aneurysms affected mainly the middle cerebral artery and its branches, followed by anterior and posterior cerebral arteries. Basilar, posterior inferior cerebellar artery and other vessels were also affected, but occurrence was quite smaller. In 66.1% of the studies the aneurysms were fusiform, 12.9% studies reported saccular aneurysms and 17.7% didn’t characterize the aneurysms. Also, in most of the reports (88.7%) the patients had more than one aneurysm.

Headache was the most recurrent symptom being present in 38.7% reports. In general, patients complained of progressive headache,

Table 1. Distribution of aneurysm occurrence by life decade.

Sex/age	11 - 19y	20 - 29y	30 - 39y	40 - 49y	50 - 59y	60 - 69y	70 - 73y
Women	9%	4.5%	15.9%	29.5%	20.4%	13.6%	6.8%
Men	25%	6.2%	15.7%	15.7%	31.2%	-	-
Total	12.9%	4.8%	16.1%	25.8%	22.5%	9.6%	4.8%

Table 2. Time gap between myxoma resection and aneurysm diagnosis. Results according to the most relevance time interval between myxoma resection and aneurysm diagnosis, distributed by intervals of months/years.

time	3 - 6m	> 6m - 1a	> 1y - 3y	> 3y - 5y	> 5y - 10y	> 10y - 20	> 20y - 25y
% of patients	8.0%	12.9%	11.2%	11.2%	9.6%	8.0%	1.6%

blunt headache, or thunderclap headache. Table 3 shows the main clinical manifestations. Visual symptoms were described as blurred vision, scintillations in the right visual field, and homonymous quadrantanopia. Motor aphasia, dysarthria, slurred speech are some related speech disorders. People complained of weakness in a variety way: one-sided limb weakness, weakness in lower or upper extremities, and only weakness. Seizures presented as generalized tonic clonic seizures, secondary generalized, focal seizure, motor seizures with secondary generalization, right upper extremity seizure followed by paralysis. Facial changes were inferolateral deviation of the right eye, deviation of angle of mouth, facial palsy, right facial pain and left ptosis. Other symptoms like behavior changes, dyspnea or respiratory distress, nausea/vomiting were also related.

In 17.7% of the studies, patients had a normal neurological exam, and the most common abnormalities in patients with an abnormal physical exam were decreased muscle strength, hyperreflexia, and hypertonia. A total of 9.6% of aneurysms were diagnosed in incidental or follow-up exams.

At the time of diagnosis of aneurysm, 40.3% of the patients already had a previous brain infarct or an hemorrhagic event, and in 45.1% cases the aneurysm diagnosis happened concurrently with some neurological event such as brain infarct or hemorrhage.

Management

We had divided the patient management in surgical or nonsurgical approaches of the aneurysms and those who had radiointervention. Table 4 shows the percentage of cases according to management. The surgical approach described in the case reports were diverse and depended on patients' features and risks. A total of 8.0% were treated with clipping, 9.6% received an endovascular approach as coil or liquid embolization, 9.6% had a surgical resection, and 1.6% were treated with coagulation via electrocautery.

Radiointervention was also diverse and regarded the same features as surgical approach. Low -dose radiation therapy, frameless stereotactic radiosurgery and whole brain radiation were the techniques reported.

Table 3. Main clinical manifestations of intracranial aneurysms in patients with atrial myxoma. Results according to the most related symptoms in the obtained reports.

Clinical manifestations	Number of patients
Headache	38.7%
Visual changes	20.9%
Speech disturbances	19.3%
Weakness	16.1%
Seizures	16.1%
Paresthesia	14.5%
Dizziness or vertigo	12.9%
Deviation or facial palsy	12.9%
Paresis or hemiparesis	9.6%
Gait disturbance	9.6%
Unsteadiness or ataxia	8.0%

Death was reported in only one study, in the 61 remaining articles patients were discharged from the hospitals and/or required medical follow up. In general, independently of the chosen approach, patients reported improvement symptoms. Complete obliteration of the aneurysms was found in 12.9% of patients, or the same size after management was kept. A few reports described worsening of aneurysms features after some approach.

DISCUSSION

Intracardiac tumors can cause life-threatening situations, ordinarily caused by embolic phenomena or as a sequelae of cardiac dysfunction[2]. The central nervous system might be the most affected site of embolism, and one can find as neurological complications of cardiac myxomas: embolism and ischaemia, neoplastic aneurysm formation (these situations can occur with hemorrhagic complications), and intracranial mass formation[7]. Cerebral aneurysm formation as a complication of cardiac

Table 4. Treatments approaches most cited in the obtained articles.

	nonsurgical approach	surgical approach	radio intervention	not described
patients	35.4%	32.2%	6.4%	25.8%

myxoma is rare, but these patients with cardiac tumors can present with a diversity of neurologic syndromes, even without cardiac symptoms[5], and these disturbances are still underdiagnosed[2].

According to the results presented above, myxomatous aneurysms occur predominantly in adults, mainly women, after cardiac myxoma resection. The disparity of occurrence between genders was already described with cardiac myxoma affecting women twice as much as men[8]. The predominant ages of occurrence corresponded to previous reports, between thirty and sixty years old[9]. Also, the aneurysms can affect anterior and posterior circulation, and manifest in a diversity of symptoms, such as headache, blurred vision, or aphasia. In most cases aneurysms' diagnosis happens after myxomas resection. It also can happen at the time of a neurological event, or after that. Neurological exam is normal in most patients and non-surgical approach is preferable in these cases.

Atrial myxoma, in addition to atrial fibrillation, acute myocardial infarction, valvular heart disease, infective endocarditis, and nonbacterial thrombotic endocarditis are the main causes of cerebral embolism originating from the heart[10]. Previous studies have shown that neurological manifestations occur in 12-45% of patients and aneurysms formation in 1-3%[9]. Tumor cells undergo embolization, and reach intracranial vessels, where they are lodged in the smaller and peripheral arteries[9]. These cells penetrate and proliferate in the endothelium, leading to weakening and dilatation of arterial walls[9]. Some studies also associated myxomatous proliferation inside the vascular lumen with aneurysmal dilatation[9]. Therefore, the pathology of formation of myxomatous aneurysm has three steps: arterial embolism and ischaemia, neoplastic aneurysm formation, and intraparenchymal metastases[11]. Neoplastic aneurysm formation can happen with or without hemorrhage[11].

The already described characteristics of these aneurysms match with the results of this research: myxomatous aneurysms are multiple, fusiform, located at distal branches on the arterial tree, mostly at the anterior and middle cerebral arteries territories[11,12]. Saccular aneurysms were also described. In our study, aneurysms were mostly diagnosed after myxomas resection, but Alrohimi et al.[13] showed that 56% of aneurysms were diagnosed previous to myxomas resection[13].

It is known that aneurysms can be a late manifestation of cardiac tumors, and the latency period between tumor resection and aneurysm detection varies between 2 and 300 months, an average of 36 months, and it occurs even in the absence of other risk factors[5]. Aneurysms may develop after many years, since tumor's resection, as a delayed complication, owing to slowness of the pathological process that involves its formation[12]. Myxomatous metastasis is also a delayed complication, and haemorrhagic stroke is not common (in general related to cerebral aneurysms)[14]. Neurological manifestations can be accute or chronic[12]. The immediate manifestation of tumor embolization is ischemic brain disease because of occlusion and stenosis of the vessels[12].

The clinical manifestations described at this study were reported by patients at the hospital admission resulting in aneurysm diagnosis. Myxoma can present with a range of symptoms, such as neurological deficits, hemorrhages, syncopes, psychiatric symptoms, headaches or epilepsy[11]. All these manifestations were found in the analyzed cases. Embolic events should be suspected at the sudden onset of neurologic deficit associated with alteration in consciousness, seizures, or hemorrhagic infarction on computerized tomography[15]. Patients with myxomatous aneurysms usually have symptoms like cerebral vasculitis or infective endocarditis, so echocardiography, computed tomography and magnetic resonance imaging of the heart are necessary in patients with suspected stroke[14]. It has already been demonstrated that aneurysms can present stroke, transient ischaemic attack, subarachnoid hemorrhage, intraparenchymal hemorrhage, headaches, and neurological deficits, similar to the clinical manifestations shown above[11].

There are no guidelines that determine the approach for patients with intracranial aneurysm followed by a cardiac myxoma[5]. In general, conservative management is the main choice for these patients, mainly because of the poor existing data about the natural history of myxomatous aneurysms, and the lesions seem to be stable on radiographic follow-up or have a spontaneous regression[16]. As usually the aneurysms are multiple and fusiform,

they cannot be coiled or clipped, so if they are stable, conservative management is an appropiate choice[17]. Surgical approach can be considered in patients with hemorrhage, and resection of aneurysms located in non-eloquent areas has been described[11,13].

The cardiac tumor's resection can prevent neurological complications but does not prevent the risk of cerebral aneurysm[13]. "Metastasize and Infiltrate" theory is the major explanation for this phenomenon: myxoma fragments metastasize to the brains, these cells infiltrate the vessel walls and damage the elastic lamina, creating vessel dilatation that results in aneurysm formation[5].

Other options to be considered are chemotherapy and radiointervention: chemotherapy results were questionable; radiation therapy combined with chemotherapy could degrade myxoma metastasis cells, so it can prevent the myxomatous aneurysms[18]. Irradiation with doxorubicin and ifosfamide has better results, compared with chemotherapy[9].

Medical management, as anticoagulation, is ineffective for the prevention of embolic phenomenons related to cardiac myxoma, therefore echocardiography should be performed in patients with suspected cardioembolic stroke[9]. Penn et al.[16] recommended radiographic follow-up after lesion diagnosis, and if the patient presents with neurological symptoms, MRI and/or MRA, should be performed on presentation and repeat imaging at 3 months[16]. The lesions detected initially demand a closer follow-up with a 3 months interval to confirm stability. Once confirmed stability, 6 months or one-year interval can be considered[16].

As a result of this study, we observe the knowledge gap about neurological manifestations of atrial myxoma, mainly aneurysm formation. This stems from the rarity of these occurences, in the meantime it can cause life-threatening situations and/or neurological consequences for patients. In the literature, most studies about this theme are case reports, so it is important to keep watching closely these patients and studying the best way to manage them. The poor quantity and quality of reviews and studies about this condition was the biggest limitation of our study. Updated data about aneurysm formation and patient management are poor. As a result, we did not obtain a large sample of case reports, as we expected, to build this research.

CONCLUSION

Intracranial aneurysms in patients with atrial myxoma are a rare condition, but it can cause damage. Women are more affected than men, and the aneurysms occur mostly around the 5th (women) or 6th (men) decades of life. The majority of aneurysms were diagnosed after the myxoma's resection. In general, they are fusiform, and the most affected vessels are middle cerebral artery and its branches, anterior and posterior cerebral arteries. Headache is the main symptom. Treatment and management are still controversial, only 32.2% were treated surgically. But, in general, patients had a neurological improvement and were discharged from hospitals for follow-up. Death occurred in only one report.

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Review

Malignant Cerebellar Large Cell Lymphoma: case report and systematic review

Linfoma Maligno de Grandes Células Cerebelar: relato de caso e revisão sistemática

Raiza Marques Vieira Campos[1]
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Osmi Hamamoto[3]

ABSTRACT

Introduction: *primary CNS lymphomas are considered non-Hodgkin type, involving the nervous system without systemic involvement. Risk factors include prior viral infection, immune dysfunction, and family history. In recent decades, its incidence has been increasing in young immunosuppressed individuals.* **Methodology:** *the authors present a rare case of a patient with cerebellar large B-cell lymphoma and a literature review from the last ten years on the subject, in the PubMed and SciELO databases.* **Case report:** *we report a rare case of cerebellar large B-cell lymphoma in a young patient with HIV/AIDS reported during hospitalization, describing the actions taken by the neurosurgery team at Hospital das Clínicas de Marília according to surgical complications, as well as the patient stage.* **Discussion:** *PCNSL constitute a rare condition, in which infratentorial involvement has been described in few cases in the world. They have a high degree of malignancy and high recurrence rates. If left untreated, life expectancy is very low.* **Conclusion:** *due to the increasing incidence in both immunocompromised and immunocompetent patients and the highly aggressive nature of these tumors, early diagnosis is necessary. The authors report that even teamwork with infectious diseases, intensive care and pathology were not able to increase survival in the reported case.*

Keywords: *Cerebellar B-cell lymphoma; Cerebelar primary neoplasm*

RESUMO

Introdução: *os linfomas primários do sistema nervoso central (PSNCL) são considerados do tipo não-Hodgkin sem envolvimento sistêmico. Os fatores de risco incluem infecção viral prévia, disfunção imunológica e história familiar. Nas últimas décadas, sua incidência vem aumentando em indivíduos jovens imunossuprimidos.* **Metodologia:** *os autores apresentam um caso raro de paciente com linfoma de grandes células B cerebelar e uma revisão da literatura dos últimos dez anos sobre o assunto, nas bases de dados PubMed e SciELO.* **Relato de caso:** *relatamos um caso raro de linfoma de grandes células B cerebelar em paciente jovem com HIV/AIDS durante sua internação, descrevendo as ações tomadas pela equipe de Neurocirurgia do Hospital das Clínicas de Marília.* **Discussão:** *o PSNCL constitui uma condição rara, na qual o envolvimento infratentorial tem sido descrito em poucos casos no mundo, apresentam um alto grau de malignidade, altas taxas de recorrência e sobrevida muito baixa, quando não tratado.* **Conclusão:** *devido ao aumento da incidência e à natureza altamente agressiva desses tumores, o diagnóstico precoce é necessário. Os autores relatam que mesmo com esforços da equipe multidisciplinar e rapidez nas ações tomadas conforme intercorrências surgiam, não foi possível aumentar a sobrevida no caso relatado.*

Palavras-chave: *Linfoma de células B cerebelar; Neoplasia primária cerebelar*

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INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is an uncommon form of non-Hodgkin's lymphoma that can affect the brain, meninges, spinal cord or eyes, representing 3% of intracranial neoplasms. Only 9% of PCNSL is found in the cerebellum, generally presenting as a single lesion in 60-70% of cases[1]. It is a less common pathology in immunocompetent patients and the average age of diagnosis in these patients is 50 to 65 years. Frequent symptoms include personality changes, aphasia, focal neurological deficit, increased intracranial pressure, muscular deficit, seizures, ataxia, emesis, confusion and visual changes. On MRI, lymphomas usually show iso or hyposignal on T2 and restricted diffusion, as they have high cellularity. When they do not present these characteristics, the diagnosis can be challenging and other differential diagnoses must be considered. The choice of treatment depends on multiple factors, such as the patient's age, previous treatment and response, and comorbidities. The role of surgery in these cases is limited, but should be considered in cases of evident increase in intracranial pressure[2,3].

In this article, we describe a case of cerebellar PCNSL in a young patient not known to be immunocompromised before hospitalization, in addition to bringing together in a systematic review, from the last 10 years, cases described in the literature to compare their clinical, histopathological and prognostic characteristics. This study provides a reference for the diagnosis and treatment of this type of disease.

METHODS

This study was based on the methodological procedures described in Preferred Report Items for Systematic Reviews and Meta-analysis (PRISMA) of the experimental type to identify, select and critically evaluate research already published on the exposed topic (Figure 1).

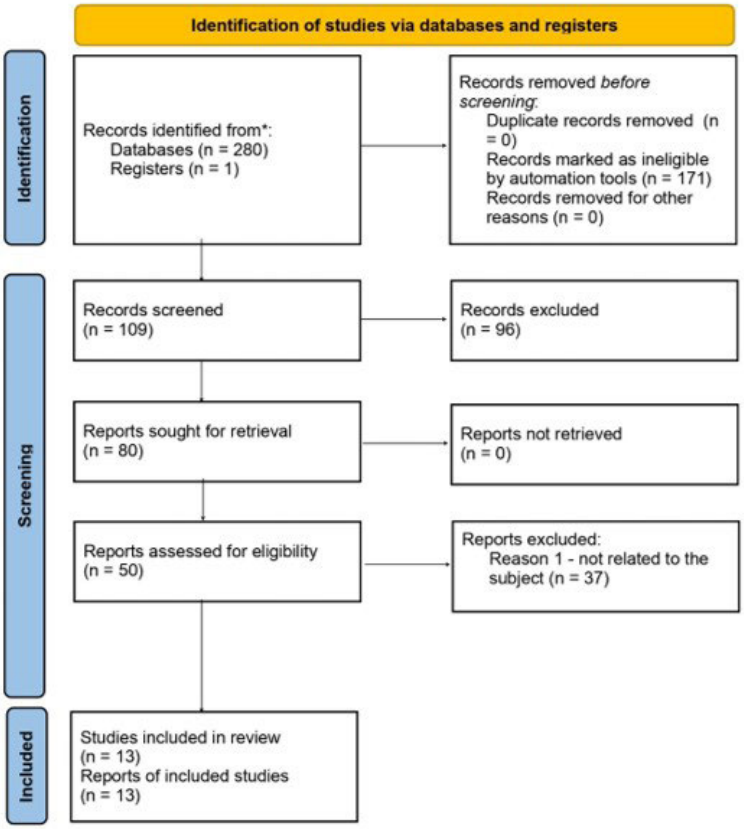

Figure 1. Literature search according to PRISMA guidelines.

The review was carried out on the original articles available in the PubMed and Scielo databases, thtat were selected using the term: "cerebellar B-cell lymphoma", which was determined based on previous studies on the topic and analysis of the reported case. The selection criteria were studies published between 2013 and 2023, in English or Portuguese, and articles available in full. Articles that were not related to the topic studied or the research question were excluded.

RESULTS

Table 1 compares the reports found in the literature. These are studies with reports from one or more patients comparing common factors, including age, sex, personal history, initial clinical picture, imaging examination, management and outcome (Table 1).

Table 1. Description of clinical characteristics, surgical procedure of choice and outcome of case reports found in the literature.

Author	Study type	Sex	Age	Previous disease	Clinic	Image exam	Treatment	Outcome
Beraldo et al., 2019[1]	CR	Female	52	none	Dizziness and left motor incoordination	Brain MRI: hyperintense lesion on T2 in the left middle cerebellar peduncle	Open biopsy and resection, dexamethasone and four cycles of chemotherapy	After 3 months, the patient returned with decreased consciences level and new lesion. The patient died five days after her relapse
Ghannam et al., 2018[4]	CR	Male	71	none	Dizziness, nausea, vomiting and gait imbalance	Brain CT: three intensely enhancing masses in the right cerebellar hemisphere	The patient underwent right suboccipital craniotomy with partial resection plus chemotherapy	No residual disease seen on head CT scans. Improvement in symptoms but still reports balance problemas and blurry vision
Pancetti et al., 2023[5]	SC	Male	76	None	Frontal headaches, dizziness, nausea and vomiting	Brain MRI: mass in the left cerebellar hemisphere with abnormal blood flow	Posterior craniotomy for tumor excision and chemotherapy	After 2 cycles of chemotherapy the patient achieved complete remission
Pancetti et al., 2023[5]	SC	Female	65	Dyslipidemia, alcoholism, heavy smoking and 2 spontaneous miscarriages	Asymptomatic	Brain MRI: one lesion in the right hemisphere with a mass effect on the fourth ventricle and a second one in the left cerebellar peduncle	Posterior craniotomy with partial cerebellar tumor excision and chemotherapy	After 2 months of chemotherapy the patient achieved complete remission
Pancetti et al., 2023[5]	SC	Female	65	Previous diagnosis of meningioma, treated with surgery	Long-standing headache and nausea	Brain MRI: expansive lesion in the right cerebellar hemisphere close to the dentate nucleus	Stereotactic biopsy, chemotherapy and auto-transplant of autologous steam cells	18 months after the diagnosis the patient achieved complete remission
Zhou et al., 2015[2]	CR	Male	80	Positive for Epstein-Barr virus	Cervical lymphadenopathy, cough, fatigue and anemia requiring transfusion	Brain MRI: ring-enhancing mass lesion in the left posterior cerebellum. There is mild edema around the lesion as well as hemorrhage or mineralization	Stereotatic biopsy, one cycle of rituximab followed by one cycle of rituximab, methotrexate and vincristine	The patient's clinical course was complicated by biopsy related subdural hemorrhage and multiple infections. The patient died 4 months after the diagnosis of B-cell lymphoma
He et al., 2022[3]	SC	Male	22	smoking	Dizziness, headache, nausea and vomiting	Brain MRI: cerebellar mass lesions within the bilateral cerebellar hemispheres with strong enhancement	Right cerebellar tumor excision with complete resection and chemotherapy	PCNSL could not be suppressed by this therapeutic strategy, and the tumour invaded other brain sections. This patient died within 9 months.

Table 1. Continued...

Author	Study type	Sex	Age	Previous disease	Clinic	Image exam	Treatment	Outcome
He et al., 2022[3]	SC	Male	26	smoking	dizziness and unsteady gait	Brain MRI: high enhancement signal in the right cerebellum	Right cerebellar tumor excision with complete resection and chemotherapy	The patient has survived and is generally in good condition
He et al., 2022[3]	SC	Male	54	none	Occipital sore	Brain MRI: multiple nodular signals with low T1 and slightly high T2 in both cerebellar hemispheres. The FLAIR sequence showed annular hyperintensity, and enhancement was very evident on the enhanced scan	Right cerebellar tumor excision with complete resection and radiotherapy	The patient has not experienced tumour progression and is generally in good condition
Jha et al., 2015[6]	CR	Female	63	Mastectomy for carcinoma breast and pulmonary tuberculosis	Seizures	Brain MRI: large, well-defined lobulated lesion in the left cerebellar hemisphere showing a moderate enhancement with central necrotic areas and associates mass effect on the dorsolateral aspects of the pons and medulla	Left retromastoid craniotomy and tumor excision plus chemotherapy	The patient was lost to follow up
Harley et al., 2018[7]	CR	Female	40	History of MG and thymectomy. She had been on azathioprine treatment 175 mg once per day for 8 years	3 months history of global headaches	Brain MRI: demonstrated a left posterior fossa rim enhancing lesion, measuring 27 21 20 mm,	She underwent a stereotactic left retrosig- moid craniotomy and resection of the lesion	When the diag- nosis was confirmed, azathioprine was discontinued but pyri- dostigmine was continued. Unfortunately the patient developed a recurrent lesion at the site of resection 5 weeks postoperatively. She was treated with rituximab and methotrexate followed by cytarabine. At six months postoperatively the patient has minor residual fatigue, but no headache and no neurological deficits.
Galarza Fortuna et al., 2019[8]	CR	Female	78	History of estrogen and progesterone receptors positive, right breast ductal cell carcinoma in situ, which was fully excised.	Progressive right-sided ataxia of 1 week.	Noncontrast head CT showed an iso-hypodense ill-defined lesion in the right cerebellum measuring approximately 1.6 cm associated with surrounding edema and mild mass effect on the fourth ven- tricle. A follow-up brain magnetic resonance imaging (MRI) showed multiple posterior fossa enhancing lesions and an additional punctate enhancing lesion in the left thalamus, suspicious for metastatic carcinoma	Right-sided posterior fossa craniotomy with excisional biopsy of the right cerebellar lesion plus pre-irradiation chemotherapy with high-dose methotrexate, rituximab, and temozolomide for 6 cycles, followed by low-dose whole-brain radiation and post-irradiation temozolomide	A follow-up brain MRI showed interval resolution of the multiple enhancing lesions in the posterior fossa, with no evidence of residual or new foci of primary CNS lymphoma

Table 1. Continued...

Author	Study type	Sex	Age	Previous disease	Clinic	Image exam	Treatment	Outcome
Yamamoto et al., 2015[9]	CR	Female	70	Diabetes Mellitus	Progressive gait disturbance. Neurological examination revealed right-sided dysmetria and an unstable wide gait	CT) showed ill-defined mixed density (iso- and hypo) lesion in the cerebellum. Magnetic resonance imaging (MRI) revealed an irregularly shaped and relatively homogenously enhanced mass with surrounding brain edema. This intra-axial mass was located mainly in the cerebellar vermis and extended to the right hemisphere of the cerebellum. A diffusion-weighted image showed mild fluid restriction and a map of regional cerebellar blood volume from a perfusion-weighted image indicated increased blood flow	The patient underwent 5-ALA-induced fluorescence guided surgery. the fluorescent tumor tissue was partially resected.	The patient underwent the first course of high-dose methotrexate therapy (HD-MTX). Because of mild renal dysfunction, the patient could not receive the next course of HD-MTX. Thus, the patient underwent subsequent radiotherapy. The patient's condition improved without any other neurological deficit. No recurrence of the tumor was detected on MRI performed 21 months after the surgery
Franzini et al., 2023[10]	CR	Male	60	None	Dysarthria, mental slowing and gait instability. Neuro- logical examination showed wide-based gait, adiadochokinesia, dysmetria at the finger-to-nose test in the right limb, and increased instability with eyes closed.	Brain MRI: characterized the lesion as isointense on T1 and hyperintense on T2 weighted sequences. A strong homogeneous contrast enhancement was observed in the central part of the lesion. MRI spectroscopy showed a non-specific neoplastic pattern	A trial of high-dose intravenous steroid was started with the transient reversal of the cerebellar syndrome. Then, they performed an open surgical biopsy for histological diagnosis. In addition, they proceeded with the resection of the central contrast-enhanced part of the tumor.	Post-operative MRI showed the nearly complete resection of the central contrast-enhanced area of the tumor. The patient completely recovered his neurological status and was referred to an oncologist for adjuvant therapies.
Datta et al., 2013[11]	CR	Female	55	None	Symptoms of ataxia and disorientation of 1 week duration. She was suffering from headache and vomiting for four months. Concurrently, she had a weight loss of 11 kg, daily fever and chills over the same duration. Clinical examination revealed slurred speech, finger to nose ataxia worse on the right side and truncal ataxia, with no other significant neurological deficits.	T2- weighted axial, T1-weighted and gadolinium- enhanced T1- weighted axial magnetic resonance imaging (MRI) scans of brain showed a contrast enhancing mass with peritumoral edema in the right cerebellar hemisphere	Intravenous dexamethasone was initiated and a subtotal resection of the cerebellar lesion was performed. Cytotoxic therapy with carmustine 200 mg IV 6 weekly three cycles followed by external beem radiation therapy (EBRT) 30 Gy.	No recurrence was noticed in one year follow-up.

In relation to sex, we can observe a small predominance of females in the reported cases, at 53.3%. Regarding age, the fact that lymphomas are a pathology strongly related to aging is corroborated, as 60% of cases increase progressively after the age of 40. Regarding personal history, all reported patients were immunocompetent, confirming the premise that PCNSL has been growing in this population, when compared to immunocompromised patients, mainly due to greater access to new therapies in autoimmune diseases and HIV. However, there is a relationship between a history of previous neoplasia and subsequent development of PCNSL, with 26.6% of cases. Clinically, the most prevalent findings were vertigo (33.3%), motor incoordination (33.3%), nausea and vomiting (33.3%) and headache (33.3%), followed by gait imbalance (26.6%) and disorientation (20%). On head CT, these tumors usually present as a single hyper- or isoattenuated lesion, while on MRI, they tend to be hypo- or isointense on non-contrast T1 sequences and hyper- or isointense on non-contrast T2 sequences. The proposed treatment for the reported patients was mostly surgery for tumor resection (73.3%) with adjuvant chemotherapy (66.6%), of which, among those who received this treatment combination, they achieved a 57% survival rate. Other treatments were considered together, such as radiotherapy (20%). It is noted that the use of corticosteroids – 20% of patients – was related to partial resection of lesions in 100% of cases, which corroborates the data found in the literature that lymphomas are sensitive to corticosteroids, leading to apoptosis and changing cells in the lesion, reducing the diagnostic yield of the biopsy and altering surgical success rates.

CASE PRESENTATION

Male patient, 40 years old, formerly deprived of liberty, admitted with a history of disabling sudden rotational vertigo, associated with holocranial headache with severe stitches and episodes of emesis for 5 days. He reported being a smoker, fashion designer and former drug user. On neurological examination, he was alert, conscious and oriented, in an antalgic position, isochoric and photoreactive pupils, preserved strength and reflexes, stiff neck, gait ataxia.

The initial head tomography demonstrated a hypoattenuating cerebellar lesion on the right, without contrast enhancement, measuring 3.6 x 1.7 x 1.5 cm, a tenuous hyperattenuating area posteroinferior to the IV ventricle (Figure 2). On MRI, an expansive formation measuring 4.3 x 3.3 x 2.5 cm was observed, located in the right hemisphere and cerebellar peduncle, with heterogeneous signal in all sequences and hypointense foci in SWI, with strong ring impregnation with gadolinium and minimal peripheral diffusion restriction, promoting compression of the IV ventricle and the pons, in addition to mild bulb deformity, likely neoplastic lesion (Figure 3).

The patient was hospitalized for symptoms and underwent primary lesion screening, cultures and serology. Computed

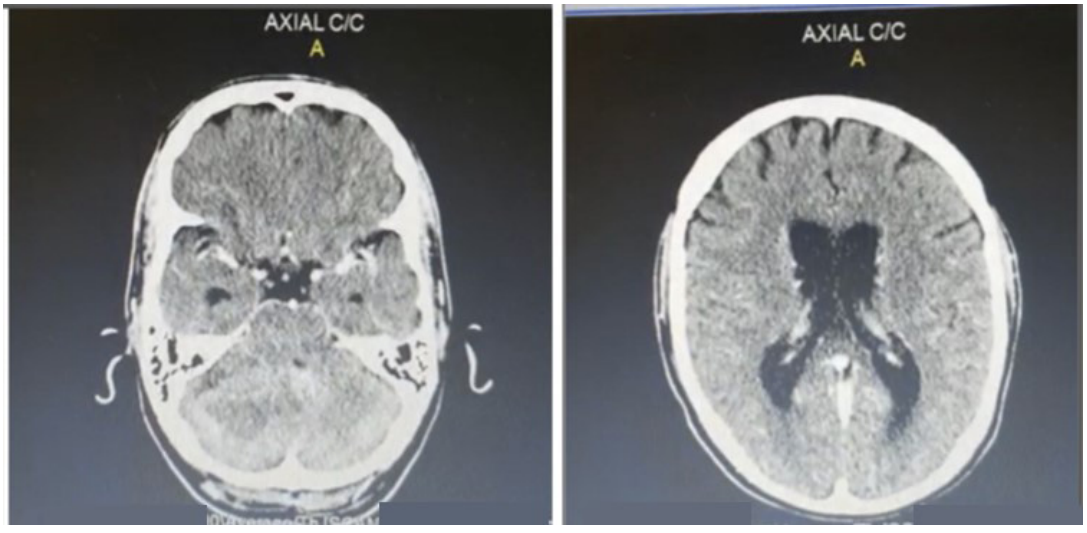

Figure 2. CT (computerized tomography). Right cerebellar hypoattenuation, without contrast enhancement, tenuous posteroinferior hyperattenuation area of the fourth ventricle.

tomography of the abdomen was unremarkable, CT of the chest showed left axillary lymph node enlargement. Non-infectious CSF, negative blood cultures (for bacteria and fungi), negative serologies for hepatitis A, B and C; VDRL negative, serological reaction for toxoplasmosis IGG + and IGM negative and HIV positive. Bactrim and empirical regimen for neurotoxoplasmosis were started, with CD4 collection.

The patient developed a worsening headache associated with episodes of emesis, vertigo and mental confusion. A new head CT revealed an infratentorial mass effect and CSF transudation. External ventricular shunt (EVD) was performed with an improvement in the level of consciousness. After 3 days, drowsiness, disorientation, intense holocranial headache, bilateral orbital edema and hyperemia; presented dysphagia and bloody emesis. On examination, Glasgow 13, disoriented, slurred speech, paralysis of the IX and XII cranial nerves, with head CT showing a normopositioned catheter, maintaining ventricular dilation (Figure 4). The following morning he developed a worsening level of consciousness, Glasgow 8 and angioedema. Orotracheal intubation was performed following neuroprotection, with glottis edema observed during the procedure. After two days, the patient underwent resection of the cerebellar lesion. A fresh biopsy revealed the absence of malignancy criteria, compatible with an infectious process. Empirical treatment was initiated for bacterial, fungal and tuberculosis infections.

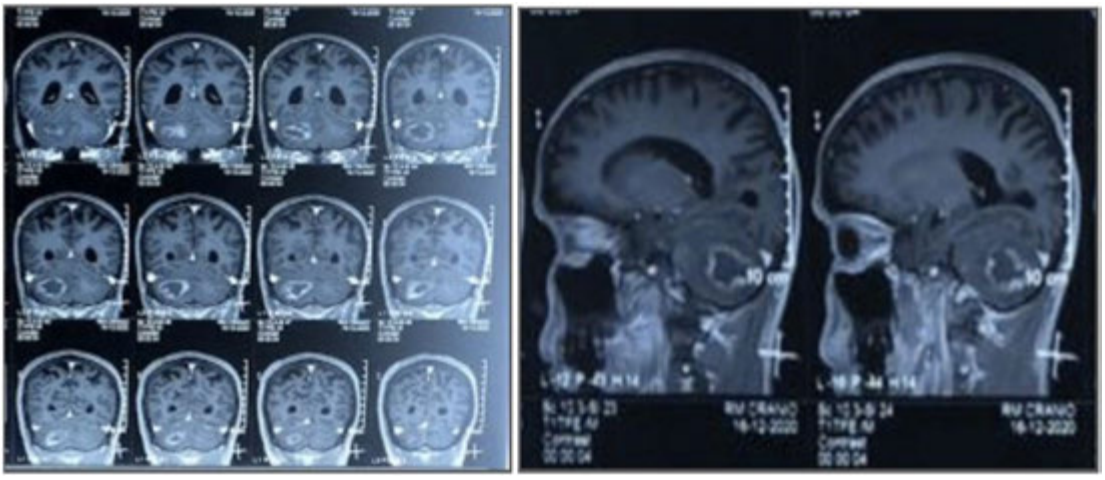

Figure 3. MRI (Magnetic resonance imaging). Expansive formation, located in the right hemisphere and cerebellar peduncle, with heterogeneous signal in all sequences, promoting compression of the IV ventricle and pons, in addition to mild bulb deformity.

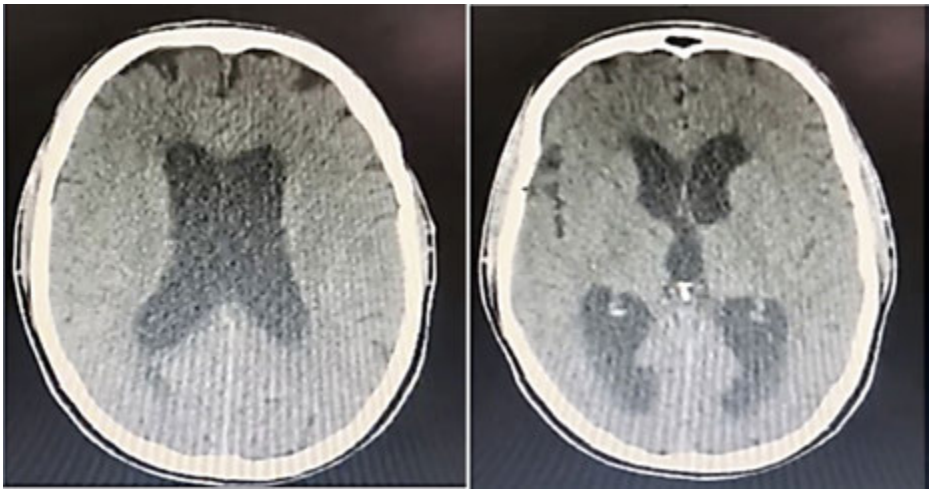

Figure 4. CT (computerized tomography). Infratentorial mass effect and cerebrospinal fluid transudation. External ventricular shunt conduct.

After two days, he was extubated without complications, maintaining Glasgow 15, however, a few hours later, he experienced a sudden episode of emesis, followed by a lowering of the level of consciousness and Cushing's triad, being intubated and sedated with a reversal of the condition. Functioning EVD, maintained at 10 mmhg, with 150ml of clear output in the last 24 hours. During the night he developed D>E anisocoria, with reversal after neurointensive measures.

He underwent a new head CT, which showed that the patient did not present ventricular dilation (Figure 5). The following day, the patient developed loss of brain stem reflexes, the EVD, which was 10 mmHg, had a flow rate of 450 ml, bloody, however the patient died a few hours later.

Anatomopathology and immunohistochemistry confirmed the diagnosis of diffuse large B-cell lymphoma of the non-germinal center type (Figure 6).

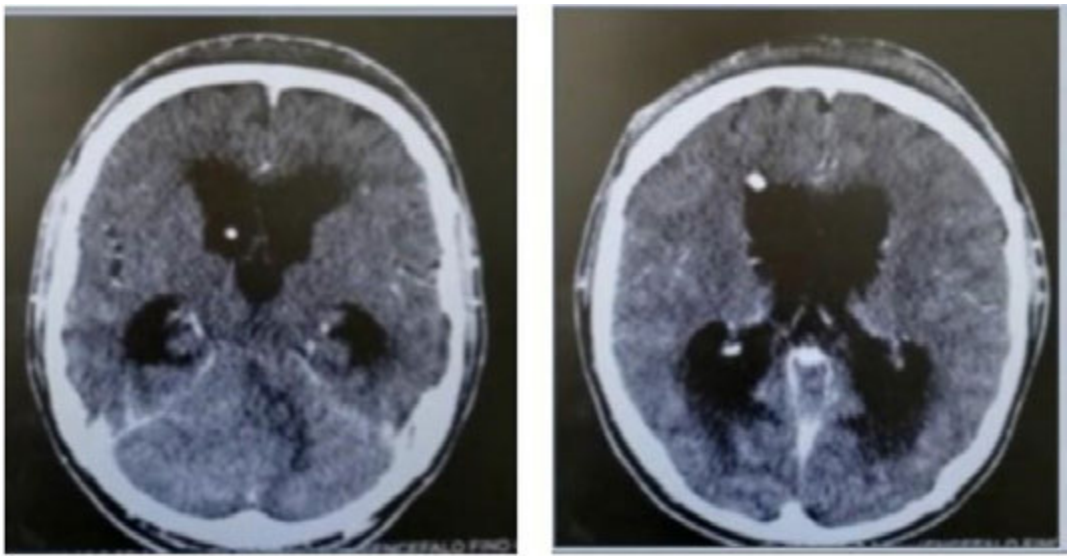

Figure 5. MRI (Magnetic resonance imaging). Resection of the cerebellar lesion was performed, in the frozen section there were no malignancy criteria, compatible with an infectious process.

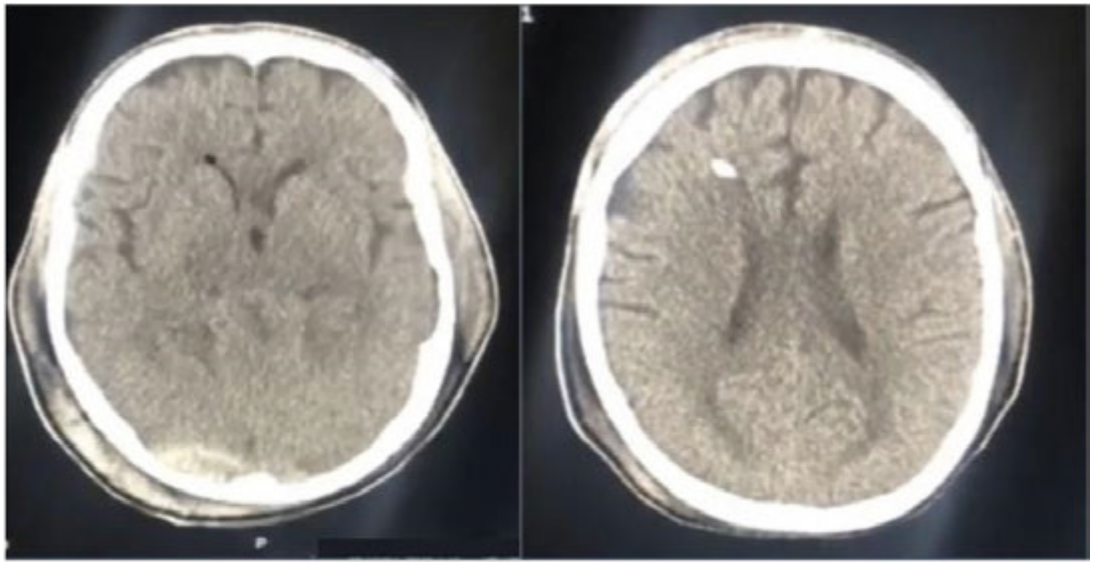

Figure 6. CT (computerized tomography). Absence of ventricular dilation.

DISCUSSION

PCNSL is a rare intracranial neoplasm with an annual incidence of 0.5 cases per 100,000 people[1]. Of these, only 13% are located in the infratentorial brain, of which 9% affect the cerebellum. The vast majority of cases are diffuse large B-cell lymphomas, accounting for approximately 90%[4]. PCNSL generally presents as a single focal lesion, however, approximately 18% to 30% of cases in immunocompetent patients presented multiple lesions, which are often supratentorial[8].

In immunocompetent patients, the average age at diagnosis is 50-65 years, with a male to female sex distribution of 1.2: 1, while in immunocompromised patients, the average age is around 30-35 years, with a clear predominance male, with 7.4:1. The incidence of PCNSL increases exponentially with aging, with three possible explanations for this phenomenon: first, immunological dysfunction increases in older patients, mainly due to thymic involution; second, several genes and molecules undergo changes as we age, promoting the development of tumors; and third, the incidence of chronic inflammation may gradually increase with aging[12]. Immunocompromising in these patients is typically secondary to HIV, organ transplantation, or primary immunodeficiency syndrome.

More recent studies show a significant decrease in PCNSL cases among patients with HIV, justified by greater access to antiretroviral therapy[8]. The incidence in the immunocompetent population has increased more than 10-fold in recent years[13]. In both groups the outcome without therapy is high mortality, but overall survival for treated patients is much better for immunocompetent patients (19 months) than for immunosuppressed patients (2.6 months)[13].

The most frequent symptoms involve neuropsychiatric, signs of increased intracranial pressure – such as headache, nausea and vomiting – seizures and ocular symptoms[4], determining a diagnosis can be challenging because of the absence of typical clinical symptoms, the heterogeneous pathological morphology and the lack of specific exams, in addition to the variable appearance on imaging exams.

Image-guided stereotactic biopsy, including immunohistochemistry and pathology, remains the gold standard method for diagnosing PCNSL. From a histopathological point of view, diffuse large B-cell lymphomas exhibit diffusely growing tumors with medium to large perivascular aggregates, atypical cells with nuclear pleomorphism and often prominent nucleoli, and, in some cases, extensive necrosis[5].

From a molecular point of view, this tumor carries somatically rearranged and hypermutated immunoglobulin genes, with frequent rearrangements of the BCL6 gene. In many cases, we have a loss of expression of HLA class I and II proteins, which explains the ability to grow in immunoprivileged sites[5].

In some situations, pathological evaluation may be compromised, such as in patients with intracranial expansive lesions who are frequently treated with corticosteroids, to which lymphomas are sensitive. The use of corticosteroids often leads to apoptosis and morphological changes in lymphoma cells, which can decrease the diagnostic yield of biopsy[8].

Unfortunately, it is an aggressive tumor with high recurrence rates after treatment, and without treatment, survival is expected to be only 3-6 months. Surgical excision of these tumors is rarely possible due to their deep location, with a significant risk of postoperative neurological complications, and should be used in cases of solitary lesions and in cases of increased intracranial pressure. The main disadvantage when approaching a PCNSL in the posterior fossa by open surgery is that this tumor may appear indistinguishable from normal cerebellar parenchyma, causing the surgeon to identify pathological tissue based solely on image-guided neuronavigation and frozen section biopsy. time-consuming[11].

It is known that PCNSL are highly sensitive to radiation. Therefore, patients must be evaluated regarding the possibility of radiotherapy, depending on individual criteria such as comorbidities and risk factors that contraindicate radiation. Furthermore, some chemotherapy drugs such as methotrexate, procarbazine and cytarabine are being widely used as therapeutic proposals[3]. However, even with timely therapeutic intervention, the prognosis of these tumors remains poor.

CONCLUSION

PCNSL is a rare disease with increasing incidence in both immunocompromised and immunocompetent individuals.

The highly aggressive nature of these tumors requires diagnosis and intervention as soon as possible, mainly due to the scarcity of clinical and imaging resources for diagnostic confirmation, making the use of biopsy crucial. Involvement of the cerebellum and other deep structures, such as periventricular regions, basal ganglia and brain stem, is associated with poor prognosis and reduced survival, which explains the importance of the lesion site and the description of this case. Furthermore, this pathology presents a challenging diagnosis, given the heterogeneity of clinical symptoms associated with imprecise characteristics in imaging exams, making it common for patients to have mistaken management. We present a rare case of cerebellar large B-cell lymphoma in a patient not known to be immunocompromised, with an infectious-looking lesion on fresh biopsy with treatments corresponding to the suspicion, with rapid evolution with cognitive deterioration and death.

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Evaluation of Motor Function and Quality of Life In Patients with Cerebral Palsy Undergoing Selective Dorsal Rhizotomy

Evaluación de la Función Motora y la Calidad de Vida en Pacientes Con Parálisis Cerebral Sometidos a Rizotomía Dorsal Selectiva

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ABSTRACT

Background: *Cerebral palsy (CP) consists of a group of permanent neurological deficits of the nervous system. Thus, the main objective of management of CP is to mitigate spasticity, as it has a high potential to generate contractures, stiffness, dislocations, pain and deformities. More severe forms can be curbed by selective dorsal rhizotomy (SDR).* **Objective***: This study aims to evaluate the SDR outcomes and changes in the quality of life (QoL) of individuals with CP undergoing the procedure.* **Methods***: systematic review study with guiding question elaborated using the PICO strategy. Complete works available in Portuguese and English were selected, assigning 10 years. After the selection and eligibility process, 9 articles were selected.* **Results and discussion***: In SDR, electroneuromyography is used to assess the degree of hyperactivity of nerve roots from L1 to S2 and the response in the musculature of the corresponding segment. Each radicle is stimulated separately and only those with spastic activity are sectioned. The effect achieved is a reduction in the overstimulation of the muscles of the lower limbs. Studies show that SDR is accompanied by an enrichment of motor function, a significant reduction in spasticity and an increase in range of motion.* **Conclusion***: SDR is the most effective alternative for the treatment of spasticity in patients with CP with GMFCS level II or III due to the significant improvement in QoL provided by the reduction of spasticity and stiffness and the functional evolution. This reduces the need for further surgical interventions and improves independence in activities.*

Keywords: *Rhizotomy; Cerebral palsy; Muscle spasticity; Quality of life*

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RESUMEN

Introducción*: La parálisis cerebral (PC) consiste en un grupo de déficits neurológicos permanentes del sistema nervioso. Así, el principal objetivo de la conducción de la PC es mitigar la espasticidad, ya que tiene un alto potencial para generar contracturas, rigidez, luxaciones, dolor y deformidades. Las formas más graves pueden frenarse mediante la rizotomía dorsal selectiva (RDS).* **Objetivo***: El objetivo de este estudio es evaluar los resultados de la RDS y los cambios en la calidad de vida de las personas con PC sometidas a este procedimiento.* **Metodología***: Estudio de revisión sistemática cuya pregunta guía fue elaborada utilizando la estrategia PICO. Fueron seleccionados trabajos completos disponibles en portugués e inglés, con asignación de 10 años. Tras el proceso de selección y elegibilidad, se seleccionaron 9 artículos.* **Resultados y discusión***: En la SDR, la electroneuromiografía se utiliza para evaluar el grado de hiperactividad de las raíces nerviosas de L1 a S2 y la respuesta en la musculatura del segmento correspondiente. Cada radícula se estimula por separado y sólo se seccionan las que presentan actividad espástica. El efecto conseguido es una reducción de la sobreestimulación de los músculos de los miembros inferiores. Los estudios demuestran que la SDR va acompañada de un enriquecimiento de la función motora, una reducción significativa de la espasticidad y un aumento de la amplitud de movimiento.* **Conclusiones***: La SDR es la alternativa más eficaz para el tratamiento de la espasticidad en pacientes con PC con GMFCS nivel II o III debido a la importante mejora en la calidad de vida proporcionada por la reducción de la espasticidad y rigidez y la evolución funcional. Esto reduce la necesidad de nuevas intervenciones quirúrgicas y mejora la independencia en las actividades.*

Palabras clave: *Rizotomía; Parálisis cerebral; Espasticidad muscular; Calidad de vida*

INTRODUCTION

Cerebral palsy (CP) or non-progressive chronic encephalopathy consists of a group of permanent neurological disabilities of the nervous system[1-3]. This condition encompasses a heterogeneous group regarding etiology, clinical signs, and severity of impairments. Regarding etiology, it is multifactorial and it can result from pre-natal developmental malformations (cord malformations, alterations of maternal circulation, and uterine tumors) and perinatal central nervous system lesions (influenced by maternal characteristics such as maternal age, anesthesia, and placental anomalies), fetal factors (prematurity, twinning, and malformations), or postnatal factors (anoxia)[1,4,5]. These factors trigger various alterations in neurological development, such as movement and postural disorders and altered sensory perception that arise in the first years of life.

This encephalopathy can be classified according to the type of lesion and its main clinical characteristics, spastic subtypes (diplegia, hemiplegia, and quadriplegia), dyskinetic, and ataxic[6,7]. The spastic subtype is the most common, responsible for 70% of cases. Spastic CP is caused by damage to the cerebral motor cortex – which controls voluntary movement – and the pyramidal tracts – responsible for transmitting signals to muscles. Therefore, spasticity is a motor disorder characterized by the presence of high tone (increased myotatic reflexes, clonus, plantar reflex in extension – Babinski sign) and is caused by a lesion in the pyramidal system, which consists of an exacerbation of the medullary reflex arc in the absence of inhibitory influences from upper pathways[8-10].

Although this childhood neuromuscular disorder is not neurodegenerative, the consequent musculoskeletal involvement can increase disabilities as the nervous system matures. As previously discussed, CP involves disorders in voluntary motor function and a wide variety of symptoms that make up the upper motor neuron syndrome[2,11,12]. Various additional symptoms accompany primary motor abnormalities, including altered sensory perception, intellectual disability, communication difficulties (dysarthria), palate and tongue difficulties (dysphagia), as well as seizures and musculoskeletal complications[13].

Thus, the main objective of managing cerebral palsy is to alleviate spasticity, as it has a high potential to generate contractures, rigidity, dislocations, pain, and deformities, as well as impairing activities of daily living[14].

Treatment of chronic pain resulting from musculoskeletal dysfunctions, spasticity, deformities, and other associated comorbidities involves physiotherapy and occupational therapy, oral therapies, and the use of muscle relaxants such as baclofen

and tizanidine, as well as the use of benzodiazepines. Refractory pain can be treated with the administration of Botulinum Toxin A and intrathecal baclofen[2,15].

The most severe or widespread forms of spasticity can be curtailed through neurosurgical treatment, through selective dorsal rhizotomy (SDR), complementing and assisting the various existing therapeutic modalities. SDR effectively reduces sensory input in reflex arcs responsible for muscular hypertonia and preserves voluntary movement. This procedure can be isolated, or it can be combined with other treatments, such as intramuscular botulinum toxin application – causing flaccid paralysis of the affected muscle – and with intrathecal administration of baclofen – increasing inhibitory activity on muscle tone – in order to offer functional improvements and positively impact the QoL, comfort, and care of patients[2,15].

Due to the heterogeneity of CP regarding the severity of neuromuscular and musculoskeletal impairment, the Gross Motor Function Classification System (GMFCS) is used to plan the rehabilitation of children with CP[16]. This classification is based on voluntary initiated movement, with emphasis on sitting, transfers, and mobility, and it is possible to classify the child or adolescent with CP into five levels, ranging from I, which includes minimal or no dysfunction regarding community mobility, to V, where there is total dependence requiring assistance for mobility[1,17,18].

Therefore, children who fall into level II have limitations regarding their ability to run and jump or walk long distances. Children in level III usually need mobility equipment to assist them with walking. Children at level IV are usually transported in a manual or motorized wheelchair. At level V, there is a severe limitation in controlling the head and trunk, requiring extensive assistive technology and physical assistance[19].

In addition to using this functional level standardization system in rehabilitation planning, cranial and spinal magnetic resonance imaging is performed to ensure that the condition does not run with other factors that cause spasticity or that prevent the procedure from being performed[15].

For patients with spastic diplegia who present mild to moderate motor impairment (GMFCS level II or III), without significant weakness, and are cognitively capable and motivated to participate in postoperative rehabilitation, selective dorsal rhizotomy can be performed as an alternative or in conjunction with antispasticity therapy to improve gait[2,15,20,21]. Furthermore, SDR is an alternative option for non-ambulatory children (levels IV and V) to treat refractory spasticity, provide comfort, and promote participation in daily activities[21-23].

Thus, this paper aims to explain the available evidence related to selective dorsal rhizotomy in patients with cerebral palsy, while also evaluating its outcomes and the change in QoL of individuals undergoing the procedure.

METHODOLOGY

This is a systematic review study conducted in five stages, such as: (1) defining the research question and identifying the databases for consultation, (2) establishing eligibility criteria and searching for potentially eligible primary studies in the literature, (3) analyzing and evaluating study eligibility, (4) extracting relevant data, (5) discussing the synthesis of results and presenting the study.

Based on the theme and objective of the study, the research question was formulated using the PICO acronym strategy (Population: humans with cerebral palsy; Exposure: selective dorsal rhizotomy treatment; Comparison: without selective dorsal rhizotomy treatment; Outcome: improvement in QoL), and descriptors were listed based on the PICO elements to search for literature and define the guiding question: "Does selective dorsal rhizotomy treatment in individuals with cerebral palsy improve motor function and quality of life?"

Eligible study searches were conducted from December 17th, 2022, to December 31st, 2022, in the Virtual Health Library (VHL) database, using the PICO elements to obtain specific and controlled descriptors available in the Health Sciences Descriptors/Medical Subject Headings (DeCS/MeSH) database, for the keywords rhizotomy, cerebral palsy and QoL, which were combined using Boolean operators AND.

Complete works available in Portuguese and English were selected, with a temporal range of 10 years (2012-2022). Inclusion criteria were original articles whose main subject was related

to selective dorsal rhizotomy and cerebral palsy. Exclusion criteria were duplicated works, incomplete works, works without methodological description, study protocols, and articles outside the temporal range of the study.

The selection process began with reading the titles and abstracts of the articles, applying inclusion and exclusion criteria. Then, the selected articles underwent a second analysis, with the reading of the full text, to select articles that truly complied with the eligibility and exclusion criteria, methodology and theme.

RESULTS

From the use of the descriptors mentioned above, 17 articles were identified in the defined database for the search. After the process of selection and eligibility of the found works, 9 articles were selected for the systematic review (Figure 1).

Table 1 summarizes the studies selected to compose this systematic review. The main items included are author(s) and year of publication, study design, objectives, methodology, and main results.

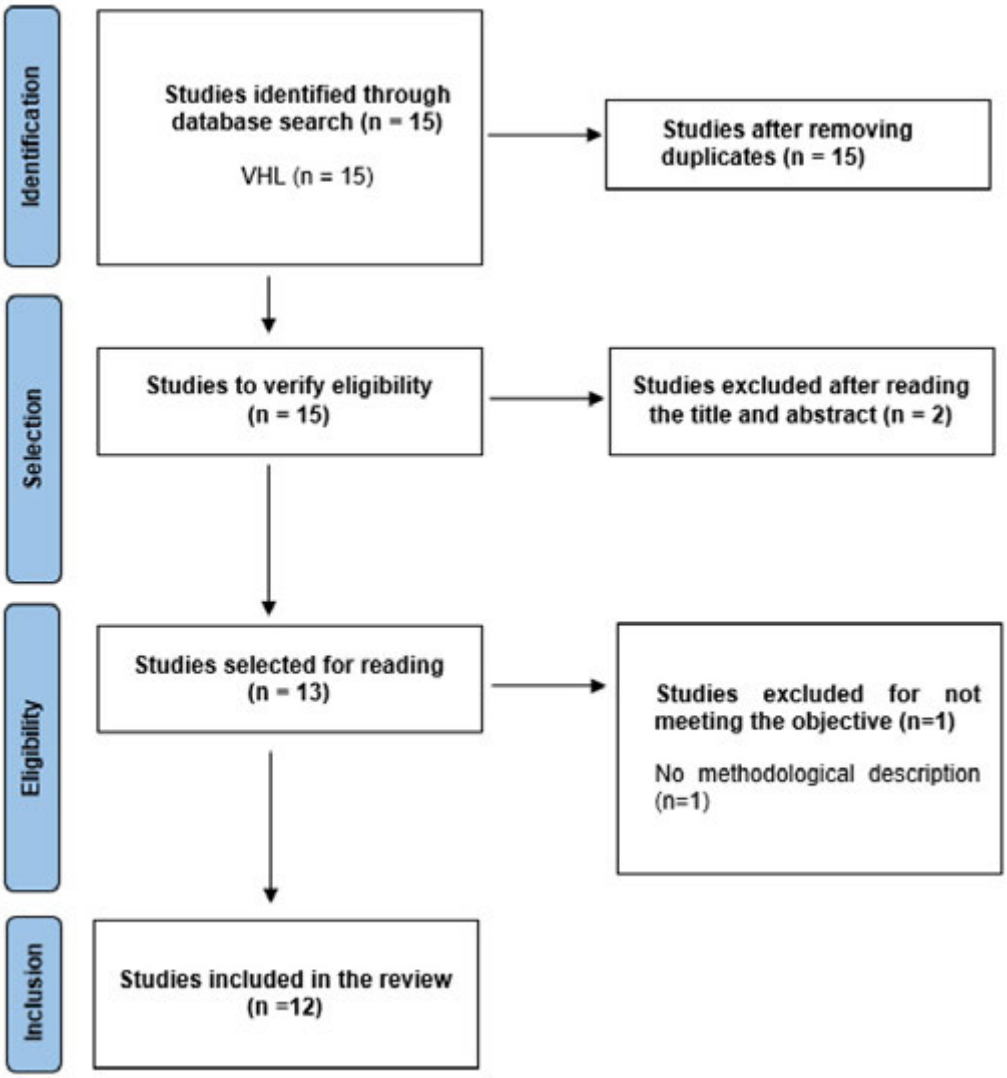

Figure 1. Schematic representation of the study selection stages.

Table 1. Studies found for systematic review.

Author and year of publication	Study design	Goals	Methodology	Main results
Gillespie et al.[21]	Prospective study.	To investigate the effect of age category, sex, GMFCS level, and presence of dystonia on changes in eight function test parameters 24 months after SDR.	Children aged 3 to 18 years with bilateral CP with spasticity who underwent SDR at a tertiary pediatric neurosurgery center between 2012 and 2019 were selected.	SDR can improve gross and fine motor function, mobility and self-care, QoL and overall outcome based on extensive testing of scoring parameters at 24 months.
			A linear mixed-effects model was used to assess longitudinal changes.	Atypical patient populations can benefit from SDR if properly selected.
				Multicenter prospective registries investigating the effect of SDR are needed.
Hurvitz et al.[24]	Prospective study.	To assess outcomes, interventions, life satisfaction, and subjective impressions of SDR in older adolescents and adults who underwent the procedure as children.	A survey was applied to older adolescents (16–20 years) and adults with CP who underwent SDR between 1986 and 2000 at two academic centers.	Most adults who underwent SDR as a child would recommend the procedure to others. Very few reported negative impressions of the procedure.
			Patients or their caregivers participated in telephone or clinic interviews.	Life satisfaction levels were generally high.
			Subjective impressions of SDR and a history of post-SDR medical interventions were obtained.	The prevalence of pain was similar to that reported in the literature for adults with cerebral palsy.
			Current functional status, history and pain assessments, educational achievement, living situation, and subjective health status were also recorded.	Despite the SDR, other interventions, both surgical and non-surgical, were used in most patients.
MacWilliams et al.[25]	Retrospective study.	To understand the long-term effects of comprehensive spasticity treatment, including SDR, in individuals with spastic CP.		Spasticity was effectively reduced at the long-term assessment in the group given SDR and remained unchanged in the group without SDR.
			Children were matched by age group and spasticity at baseline.	There were no significant differences between the groups on any measure except the Gait Deviation Index and walking speed.
			Children at one center underwent spasticity treatment including SDR (n=35) and antispastic injections.	The SDR group underwent more subsequent orthopedic surgeries and antispastic injections in the lower limbs.
			Children at two other centers had no SDR (n = 40) and limited antispastic injections.	
			Participants returned for comprehensive long-term evaluation (age ≥21 years, follow-up ≥10 years).	
			Assessment included spasticity, contracture, bone alignment, strength, gait, walking energy, function, pain, stiffness, participation and QoL.	

Table 1. Continued...

Author and year of publication	Study design	Goals	Methodology	Main results
Munger et al.[26]	Retrospective study.	Examine the long-term results of SDR 10 to 17 years after surgery.	Participants who underwent SDR had spastic diplegic CP, completed baseline gait analysis, and were 16 to 25 years of age at follow-up.	SDR and non-SDR groups had significant improvement in gait pathology over time.
			Control (non-SDR) participants were matched on key clinical parameters at baseline but did not undergo SDR.	The non-SDR group had significantly better gait compared to the SDR group at follow-up.
			All participants completed six surveys assessing pain, QoL, participation, function, and mobility. Treatment history for lower limb surgery and antispasticity injections was tabulated.	The groups had similar levels of energy cost, pain and QoL.
			A subset of each study group returned for gait analysis, including kinematics, metabolic energy expenditure, and physical examination.	Non-SDR participants underwent significantly more orthopedic surgeries and anti-spasticity injections than SDR participants.
			The Gait Deviation Index (GDI) was calculated to measure gait quality.	The use of a clinically similar control group highlights that different courses of treatment can result in similar outcomes in young adulthood.
Robins et al.[27]	Prospective study.	To present complete data for CPQoL results for patients undergoing RDS at a single institution at 2 years of follow-up.	Patients were operated on for a period of 5 years by the same surgeon using the same technique at a single institution.	Statistically significant improvement was seen in five of the seven CPQoL domains and was maintained up to 2 years after SDR.
			CPQoL questionnaires were completed by patients and family members preoperatively and at 6 months, 1 year, and 2 years after surgery.	
Spazzapan et al.[6]	Retrospective study.	To present the surgical technique and short-term results of a newly created surgical treatment in Slovenia.	A retrospective analysis of all patients who underwent SDR from 2017 to 2019 was performed. The median follow-up was 10 months.	There were no complications regarding wound healing, CSF leak or neurological disorders.
			The motor functions of all children were classified by the GMFCS GMFM-88.	Despite the relatively short follow-up, initial results confirm the effectiveness of SDR.
Summers et al.[20]	Prospective study.	To assess gross motor function before and after SDR and postoperative QoL in a study commissioned by NHS England.	Observational study in five hospitals in England that were contracted to perform SDR in children aged 3 to 9 years with spastic diplegic CP.	SDR improved function and QoL at 24 months after surgery in children with cerebral palsy classified as GMFCS levels II and III.
				Based on these findings, an interim national policy decision was made that SDR would be funded for eligible children in England from 2018.

Table 1. Continued...

Author and year of publication	Study design	Goals	Methodology	Main results
Tedroff et al.[28]	Prospective study.	To evaluate the long-term effects of SDR 15 to 20 years after surgery in patients with CP.	Eighteen children with bilateral spastic CP were prospectively evaluated after SDR.	The effect of normalized muscle tone in the lower extremities after SDR was sustained after a median of 17 years.
			Assessments include the Modified Ashworth Scale for Spasticity, the Gross Motor Function Measure (GMFM-88), the Wilson Mobility Scale, the Health Survey of Health-Related QoL, SF-36v2, and the Brief Inventory of Pain.	Improved gross motor function ability, according to the GMFM score, was observed at the 3-year follow-up, after a gradual decline followed.
				The spasticity-reducing effect of SDR does not improve long-term functioning, nor does it prevent contractures, but it may reduce the pain often experienced by individuals with CP.
Veerbeek et al.[29]	Retrospective study.	To determine the physical status, mental health and health-related QoL (HRQoL) of adults with CP who underwent SDR for at least 25 years, compared to matched typically developing (TD) individuals.	Adults with CP were recruited from a database of children who underwent SDR performed using the technique introduced by Professor Warwick Peacock between 1981 and 1991.	Normalized lower limb muscle tone was maintained 25-35 years after SDR.
		Investigate relationships between physical status and other outcome measures.	These individuals were matched for age, sex, body mass index, and socioeconomic status to a cohort of TD adults of a similar background.	Whereas the lower scores for physical assessments are in line with findings in other CP populations, notably, relatively good mental health scores and HRQoL were reported in this CP group despite their physical limitations.
			The parameters evaluated were muscle tone of the lower limbs, passive range of motion, muscle strength, selectivity, functional mobility and dynamic balance (Timed Up and Go test [TUG]), HRQoL (SF-36) and levels of anxiety and depression.	The strong correlation between muscle strength and TUG suggests that strength training after SDR may be of value in improving functional mobility and balance.

DISCUSSION

SDR is considered and widely accepted as a standard neurosurgical procedure for the treatment of spasticity associated with CP. A number of studies have reported the efficacy of SDR in reducing spasticity[6,20,25-29].

SDR involves partial sectioning of the sensory roots using electrophysiological stimulation. At each vertebral level to be addressed, a linear incision is made to expose the spinal cord and visualize the medullary cone and cauda equina. Electroneuromyography is used to evaluate the degree of hyperactivity of the nerve roots from L1 to S2 and the response in the corresponding segment's musculature, with care given to S2 to S4 to protect bladder and sexual function. Each radicle is stimulated separately, and only radicles that present spastic activity are cut[15,20,21,30,31].

The effect achieved is the reduction of the overstimulation of the lower limb muscles, generally resulting in a decrease of two levels on the Ashorth spasticity scale in the spastic muscle group

of the lower limbs[3]. This scale qualitatively assesses the degree of spasticity, measured according to the resistance to passive movement of a segment moved rapidly by the examiner[32]. Therefore, the earlier the surgery is performed, the lower the chances of the patient having musculoskeletal disabilities[6,21].

Data on the results of a large observational study of this type of procedure and long-term cost data in children who have undergone it or not show that rhizotomy is cost-effective, generating benefits in functionality, range of motion, pain, and spasticity, reducing care costs. Surgical intervention is less expensive than managing possible complications in patients who have not undergone this procedure, considering the improvement in clinical condition and QoL[2,33].

Studies show that SDR is accompanied by significant improvement in several parameters, such as motor function improvement, significant reduction in spasticity, and increased range of movement[6,21,26,28,29]. These benefits were reflected in GMFM scores after SDR, which increased linearly during the observation period after surgery[6,20,21,28]. Specifically, the QoL improved in terms of feelings about functioning, participation and physical health, emotional well-being and self-esteem, pain, and the impact of disability and family health[2,20,33].

Regarding motor function, SDR has traditionally been used in the management of GMFSC grades, a widely used tool to establish a child's function level and guide treatment[27].

In the context of CP, SDR is reserved for improving gait in children diagnosed with GMFCS grades II and III. In more severe non-ambulatory GMFCS grades IV and V, the main goal of treatment is to facilitate nursing care, usually using intrathecal baclofen pump (ITBP). Thus, in non-ambulatory CP, the child and caregiver's objectives should be carefully considered as not all children will have benefit from reducing spasticity as some may rely on spasticity to assist with transfers[2].

A 2019 review showed that the efficacy of the operation in severely affected children is likely best evaluated in terms of specific patient and family goals, rather than gross motor measures. In this sense, SDR aims not only to reduce spasticity but also to promote the child and caregiver's functional development and goals in a person-centered manner[22].

A review conducted by Peck et al.[2] analyzed seminal and emerging evidence on interventional therapy for chronic pain in cerebral palsy. The researchers raised the question of whether SDR could be a potential alternative in reducing spasticity and improving passive range of motion (ROM). The included studies showed that in GMFCS IV and V scenarios, although the ITBP is the treatment's basis, in moderate to severe GMFCS patients, postoperative 1-year RDS was more effective in reducing spasticity and improving ROM than ITBP.

A subsequent prospective study conducted in England investigated the Pediatric Evaluation of Disability Inventory (PEDI) assessment inventory of 42 patients followed for 24 months. This analysis is based on an interview used to monitor self-care, mobility, and social skills for children with CP. In summary, the authors concluded that PEDI self-care scores increased linearly after SDR, with a significant improvement in 24 months. Such an evolution was mainly observed in GMFCS levels I, III, and IV. The increase was greater in the age groups of 10 to 18 years but not in patients with dystonia[21].

On the other hand, a multicenter and retrospectively matched cohort study comprising 75 participants concluded that children with high levels of spasticity presented marked deviations in gait, high energy consumption, joint contractures, and low function. Moreover, high levels of spasticity were often accompanied by poor motor control, weakness, and other comorbidities associated with more severe CP[25].

The relationship between physical activity, physical health, gross motor function, and selective motor control was also investigated. The summary of the physical component showed correlations with the individual's GMFCS level, the Physical Activity Scale, and the total change in GMFM throughout the follow-up, indicating that individuals who reported better physical health were those with higher gross motor performance, more physically active, and with improvements in GMFM[28].

A cohort study with 35 participants suggested that many of the long-term outcomes of surgical treatment in the domains of the International Classification of Functioning, Disability and Health (evaluations of spasticity, range of motion, and gait patterns) are not significantly different from those obtained with alternative treatments. When viewed in isolation, without comparison with a clinically similar control group, SDR appears to be an appropriate

intervention for achieving improvements in various domains of the ICF that last until early adulthood. In the long-term follow-up, spasticity, gait, and function improved. Energy consumption showed a decreasing trend. Pain interference was low, and QoL was high. However, when comparing these improvements with a clinically similar control group, it seems that surgical intervention was not the only way to achieve these improvements[26].

The results suggest that, although SDR may lead to a high QoL, low pain, and improvements in gait and function as a young adult, other courses of treatment may result in similar outcomes. Despite the clear contribution that SDR provides to people with CP, the onset of declining function and comfort will likely occur in adulthood, and continuous monitoring of outcomes is necessary.

Regarding the decline of benefits and early aging, improvements in spasticity, when compared with the baseline, have been shown to persist for up to 20 years after the procedure, while other benefits, such as increased ROM and gross motor function, persisted only temporarily, gradually decreasing some years after the procedure[2]. It has also been found that many adults with CP experienced a functional decline in early adulthood accompanied by chronic pain and fatigue, a phenomenon that has been called early aging[24].

In theory, early-life spasticity treatment could improve several of the factors associated with this phenomenon. Abnormally increased tone interferes with motor control, decreasing gait efficiency and increasing energy expenditure. Spasticity also contributes to contracture and joint displacement, leading to arthritis and pain. These findings are supported by a cohort study conducted by Hurvitz et al.[24] revealing that rhizotomy did not eliminate the need for interventions, with more than half of the patients reporting the need for medication, injections, or pump implants.

Meanwhile, chronic pain is common in adults with CP, being associated with increased psychological distress and decreased life satisfaction. Participants who reported constant pain noted that this led to frustration due to loss of independence and difficulty to participate in activities and subsequently evaluated their life satisfaction at a lower level. However, whether they would require higher doses of medication or more combined interventions if they had not undergone surgery remains a question[2].

On the other hand, Tedroff et al.[28] prospectively followed 18 children with CP who underwent SDR in Sweden between 1993 and 1997, focusing on the outcome 15 to 20 years after the procedure. To assess the severity of pain and the interference of pain with general activities, the Swedish version of the Brief Pain Inventory – Short Form was used, which consists of two parts, the first containing eight items concerning pain location, pain intensity, analgesics used, and pain relief. In the second part, the individual is asked about pain interference with activities of daily living. In this study, 50% of participants reported pain; however, both the interference and severity of pain were low (<2 composite scores). This is lower than that reported previously in adults with CP. The results reveal a group of young adults with CP where pain seems to be a minor problem than previously reported in a series of studies. This may be an effect of the reduction of spasticity.

Thus, although these benefits decrease over time, the effectiveness of SDR is still noticeable compared to the baseline before the procedure[2].

In a retrospective analysis, Spazzapan et al.[6] selected children who underwent SDR between 2017 and 2019 and routinely evaluated them preoperatively, one month after surgery, and six months after surgery. The motor functions of all children were classified using the GMFCS, and spasticity was evaluated by the scale that assesses resistance during passive stretching of soft tissues (MAS). In the first few weeks after surgery, lower limb function and gait worsened due to paresthesias, loss of rigidity, and postoperative pain. The children were routinely transferred to rehabilitation hospital. At three months of follow-up, there was already an improvement in the GMFM score, and at six months of follow-up, the mean MAS scores were 0 for all evaluated muscles. The results showed that all children improved their gross motor functioning in the GMFM test.

Regarding QoL and daily activities, SDR aims to improve functional outcomes for patients with CP by reducing lower limb tone. Sustained reduction in spasticity has been widely reported. Numerous articles have found that most CP patients who undergo RDS are satisfied and rate their personal health as good[20,24,27-29].

QoL assessment is a complex task due to the need to balance the subjective perception about QoL for each child/family, along with the need to consider disease-specific factors as well as general measures of health, functioning, and the impact of a disability.

The CPQoL questionnaire was developed as a specific tool for assessing QoL in the condition of cerebral palsy and is designed to be completed by parents and completed by the patient at a later date. It is based on the International Classification of Function and the WHO definition of QoL by assessing the domains of "social well-being and acceptance", "feelings about function", "participation and physical health", "developmental well-being and self-esteem", "access to services", "pain and impact of disability", and "family health". It is also crucial for assessing the impact of surgical intervention on patient and family QoL[27].

To better understand QoL outcomes after SDR, Robins et al.[27] followed a cohort of 78 children with complete data preoperatively and at 6 months, 1 year, and 2 years post- SDR using a standardized QoL measure. They found that SDR has a beneficial effect on QoL in five of the seven domains for CPQoL. These were "feelings about functioning," "participation and physical health," "emotional well-being and self-esteem," "access to services," and "pain and impact of disability." All of these domains showed improvement at 6 months postoperatively that was maintained at 2 years after SDR. Surgical intervention did not have a statistical significance on feelings of "social well-being and acceptance" and "family health" as these two domains are highly complex and multifaceted and affected by numerous factors beyond the patient's physical functioning. "Social well-being and acceptance", for example, are influenced by the presence of other comorbidities (including difficulties), school and socio-environmental factors, and support structures. In addition, the analysis revealed that improvement in the gross motor function measure was observed to be greater in GMFCS level II and III children. Improvements in activities of daily living, self-care, and independence were reported[20,27].

In a 2013 descriptive study, the authors assessed the long-term perceptions of 88 older adolescents (16-20 years old) and adults with CP who underwent SDR as children. Overall or general life satisfaction was assessed using the Diener Satisfaction with Life Scale (SWLS), which rates 5 statements on a 7-point scale. SWLS scores were a predictor and overall health showed a tendency to be a predictor, with better scores on these parameters associated with increased odds of recommending rhizotomy to others[24].

When asked about their subjective impression of the procedure, the majority (65%) of the individuals interviewed believed that the SDR had a beneficial impact and reported that they would recommend the surgery to others. However, for 8% of the participants the surgical intervention decreased their QoL, citing pain and no effect as reasons. Most patients who reported decreased QoL were in the GMFCS levels with greater motor limitation[24].

In this study population, there was a high prevalence of both pain and post- SDR medical and surgical treatments for spasticity. However, despite continued residual pain and spasticity, most patients were satisfied with their lives and reported good to excellent health[24]. The hypothesis raised is that reduced spasticity and less pain may result in higher perceived health-related QoL and higher overall scores. When compared to the age-standardized sample, the study group exhibited a lower physical component summary but a higher mental health component summary, showing that they perceived their physical health to be worse and their mental health to be better when compared to the control group[28].

Additionally, a 2021 cross-sectional study conducted by Veerbeek et al.[29] investigated health concepts and their perceived impacts on QoL in adults with CP undergoing SDR in South Africa between 1981 and 1991. The concepts assessed were physical functioning, limitations in usual activities due to physical health problems, general health, vitality (energy and fatigue), social functioning, limitations in usual activities due to emotional problems, and general mental health (psychological distress and well-being).

The primary results discussed were that adults with CP perceived relatively good health-related QoL in all domains. Additional results included that although some study members had disability, were more dependent, and faced more difficulties in daily activities and social roles, they were satisfied in carrying out these lifestyle habits. In reference to mental health, only limited symptoms of anxiety and depression were found. These results reveal that adults with CP more than 25 years after SDR have good mental health, regardless of physical challenges[29].

CONCLUSION

The results obtained corroborate that selective dorsal rhizotomy is the most effective alternative for the treatment of spasticity in cerebral palsy patients with GMFCS level II or III due to the significant improvement in QoL provided by the reduction of

spasticity and muscle stiffness and by the functional evolution and mobility of the patient.

Studies show that surgical intervention can potentially lead to improvements in gross motor test and general function, mobility, QoL and self-care scores after the neurosurgical procedure. This reduces the need for further surgical intervention and improves independence in activities of daily living.

Therefore, most adults who underwent SDR had a positive impression of the surgery and would recommend it to others. Very few reported negative impressions of the procedure. Levels of satisfaction with life post- SDR were generally high.

Further large retrospective and prospective controlled studies or multicenter collaborations are needed to define the benefits of SDR, particularly with regard to long-term follow-up, but the data from the present study suggest generating an overall positive impression and a lack of negative consequences of SDR.

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Pediatric Ependymoma Treatment: where are we today?

Tratamento para Ependimoma Pediátrico: revisão de literatura

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ABSTRACT

Background: *Ependymomas are the second most common pediatric central nervous system tumors with origin from glial cells, with a high incidence in the 0-4 age group. They are histologically classified into grades I, II and III by the World Health Organization (WHO) and, by associating this classification with other characteristics of the tumor and the patient the best option of treatment is constructed, individualizing each situation.* **Objective:** *This study aims to conduct a literature review of current treatments for pediatric ependymomas.* **Methods:** *The review was made searching the National Library of Medicine (Pubmed), Scientific Electronic Library Online (Scielo), and Latin American and Caribbean Literature in Health Sciences (Lilacs) databases with the keywords "tratamento ependymoma pediátrico" and "ependymoma treatment pediatric", including texts in Portuguese and English, from 2018 to 2022, regardless of gender and age group of the child. Abstracts, editorials, duplicate articles, chapters, non free access articles and those that lack treatment innovations were not included.* **Results:** *At the end, 17 articles were selected for the review, which concluded that the main treatment remains the total resection, and when this is not possible, surgical reapproach and/or radiotherapy, which is essential in subtotal exeresis, metastases and inoperable cases. Finally, there is a need for studies with a larger cohort, evaluating the different treatments and their effectiveness in different cases.*

Keywords: *Ependymoma; Pediatric brain tumor; Cancer treatment; Pediatric neurosurgery*

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RESUMO

Introdução: *Ependimomas são o segundo tumor pediátrico mais comum do sistema nervoso central, com origem das células da glia, e têm alta incidência na faixa etária de 0 a 4 anos. Foram classificados em graus I, II e III pela Organização Mundial de Saúde, em 2016, e a partir desta classificação juntamente com as características do tumor e a evolução do paciente, é individualizada e construída a melhor linha de tratamento para cada situação.* **Objetivo:** *revisar a literatura sobre os tratamentos existentes para ependimomas pediátricos.* **Método***: Foi realizada uma revisão sistemática da literatura com pesquisa nos bancos de dados Pubmed, Scielo e Lilacs com os descritores "tratamento ependimoma pediátrico" e "pediatric ependymoma treatment", utilizando textos em inglês e português no período de 5 anos (2018 a 2022), independente do gênero e faixa etária da criança, sendo excluídos resumos, artigos não disponíveis gratuitamente, editoriais, cartas ao editor, artigos duplicados, capítulos de livro e ausência de inovações nos tratamentos.* **Resultados:** *Ao final, 14 artigos foram selecionados para a revisão, dos quais se conclui que o tratamento principal continua sendo a exérese total e, quando não for possível, a reabordagem cirúrgica e/ou radioterapia, sendo esta essencial na exérese subtotal, metástases e casos inoperáveis. Por fim, vê-se a necessidade de estudos com maior coorte, avaliando os diferentes tratamentos e sua eficácia em casos diversos.*

Palavras-Chave: *Ependimoma; Tumores cerebrais pediátricos; Tratamento do câncer; Neurocirurgia pediátrica*

INTRODUCTION

Ependymomas are the second most common tumors of the central nervous system (CNS) from glial cells origin and correspond to approximately 5-10% of all intracranial pediatric tumors, with a higher incidence in the 0-4 years age group[1]. The location can be anywhere in the CNS but more than half of pediatric ependymomas are located in the posterior fossa (PF), a small amount in the supratentorial (ST) and also be extracranial in spinal cord ependymomas[2]. ST ependymomas generally present in older children are primarily extraventricular and have a better prognosis when total resection is performed[3].

The 2016 World Health Organization (WHO) classification system, separates ependymomas into grades I (myxopapillary), grade II (classic), grade III (anaplastic) and RELA fusion-positive ependymoma (grade II or III). Using the WHO classification along with the patient's age, location and molecular genetics, it's possible to establish a more accurate treatment and prognosis for the children[4]. The new 2021 WHO classification of tumors (Table 1) defines specific types of ependymoma and two additional types that consist of tumors with particular locations, but that cannot be assigned to another, molecularly more specific type. Together, ten different ICD-O diagnosis are available to classify ependymal tumors. Whether a CNS tumor shall be defined as ependymoma and, is no longer solely dependent on the tumor morphology. For the diagnosis of many ependymoma types, the presence of a certain molecular feature or profile is now essential[5,6]. This research aims to review current treatments for pediatric ependymomas and their improvements, since such knowledge is extremely important for the medical profession in the elaboration of conduct in these oncological patients.

Table 1. WHO Classification of Tumors of the Central Nervous System (2021).

Ependymal tumors	Grades
Supratentorial ependymoma	3
Supratentorial ependymoma, ZFTA fusion-positive	2, 3
Supratentorial ependymoma, YAP1 fusion-positive	2, 3
Posterior fossa ependymoma	3
Posterior fossa ependymoma (PFA)	2, 3
Posterior fossa ependymoma (PFB)	2, 3
Spinal ependymoma	3
Spinal ependymoma, MYCN-amplified	2, 3
Myxopapillary ependymoma	2

METHODS

This is a systematic literature review in the National Library of Medicine (Pubmed), Scientific Electronic Library Online (Scielo), and Latin American and Caribbean Literature in Health Sciences (Lilacs) using keywords in Portuguese and English "pediatric ependymoma treatment" and "tratamento ependimoma pediátrico",

from 2018 to 2022, regardless of gender and age group of the child. In the search 184 articles were found. After a thorough reading, articles with full free texts, clinical trials, meta-analysis, controlled and randomized trials, innovative treatments, pediatric ependymomas and those that spoke of management were included. Abstracts, editorials, duplicate articles, chapters, articles not available for free and those that lack treatment innovations were not included.

RESULTS

After searching the databases mentioned in the methodology and applying the exclusion criteria, 46 publications were found in Pubmed, 2 in Lilacs and none in Scielo, resulting in 48 articles. In those, the articles that were outside the scope of the study were also excluded. A total of 14 publications remained (Figure 1 and Table 2).

DISCUSSION

Ependymoma is an aggressive tumor due to its topographic location, evolution and manifestation, it should be remembered that such tumors are found in the posterior fossa near the fourth ventricle, supratentorial and medullary canal. Histopathology in these tumors is extremely important for clinical and surgical management, as neoplastic cells have arsenals of mutations that make them untargeted and drug resistant, altering the prognosis of this patient. The 2016 classification established by the WHO, which takes into account cellular morphological findings, is still used. The treatment will take into account the aforementioned characteristics established in recent guidelines[7,11].

The primary treatment is surgical with total resection due to the high risk of recurrence if residues remain[3], but complete removal cannot always be performed, especially in tumors located in the brainstem. Tsai et al.[8], described that there is difference between the prognosis of patients with total and incomplete removal of the tumor. When complete resection is performed, the patient will have at least 10 years of survival compared to 5 years if residues remain. Neoplastic grade and age are also casuistic factors for the described probability[4].

When the tumor is not completely removed, the patient can be subjected to metastasis, new cellular growth and hydrocephalus[2]. Usually a new surgery is indicated, sometimes using adjuvant radiotherapy to contemplate the treatment[1]. Post-surgical protocols recommend magnetic resonance imaging (MRI) within 72 hours postoperatively for local cellular evaluation and analysis of cerebrospinal fluid (CSF) for follow-up and to decide conduct[11].

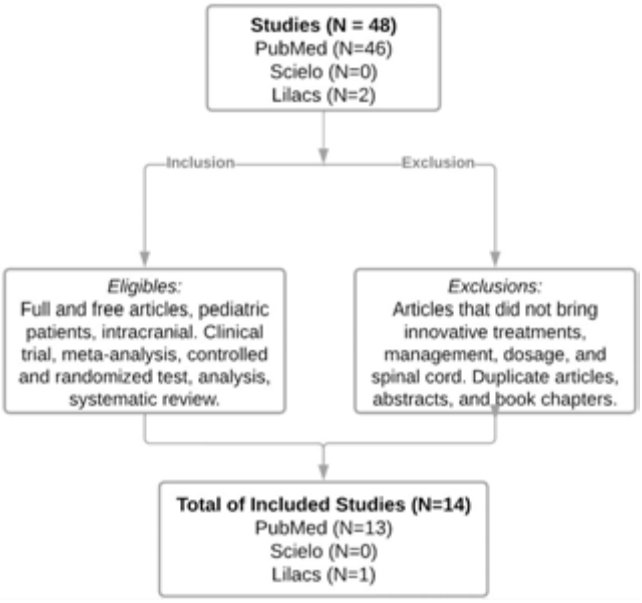

Figure 1. Selection of articles based on inclusion and exclusion criteria.

Table 2. Treatment options according to literature**;** RT (Radiotherapy); GTR (Gross total resection); CT (Chemotherapy); CRT (Conformational radiation therapy); CAR (Chimeric Antigen Receptor).

Author	Treatment	Conclusion
Thorp and Gandola[1]	Surgery + RT / CT	GTR when possible followed by focal RT. CT as an adjuvant strategy after surgery and RT has been studied and shows good promise.
Khatua et al.[3]	Surgery + RT/CT/ Targeted therapy	Maximal safe surgical resection followed by adjuvant therapy is critical. Focal irradiation has a standard role in the postoperative management of ependymomas. CT has an unclear role. Targeted therapy is promising, but needs to be studied further.
Toescu and Gandola[2]	Resective surgery + RT/Proton Beam/ Therapy/CT	Surgery with postoperative radiotherapy has more evidence and Proton beam therapy is being favored in order to avoid harmful late toxicities. Chemotherapy has an unclear role.
Rudà et al.[4]	Surgery + RT /CT/ Proton Therapy	GTR, when possible, is recommended. RT for children between 12 and 18 months and with children with poor neurological status. CT alone in children with 12 months or less is considered good practice, however, CT role remains unproven. For recurring ependymomas, chemotherapy showed a low response rate. Proton beam therapy needs to be studied further.
Sierra Benítez et al.[7]	Surgery +/- RT with or without CT	36.4% of total resection and 63.6% of subtotal resection. Global survival of 81%. At the end of the first year of treatment, most patients showed a tendency towards stability.
Louis et al.[5]	Classification of ependymomas	It is expected that studies of the molecular characteristics of ependymoma will allow more narrowly defined tumor groups.
Tsai et al.[8]	Surgery + RT	Favorable long-term survival for patients with spinal MPE after surgery and adjuvant RT.
Combs et al.[9]	Surgery + Fractionated Stereotactic Radiotherapy (FSRT)	FSRT is well tolerated and highly effective in the management of ependymal tumors, including reoccurrences.
White et al.[10]	CT in children younger than 4 yo	The initial response to the VETOPEC regimen is encouraging and warrants study of further dose escalation.
Seo et al.[11]	Surgery + RT Intensity-modulated radiotherapy (IMRT) / CT	GTR when possible. IMRT exhibits great local control and less toxicity than 3D conformal RT/CT efficacy on ependymomas is controversial.
Lester and McDonald[12]	Subgroup specific treatments	There are no subgroup-specific clinical trials for ependymoma patients, therefore, further models are required to investigate the potential therapeutic targets
Marmor et al.[13]	ErbB transmembrane receptors.	Even though further studies are required, the mechanism of how monoclonal antibodies inhibit tumor growth are still unclear
Gururangan et al.[14]	CT: objective response to bevacizumab (BVZ) plus irinotecan (CPT-11) in cases of pediatric recurrent ependymoma	The combination was not effective in producing objective answers. Furthermore, the observed rate of disease stabilization (6-month Progression-Free Survival = 27.7%) does not appreciably improve the suboptimal responses and outcome observed with standard rescue regimens used for recurrent ependymoma
Mukherjee et al.[15]	Dietary restriction in mouses	Moderate dietary restriction may be an effective antiangiogenic therapy for recurrent malignant brain cancers
Stock et al.[16]	RT / RT with proton beam	RT with proton beams showed a higher homogeneity and reduction in affecting healthy tissues
Patterson et al.[17]	Surgery + RT / CT / CAR T cell therapy	Surgery followed up with RT has clearly shown a clear utility. The benefit with upfront chemotherapy is less understood. CAR-T cell therapy showed efficacy in xenograft models of ependymomas, however, more research is needed
Thomas et al.[18]	CAR T cell therapy	Remarkable remission rates in patients with relapsed refractory B cell malignancies, however, there are safety concerns related to this therapy, and current clinical data indicate that, when used as a monotherapy, it is not especially effective in solid tumors

Conventional radiotherapy (RT) is an adjunct therapy to surgery with remnant cancer tissues. After the onset of cancer[4], its post-surgical use showed late relapse and even cure of the ependymoma[19]. According to Combs et al.[9], in a prospective study using Fractionated Stereotactic Radiotherapy (FSRT), it was concluded that its use in recurrent cases caused less tissue damage and the rate of recurrence did not increase compared to conventional radiotherapy. The fractional use of RT is already a protocol used in children with residual neoplasia, metastasis, in inoperable cases[1,4]. The dosage will be indicated according to age, degree, location and previous ependymoma, taking care to avoid intoxication.

Chemotherapy is a classic treatment in oncology, but in ependymomas it plays a supporting role. Randomized studies evaluated some chemotherapy drugs, such as cisplatin, vincristine, cyclophosphamide and etoposide, in monotherapy dosage and double therapy with radiotherapy[3]. Studies have shown no benefits from monotherapy, however, its use in conjunction with RT improved patient survival and decreased the number of surgeries for tumor resection[3]. The VETOPEC (Cyclophosphamide/vincristine + cisplatin/etoposide + carboplatin/etoposide), ICE (Ifosfamide/etoposide/carboplatin) and Baby-POG (Cyclophosphamide/vincristine + cisplatin/etoposide) protocols showed positive results, respectively, 87.5%, 54.5% and 52% of the patients in the study had total or partial remission of the ependymoma[9,10]. Monotherapy was not as positive as compared to cocktails, but cisplatin and etoposide were the ones with promising results, in studies etoposide-induced deleterious effects in the bone marrow such as leukemia, being indicated for refractory patients[2,3,19].

OTHER TREATMENTS

Radiotherapy with proton beam

The process of releasing the proton beam has the same mechanism used in releasing x-rays, but the release of the proton beam occurs only in the target organ, surpassing the organs without interfering with healthy tissues, which is preferable because it doesn't leave damage. Khan et al.[20] described these aspects when comparing conventional RT, which sends its rays to the other organs compromising them, contrary to proton beam therapy. Studies showed a 75-85% of 5-year survival rate after gross total resection and focal RT in ependymomas, with that rate being lower in subtotal resections, young patients and metastasis[1,21]. Unfortunately proton beam RT is not available all over the world. Its access is very restricted, especially in developing countries.

Monoclonal antibody treatment

The ErbB/HER family receptors (ErbB-1, ErbB-2, ErbB-3 and ErbB-4) are physiologically expressed for the growth of organs and other organic structures, mostly mesenchymal, epithelial and neuronal cells. Its mutation or overexpression can cause impairment in embryonic development and provoke tumor cells growth, also increasing the expression of vascular endothelial growth factor (VEGF). Molecular studies found that mutations of ErBB-1 are found in cancers of breast, lung, neck and head with a high expression in gliomas. ErbB-2 was found to have cancerous effect in the formation of glioblastomas and indicates chemoresistance and poor prognosis. Target therapy with monoclonal antibodies is the best option for those cases[.15]

The VEGF is the primary target for the monoclonal antibody therapy aiming to inhibit angiogenesis, a response of adaptation from the tumor in a situation of malnutrition. A research with 13 pediatric patients with ependymomas used the Bevacizumab (BVZ), an anti-VEGF monoclonal antibody. The use of Bevacizumab (BVZ) plus Irinotecan (CPT-11) had multiple and non objective responses, in 10 patients there was a tumor progression in 2.2 months after therapy. Two patients had a stable disease for 12 months. Adverse effects were found and includes fatigue in 4 patients, hypertension in 2, epistaxis in 1, headache in 1 and avascular necrosis of bone in 1. It concluded that it didn't had a very satisfactory response in recurrent cases, but should be considered only in small tumors[14].

Immunotherapy-therapy with car t-cells

CAR T-cells are an immunotherapy that aims to specifically target cancer cells to minimize recurrence and off target effects. Ependymomas have four subtypes, two in the posterior fossa (groups A and B) and two in the supratentorial region (RELA and YAP1 fusions, according to the mutations drivers). The pediatric subtypes are the posterior fossa group B (PFB) and those in the supratentorial space. These tumors are sensitive to the action of CAR T-cells. According to Patterson's et al.[17] studies it was demonstrated increased expression of antigens (such as ErbB-2) that may be potentially effective targets for immunotherapy with CAR T-cell. The requirements for such treatment in solid pediatric brain tumors (PBT) are the expression of antigens on tumor cells but not on normal cells, to lessen the cytotoxicity and prevent immune escape. However, it's actually quite hard to have an antigen expressed only on tumor

cells, causing neuroinflammatory toxicities. In a research in mice and patient-derived orthotopic xenografts some antigens control growth in PBT without toxicity, and others cause neurotoxicity due to their expression on peripheral nerves and parenchyma[18]. However, Wykowski et al.[22] described that the therapy with EPHA2-specific CAR T-cells has shown safety in orthotopic xenografts derived from patients with medulloblastoma and ependymomas.

Ketogenic diet

The diet consists of foods that release ketone, depriving the brain and tumor of glucose, which is the raw material of functional energy for both, but the brain has other ways of extracting energy through ketone bodies, as it occurs in a fasting state, and these enter the Krebs Cycle, whereas the tumors have a difficulty using ketone bodies for their metabolism, due to mitochondrial abnormalities. Research in mice showed that a 30-40% dietary restriction led to a 79.5% reduction of tumor growth in astrocytomas. Studies have proven that the ketogenic diet has anti-inflammatory, anti-angiogenic and pro-apoptotic effects, however, it should only be used as a complementary therapy to current treatments, considering that the dietary changes do not prevent tumor growth, only retard it[11,15].

CONCLUSION

The cornerstone of treatments for ependymoma in pediatric patients continue to be surgical with total excision of the tumor. When total extraction is not possible, additional surgery or RT or both should be performed. RT is essential in neoplasia with subtotal exeresis, metastases and in inoperable cases. Chemotherapy, on the other hand, did not present such significant results until the present review, except when combined with RT. The other treatments, such as RT with a proton beam, monoclonal antibody and ketogenic diet are promising in the ependymoma, but further studies are needed.

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Retrospective Analysis of Clinical Indicators of 522 Patients Undergoing the ALIF Surgical Technique Using PEEK Cages

Análise Retrospectiva de Indicadores Clínicos de 522 Pacientes Submetidos à Técnica Cirúrgica ALIF Utilizando Gaiolas PEEK

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ABSTRACT

This review discusses the anterior lumbar interbody fusion (ALIF) procedure combined with a polyetheretherketone (PEEK) cage to treat degenerative diseases of the lumbar spine such as disc degeneration, spondylolisthesis, and pseudarthrosis, as well as their possible complications and benefits. A systematic literature review to identify, select, and analyze articles on ALIF for treating degenerative or traumatic disorders of the lumbar spine, published from 1988 until March 2021, was performed in the Public/Publisher MEDLINE database. In nine articles selected, 522 patients underwent ALIF surgery. Among all the patients surveyed, 17% had intra- and extra-operative complications and due to them, 11 (2.1%) needed reoperation. The mean Patient Satisfaction Index was 82.93% in three articles evaluating 210 patients after the surgery. Satisfactory clinical-functional improvement, considering postoperative time and patients' total recovery, was based on the Visual Analogue Scale (VAS), Oswestry Disability Index (ODI), and follow-up (mean of 18.55 months). Although standardization between studies was difficult because different types of material and methods were used in the articles surveyed, the ALIF technique has been proven to be an effective surgical procedure. Further studies are needed to standardize the variables to effectively establish response predictors of candidates for the ALIF procedure.

Keywords: *ALIF; Anterior lumbar interbody fusion; PEEK cage; Low back pain; Lumbar spine; Neurosurgery*

RESUMO

Esta revisão discute a fusão lombar intersomática por via anterior (ALIF) combinada com gaiola de polieteretercetona (PEEK) para tratar doenças degenerativas da coluna lombar, como degeneração discal, espondilolistese e pseudoartrose, bem como suas possíveis complicações e benefícios. Uma revisão sistemática da literatura para identificar, selecionar e analisar artigos sobre ALIF para tratamento de distúrbios degenerativos ou traumáticos da coluna lombar, publicados de 1988 até março de 2021, foi realizada no banco de dados Public/Publisher MEDLINE. Em nove artigos selecionados, 522 pacientes foram submetidos à ALIF. Entre esses, 17% tiveram complicações intra e extra-operatórias e, devido a elas, 11 (2,1%) necessitaram de reoperação. A média do Índice de Satisfação do Paciente foi de 82,93% em três artigos avaliando 210 pacientes após a cirurgia. A melhora clínico-funcional satisfatória, considerando tempo pós-operatório e recuperação total dos pacientes, baseou-se em Escala Visual Analógica (EVA), Índice de Incapacidade de Oswestry (ODI) e seguimento (média de 18,55 meses). Embora a padronização entre os estudos tenha sido difícil pela utilização de diferentes tipos de materiais e métodos nos artigos pesquisados, a técnica ALIF tem se mostrado um procedimento cirúrgico eficaz. Mais estudos são necessários para padronizar as variáveis para estabelecer efetivamente preditores de resposta de candidatos ao procedimento ALIF.

Palavras-Chave: *ALIF; Fusão lombar intersomática por via anterior; Gaiola PEEK; Dor lombar; Espinha lombar; Neurocirurgia*

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INTRODUCTION

The surgical technique named anterior lumbar interbody fusion (ALIF) was initially described by Capner, in the 1930s, and was developed to treat Pott's disease, the tuberculous vertebral column involvement caused by Koch's bacillus (Mycobacterium tuberculosis)[1,2]. Such a surgery consists of fostering arthrodesis between the bodies of two contiguous vertebrae by replacing the intervertebral disc with a cage, using the abdomen as an access route. Due to the possibility of restoring the biomechanical and structural integrity of the spine[1,3] this procedure had also become a new treatment option for more prevalent diseases such as disc degeneration, spondylolisthesis, and pseudarthrosis[2].

In the United States, a total increase by 168.5% was observed in ALIF completion rate between 2007 and 2014, i.e., 24.07% per year[4]. Although Brazil lacks studies dedicated to this theme to establish a national portrait, it is likely to have similar percentages.

It is important to emphasize that no significant difference was found between the arthrodesis rate promoted for the fusion of vertebral bodies of the lumbar spine using the ALIF approach and any other similar techniques[5]. However, the ALIF technique offers certain advantages, namely a shorter surgery time[6], less blood loss[3], less postoperative pain, and reduced surgical trauma to the paraspinal muscles[2]. The anterior approach allows complete re-section of the degenerated disc and contributes to eliminate the source of pain. Simultaneously, it leads to distracting and reshaping of the disc space that is affecting the regional and local spine alignment, including disc height/angle and lumbar lordosis[5].

By contrast, the anterior approach implies exposure and manipulation of structures such as the great vessels, sympathetic plexus, peritoneal contents, and ureters[3], which can provoke vascular traumas such as arterial wall dissection or venous injury[5], in addition to complications not considered serious, which tend to resolve spontaneously, such as lower limb paresthesia, retrograde ejaculation, and sympathetic dysfunctions[7]. It is worth mentioning that, in Brazil, since the surgical access is performed by a vascular surgeon, such complications have become extremely rare[8].

The main implantable option for ALIF is the polyetheretherketone (PEEK) cage. This material has been widely used for fixation, given that it is a non-absorbable, radiolucent, biocompatible compound that displays physical properties similar to those of human bone[9]. These characteristics make it more attractive compared to metal cages, in addition to allowing better image control[10].

Regarding the surgical indication, it should be considered as the main symptom reported by patients who are candidates for surgery is low back pain. This problem affects 80% of the adults at some moment in life, and it is among the top 10 causes of consultation with internists. Every year, 5% to 10% of workers miss more than seven days of work due to this condition[11]. Chronic spinal disorders have a prevalence of around 18.5% in the Brazilian population[8] and are one of the main causes of absenteeism[12], resulting in significant economic impacts. It has been estimated that back pain affects more than 100 million individuals and costs over $200 billion per year[13]. Therefore, the ALIF technique becomes more relevant considering that the surgical procedure is the last step in an attempt to relieve suffering, in clinical-functional improvement, for those who did not obtain satisfactory solutions with the conservative treatment, to restore patients' productive capacity, and to improve quality of life[6,7].

Based on these considerations, this systematic literature review aimed to compare pre- and postoperative parameters of patients that underwent ALIF using a PEEK cage, analyze variables such as functionality, pain, and patients' satisfaction rate according to validated scales, and discuss possible complications.

MATERIALS AND METHODS

A systematic literature review was carried out in the Public/Publisher MEDLINE (PubMed) database on the use of the surgical technique ALIF for the treatment of degenerative or traumatic disorders of the lumbar spine with the use of PEEK cage. The search was conducted by five independent researchers following the steps proposed in the protocol of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[14].

Aiming to increase the specificity of the systematic review, filters were applied contiguously to the Boolean descriptor, combined as follows: "ALIF" [Medical Subject Headings (MeSH) Major Topic] OR "anterior lumbar interbody fusion". For the selection of articles, the following inclusion criteria were adopted: 1) studies in English; 2) studies performed in patients over 19 years old; 3) studies that included patients who underwent autonomous single-level or multilevel ALIF using a PEEK cage; and 4) studies involving humans. The exclusion criteria were: 1) studies that used any fixation methods other than PEEK cage; 2) studies in which ALIF was used concomitantly with other lumbar interbody fusions (ALIF combined with posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), lateral lumbar interbody fusion (LLIF), extraforaminal lumbar interbody fusion (ELIF), and oblique lateral interbody fusion (OLIF); 3) cohorts including cadavers; 4) studies that could not be traced; 5) studies whose author's last name was "Alif"; and 6) meta-analyses and systematic reviews.

RESULTS

In this systematic review in the PubMed database, 307 papers were initially selected. After applying the abovementioned inclusion and exclusion criteria, nine articles were fully analyzed, encompassing 522 patients who underwent ALIF surgery (Figure 1, Table 1). The mean follow-up period was 23.18 months (minimum of 12 months and a range of 12–59 months). All patients completed a period of conservative treatment before the surgical intervention using ALIF was necessary.

As an outcome, in most studies selected, the clinical improvement of pain after the ALIF procedure was analyzed using the Oswestry Disability Index (ODI) and the Visual Analogue Scale (VAS), employed by clinicians and researchers to quantify disability due to low back pain and one-dimensional quantification of pain intensity, respectively. Additionally, the Patient Satisfaction Index (PSI) was used for the self-assessment of postoperative results.

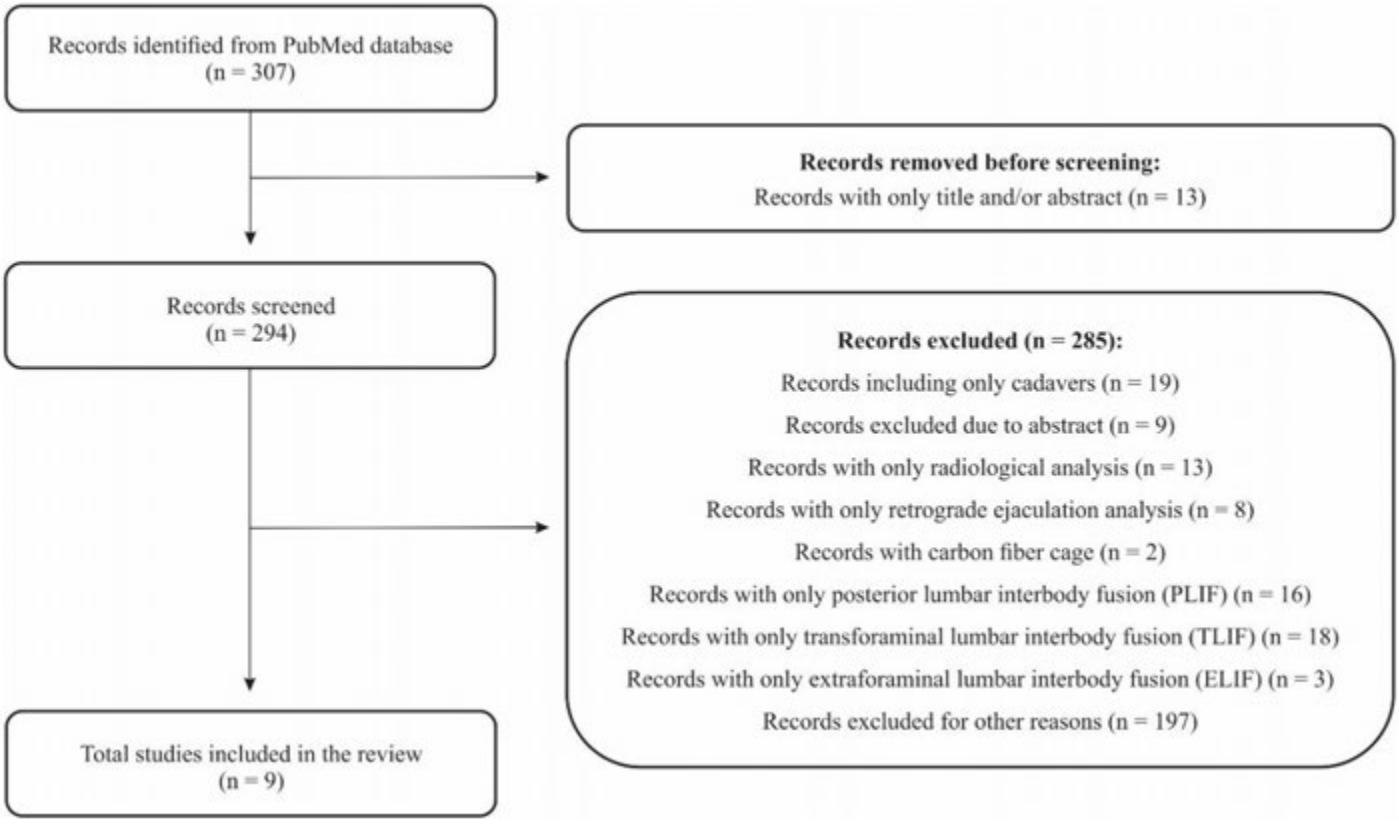

Figure 1. Flow diagram showing the study design according to the protocol of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[14].

On one hand, 345 patients (45.05% male, mean age of 53.7 years) were evaluated pre- and postoperatively applying ODI, whereas 107 patients (55.7% male, mean age of 55.7 years) were evaluated pre- and postoperatively using VAS. On the other hand, in only three articles PSI was used to evaluate 210 patients (49% male) after the surgical procedure.

Of 522 patients, a total of 89 complications were found within the articles analyzed, i.e. 17% of them had intra and extra operative complications, of which 11 (2.1%) required reoperation. Among the complications, seven patients complained of bladder dysfunction; seven had paralytic ileus; seven reported pseudarthrosis; five had superficial infections of the surgical scar, which improved after antibiotic therapy; five reported post-surgical hematomas; four had sympathetic dysfunction; three had intraoperative iliac vein injuries, which resolved without further damage; three complained of paresthesia of the lower limbs, extending to the L5 dermatome; three complained of motor complications; three reported sexual complications; two had peritoneal tears; one had an incisional hernia; one had anterior dural tear; one had abdominal wall insufficiency caused by the anterior approach, which required revision surgery; one reported temporary sensitivity disturbance in the region of the left flank correlated to the retroperitoneal approach, but the symptom disappeared spontaneously within 1 year; one had deep vein thrombosis; one reported recurrent radicular pain at L5; one had neurogenic claudication; one had lateral stenosis; one had phlebitis; one reported a sensory complication; and one had a sacral fracture.

Additionally, one patient died one day after surgery due to a previous heart problem.

Furthermore, 21 complications were attributed to the material used in the ALIF surgery: 15 patients underwent cage subsidence after a given period of cage implantation; three patients needed posterior fixations, requiring reoperations; two migrations of the plate were observed; and in one patient the screw was improperly placed.

Detailing the 11 reoperations, four patients underwent screw and rod removal due to discomfort attributed to posterior equipment after evidence of bone fusion; one required revision surgery, given the insufficiency of the abdominal wall; one required adjacent-level fusion within a 34-month observation period; one required reoperation by posterior approach due to another disease of the lumbar spine; one required reoperation to place a posterior pedicle screw percutaneously, due to constructive failure confirmed by imaging tests; one suffered a non-traumatic fracture of the upper endplate of L5, requiring posterior fixation with a pedicle screw; one underwent posterior decompression and uninstrumented fusion after imaging revealed nonunion, lateral stenosis, and residual spondylolisthesis; and one underwent revision surgery due to the detachment of the proximal hooks from their fixation points, which caused prominence of the rods and hooks.

Table 1. Characterization of the studies selected in this systematic literature review.

Reference	Experimental design	Patients (n)	Follow-up duration (months)	Age at surgery (mean ± SD; years) [range]	Male patients (%)	Complication	Reoperation	Preoperative (mean; mean ± SD)		Postoperative (mean; mean ± SD)		(%)
								ODI	VAS	ODI	VAS	PSI
Allain et al.[7]	Prospective study	65	12	57.1 ± 11.1 [35–82]	24.6	17	1	48.4	–	21.8	–	–
Jägersberg et al.[15]	Retrospective cohort	46	34	48 ± 10	47.8	11	6	–	–	–	–	75.8
Wan et al.[16]	Retrospective radiographic study	48	17	56.3	20.8	0	0	–	–	–	–	–
Rao et al.[1]	Prospective analysis	27	17	64.9 [37–84]	51.8	10	3	56.9 ± 21.7	7.6 ± 1.6	17.8 ± 16.2	2.2 ± 1.8	93.0
Ni et al.[10]	Retrospective radiographic study	68	27.5	67 ± 9	7.3	1	1	–	–	–	–	–
Mobbs et al.[6]	Clinical study	15	18	54 [33–82]	60.0	3	0	–	7.9	–	1.8	–
Phan et al.[17]	Prospective observational study	137	24	56.82	47.4	30	0	59.75 ± 24.36	–	35.23 ± 21.74	–	80.0
Norotte and Barrio[18]	Retrospective study	65	24	48 ±10	55.3	12	0	61.7 ± 9.4	6.2 ± 1.0	22.3 ± 14.3	0.5 ± 0.7	–
Kapustka et al.[5]	Retrospective analysis	51	12–59	41.7 ± 8.4 [24–59]	52.9	5	0	58	–	24	–	–
TOTAL		522				89	11					

n = number; SD = standard deviation; ODI = Oswestry Disability Index; VAS = Visual Analogue Scale; PSI = Patient Satisfaction Index.

DISCUSSION

The non-experimental surgical procedure named ALIF using PEEK cage is already consolidated in the international surgical practice and has been progressively gaining ground as a therapeutic option worldwide. It has been used to treat diseases such as disc degeneration, spondylolisthesis, and pseudarthrosis, demonstrating its effectiveness through previous prospective studies, which was also confirmed in this systematic review.

Comparing ALIF with other intersomatic spinal approaches, such as PLIF and TLIF, the anterior retroperitoneal technique decreases the risk of iatrogenic trauma to the paravertebral muscles and spinal nerves and does not involve removal of posterior bone structures[5]. It also allows the complete resection of the degenerated disc and the remodeling of the disc space using PEEK cages as well as the immediate decompression of the nerve root. Furthermore, this method allows the restoration of the lumbar lordosis angle, increases the height of the disc space, and improves sagittal balance, proposing an adequate alignment of the spine, thus making the reestablishment of the biomechanical integrity of the spine possible[1].

In contrast, the anterior approach requires exposure and mobilization of large blood vessels, peritoneal contents, ureter, and sympathetic plexus[5]. Therefore, this technique may present risks and complications involving the aforementioned structures. The most frequent complication is venous injury and rupture of the arterial wall, considered the most serious iatrogenic damage, although extremely rare[5]. Recognizing the risk, nowadays, the anterior access is performed by a vascular surgeon, which has resulted in considerable decrease in complications, reduced surgical time and bleeding, decrease in the rates of intra-operative and extra-operative complications, in addition to developing clinical-functional improvements that are beneficial to patients, especially in terms of pain relief[19].

Variables were analyzed within a study based on radiographic data from patients undergoing ALIF with PEEK, in which the anterior and posterior height of the disc, disc angle, lumbar lordosis, and foraminal dimensions were taken into account[5]. According to this analysis, anterior lumbar fusion is an effective and safe procedure for the treatment of spinal pathologies, statistically improving pain, functionality, and measures of well-being in degenerative disc diseases. Thus, ALIF is an effective treatment both clinically and radiographically[16].

The nine studies selected did not use the same quantitative and qualitative analysis standards, which limits our discussion about the improvement of patients after ALIF. Nevertheless, given the significant clinical improvement expressed by the numerical decrease in the postoperative period compared to the pre-surgical index verified using ODI and VAS in most studies, the present systematic literature review confirmed that the improvements reported by the patients proved to be significantly expressive, confirming the effectiveness of the ALIF surgery in relieving patients' pain.

CONCLUSION

Low back pain is a prevalent spinal condition and one of the main causes of demand for medical care in the world, generating economic and health impacts at global level. Based on the studies analyzed, ALIF stands out as an effective option for the treatment of this condition, and it is evident that it is a safe technique that brings significant improvement in patients' pain and quality of life. However, further prospective studies are needed to provide a real and updated picture of the ALIF technique, especially in the Brazilian context, as well as its current rate of complications and indicators of improvement and satisfaction.

This study confirmed that the ALIF technique is a surgical procedure with proven efficacy. This systematic literature review encompassed a total of 522 patients, constituting the review with the largest number of patients analyzed for this surgery in the PubMed database. Nonetheless, the discussion was limited by the discrepancy between the different types of material and methods used in the articles surveyed, making standardization between studies difficult.

Therefore, further studies that can standardize the variables are needed to allow discussing the effectiveness of this surgical procedure and to effectively establish response predictors of candidates for the ALIF procedure.

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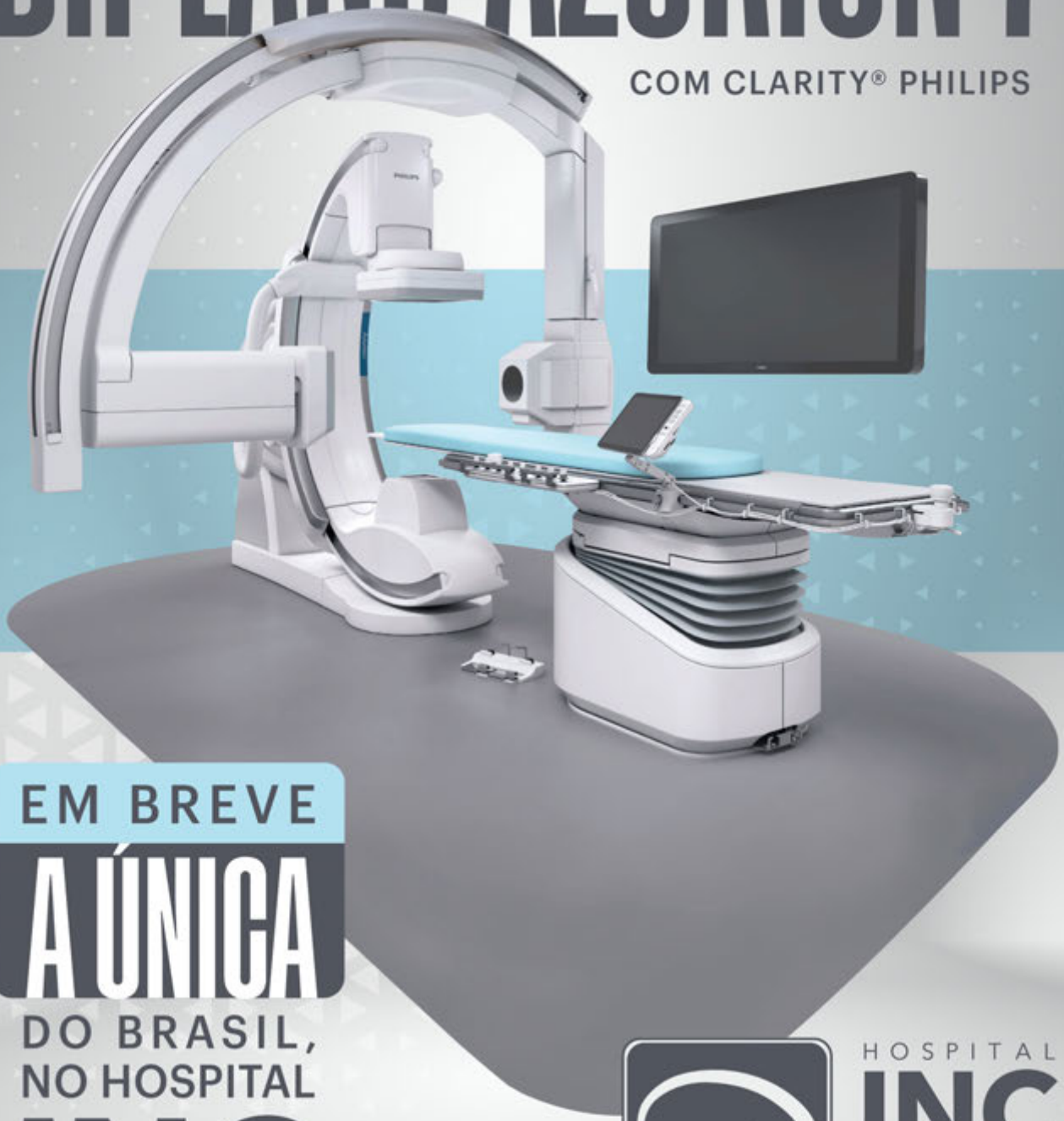

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Surgery for Candida Brain Abscesses: a case report and review of the literature

Cirurgia para Abscesso Cerebral por Candida: um relato de caso e revisão da literatura

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ABSTRACT

The Candida sp. cerebral abscess is a rare condition with high mortality rates. It is associated with immunosuppression and it should be considered as a differential diagnosis in patients who did not respond to standard treatments for other central nervous system infections. We performed a review of the literature on published cases of candida brain abscess and compared surgical to non-surgical cases. Case reports or case series were included and the data presented was analyzed. A total of 29 patients were included in the analysis. The average hospital stay was 37.7 days for the surgical group and 112.4 days for the non-surgical group (p=0.001). The overall mortality was 13.8%, with 14.3% for the surgical group and 13.3% for the non-surgical group (p=0.624). Candida sp. cerebral abscess is a rare but increasingly relevant condition. Surgical resection may alleviate local mass effects and enable a definitive etiologic diagnosis. More studies are needed to investigate the differences between surgical and non-surgical treatments.

Keywords: *Brain abscess; Brain infection; Candida sp; Surgical drainage; Surgery for brain infection*

RESUMO

Os abscessos cerebrais por Candida sp. são condições raras com altas taxas de mortalidade. Está associada à imunossupressão e deve ser considerada como diagnóstico diferencial em pacientes que não respondem aos tratamentos padrão para outras infecções do sistema nervoso central. Realizamos uma revisão da literatura sobre casos publicados de abscesso cerebral por cândida e comparamos casos cirúrgicos com não cirúrgicos. Relatos de casos ou séries de casos foram incluídos e os dados apresentados foram analisados. Um total de 29 pacientes foi incluído na análise. A média de internação foi de 37,7 dias para o grupo cirúrgico e 112,4 dias para o grupo não cirúrgico (p=0,001). A mortalidade geral foi de 13,8%, sendo 14,3% para o grupo cirúrgico e 13,3% para o grupo não cirúrgico (p=0,624). O abscesso cerebral por Candida sp. é uma condição rara, mas cada vez mais relevante. A ressecção cirúrgica pode aliviar os efeitos de massa local e permitir um diagnóstico etiológico definitivo. Mais estudos são necessários para investigar as diferenças entre tratamentos cirúrgicos e não cirúrgicos.

Palavras-chave: *Abscesso cerebral; Infecção cerebral; Candida sp, Ressecção cirúrgica; Cirurgia para infecção cerebral*

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BACKGROUND

Candida sp. infection of the central nervous system (CNS) is a rare but severe condition with mortality estimated at approximately 70%[1]. Clinical and imaging findings are not specific, so further investigation is often necessary for agent identification and treatment[1,2].

Although rare, there was an increase in *Candida sp.* infections worldwide in the past few decades[3]. Many factors contribute to this trend, including the widespread use of antibiotics and improved longevity of patients with chronic conditions, immunosuppression, central catheters and other invasive devices[1,4,5]. The estimates of neurological involvement in disseminated candidiasis range from 48–64%[6], with neurological sequelae present in 20–70% of patients[7].

Many studies have reported on the clinical and surgical treatment of this rare disorder, but the indication and treatment with en bloc resection of the lesion is still underrepresented in the literature[4,8]. In the present study, we report a case of successful combined treatment of a *Candida sp.* brain abscess resection and review other previous findings on surgically approached lesions.

CASE PRESENTATION

A 34-year-old woman with systemic lupus erythematosus (SLE), undergoing treatment with hydroxychloroquine and azathioprine, was admitted with reports of seizures that started 4 months prior to admission. Fever or other symptoms suggestive of infectious disease were not present and neurological examination was normal. Laboratory studies at clinical admission are presented in Table 1. Increased leukocyte count was observed with predominant neutrophils (81.6%), however, other infectious and metabolic panels were normal.

Table 1. Laboratory findings at admission.

Lab exam	Result
HIV	Negative
Mg	2 mmol/L
Anti-HCV	Negative
HEP B Anti HBC	Negative
HBSAG	Negative
Creatinine	1 mg/dL
Urea	56 mg/dL
K	4.5 mmol/L
Na	134 mmol/L
Anti HBS	0.06 IU/L
Hemoglobin	10.95 g/dL
Hematocrit	32.87%
MCV	88.84 fL
MCH	29.5 pg
MCHC	33.3 pg
White cells	16010 cells/mL
Neutrophil	81.60%
Lymphocyte	11.55%
Monocyte	6.19%
Eosinophil	0.02%
Basophile	0.63%
Prothrombin time	10.5 s
INR	0.88
PTT	22.2 s

HIV: Human immunodeficiency virus; Mg: Magnesium; Anti-HCV IGG: antibodies against the hepatitis C virus; Hep B anti-HBc: antibody to hepatitis B core antigen; HBSAG: Hepatitis B surface antigen; Anti- HBs: Hepatitis B surface antibody; K: Potassium. Na: Sodium; MCV = Mean Corpuscular Volume; MCH = Mean Corpuscular Hemoglobin; MCHC = Mean corpuscular hemoglobin concentration; INR: International normalised ratio test; PTT: Partial thromboplastin time.

The patient had a long clinical history of SLE and lupus glomerulonephritis, as well as other comorbidities such as hypothyroidism, panic syndrome, depression, anxiety disorder, hypertension, and pre-diabetes. She had a kidney biopsy approximately 1 year before the admission. Furthermore, the patient had previously been treated with methylprednisolone pulse twice due to increased proteinuria and nephritis. Her immunologic panel was negative for lupus anticoagulant, latex, anti-Ro, anti-La, Coombs test, and anti-Jo-1.

A contrast enhanced computed tomography (CT) scan showed a round lesion in the left frontal lobe (Figure 1). Differential diagnosis included primary glial lesions, metastatic lesions

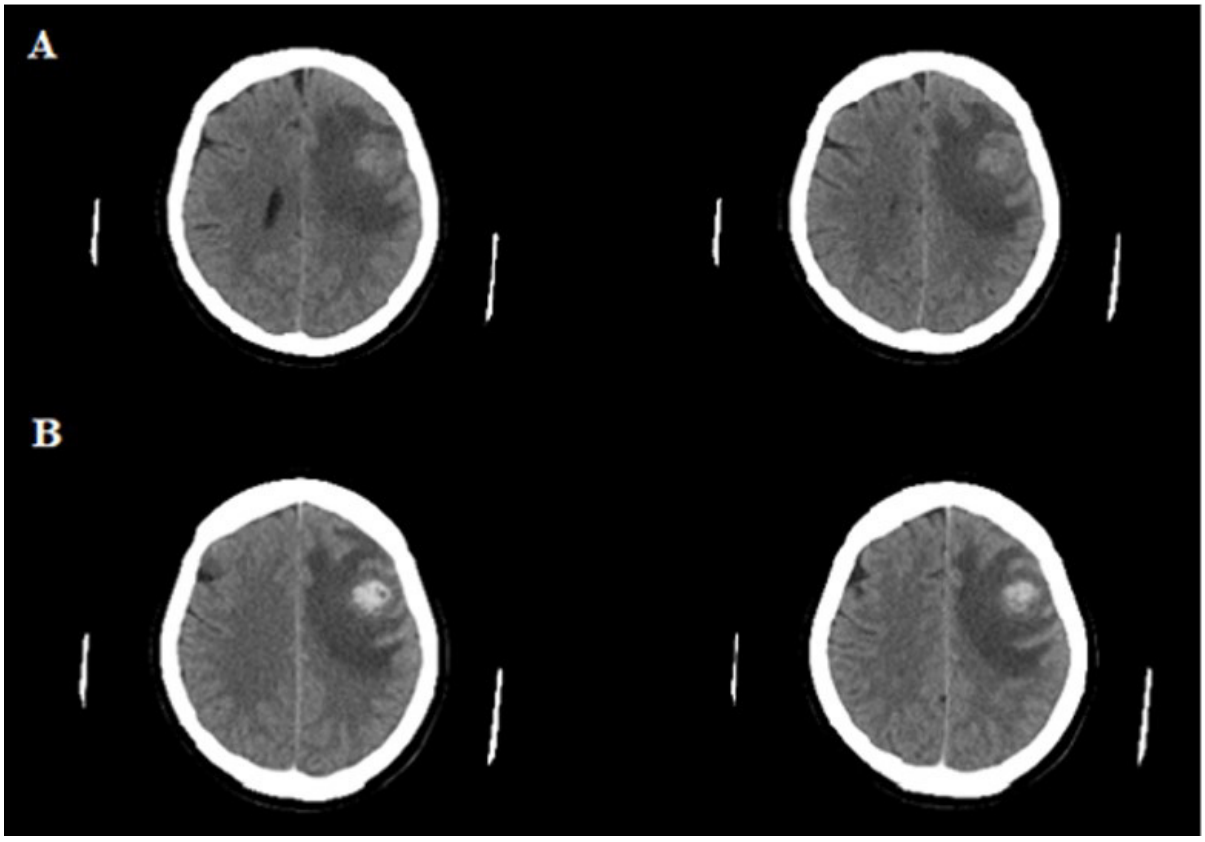

Figure 1. Computed tomography scan at admission, before (A) and after (B) contrast administration. A left frontal round lesion was observed with contrast enhancement at the grey-white matter interface, as well as digitiform edema.

and neuroinfectious lesions. Neurotoxoplasmosis (NTX) and bacterial brain abscesses were among the hypotheses due to the heterogeneous radiological aspect with peripheral enhancement on the CT scan, even though a unique lesion would be an atypical presentation for NTX.

Further investigation using magnetic resonance imaging (MRI) confirmed a left frontal nodular lesion with T2 and fluid-attenuated inversion recovery (FLAIR) iso- and hypointensities, heterogeneous contrast enhancement and diffusion restriction, as well as extensive perilesional vasogenic edema, measuring approximately 18 × 16 mm at its largest diameters (Figure 2). Diffusion-weighted images demonstrated a heterogeneous lesion and low apparent diffusion coefficient values indicating restricted diffusion. Spectroscopy showed an increase in the choline/creatine ratio and a decrease in the N-acetylaspartate peak (Figure 3), indicating neuronal depopulation, as well as a lactate peak.

Open surgical drainage was indicated. A left fronto-temporal craniotomy was performed and the lesion was identified with intraoperative ultrasonography guidance. The initial objective was to drain the lesion, but it was not possible due to its rigid consistency. Then a microsurgical dissection was performed with direct visualization of the well-defined plane around the lesion. Surgical margins were free of reminiscent material following resection.

Pathological analysis revealed suppurative areas populated by dimorphic fungal elements. Gomori-Grocott staining was positive with morphology compatible with *Candida sp.* (Figure 4). Therefore, treatment with intravenous 1mg/kg of amphotericin was maintained for 14 days. Subsequently, 150 mg/d oral fluconazole was initiated and maintained for 5 months. A similar successful approach was reported previously by Yampolsky et al.[9]. The patient developed dysarthria and transient hemiparesis in the immediate postoperative period, which were resolved completely.

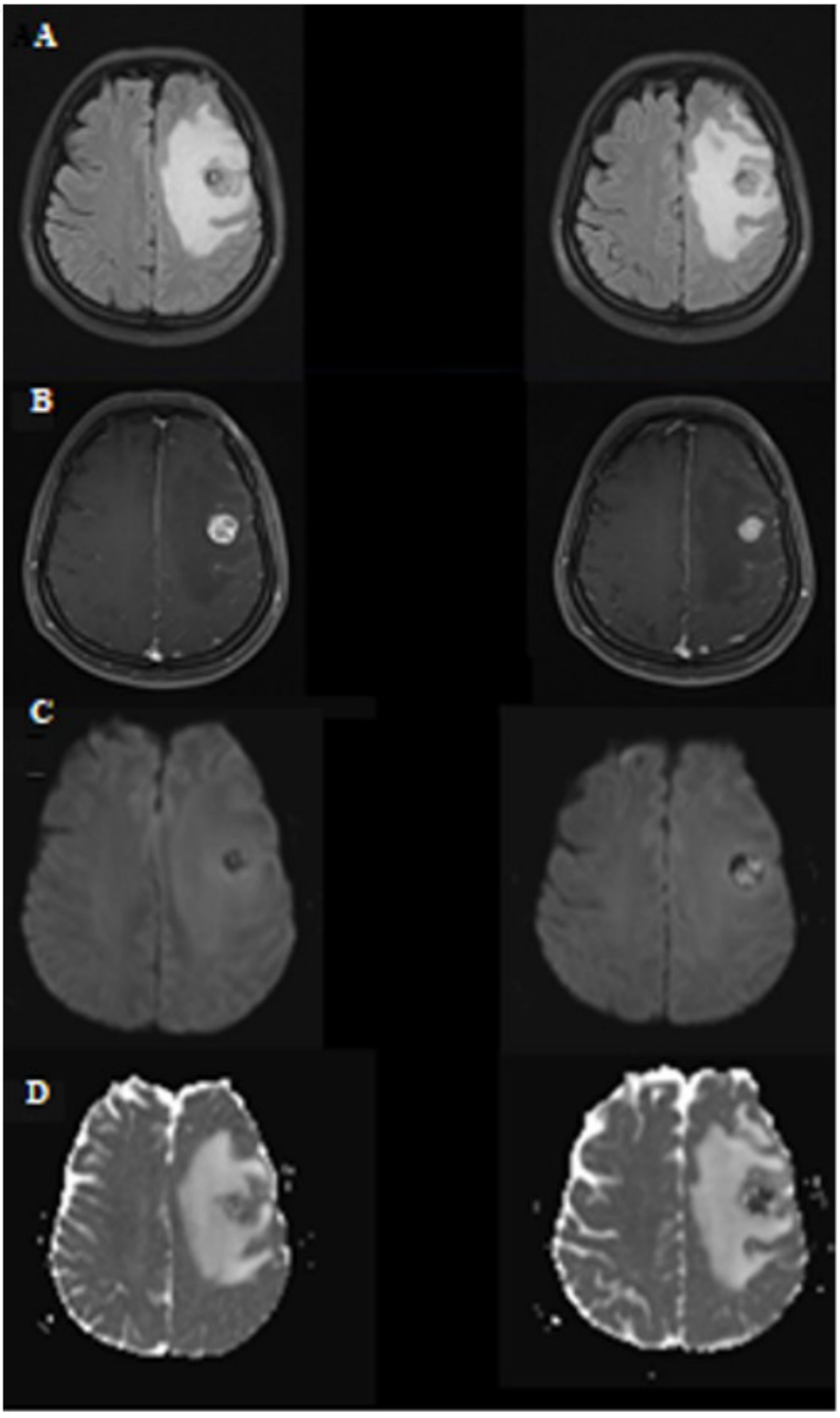

Figure 2. Magnetic resonance imaging findings using fluid-attenuated inversion recovery (FLAIR) (A), post-contrast T1 (B), diffusion-weighted imaging (C), and apparent diffusion coefficient map (D). A left frontal nodular lesion was observed at the grey-white matter interface, with iso and hypointensities by FLAIR, heterogeneous contrast enhancement, and diffusion restriction. Extensive perilesional vasogenic edema is also apparent.

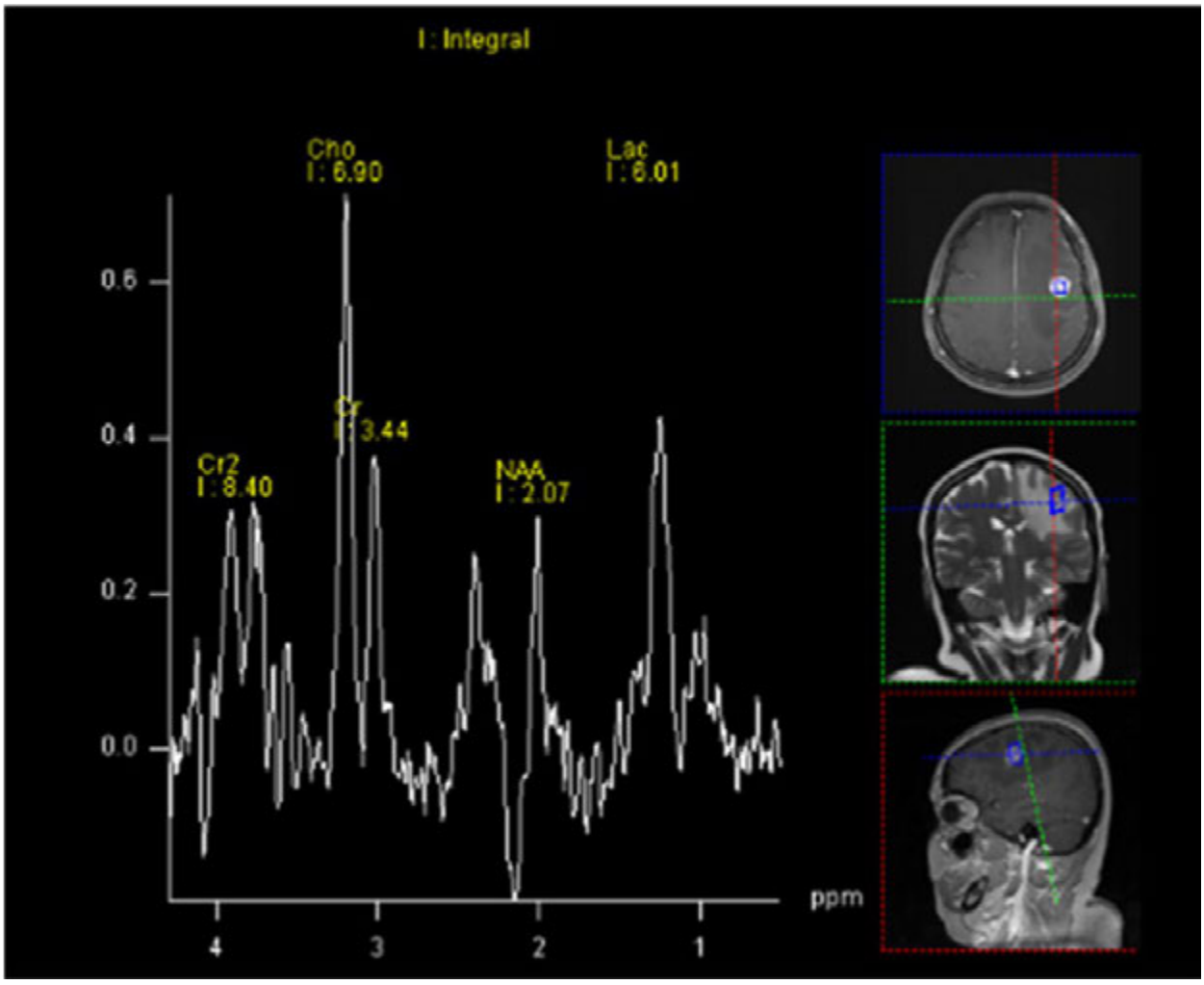

Figure 3. Magnetic resonance imaging spectroscopy with a long echo-time demonstrates an increase in the choline/creatine ratio and a decrease in the n-acetylaspartate (NAA) peak, reflecting neuronal depopulation, as well as a lactate peak at 1.3 ppm.

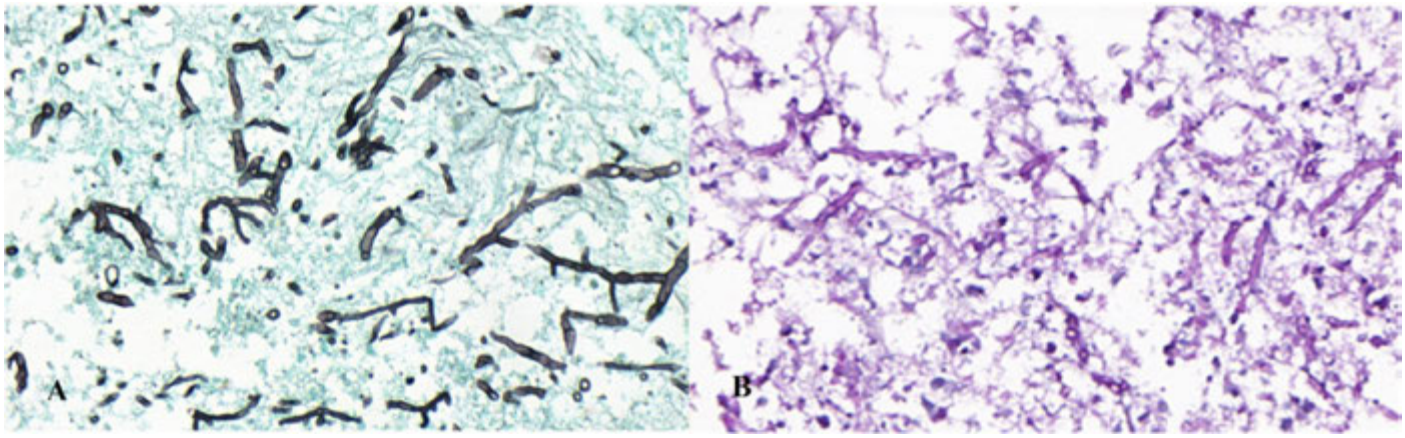

Figure 4. Grocott's silver strongly stains pseudohyphae **(A)**. Sausage-shaped chains of pseudohyphae of Candida albicans **(B)**.

METHODS

A search was performed in the MEDLINE, Embase, Google Scholar and Web of Science databases for studies presenting series of candida brain abscess patients. The following search terms were applied on October 1st, 2022: (Candida) AND (brain abscess) AND ((treatment) OR (Surgery)).

Eligibility criteria and selection of studies

Surgical and non-surgical series with full texts available online in English were included. Titles and abstracts of studies were evaluated by two authors (L.C.P.P. and R.C.) to eliminate those not relevant to the objectives of the study. In cases with duplicates, only studies with the most contemporary cohorts were considered.

Case reports or case series were included for the analysis if they confirmed *Candida sp.* in at least one pathological test (biopsy, blood or liquor culture, autopsy specimen) and had a cerebral expansive lesion compatible with a fungal infection. Studies on general brain abscess data, that did not present detailed description of the Candida abscess cases were excluded. Articles limited to radiological discussion were excluded.

Data on age, sex distribution, mortality, length of hospitalization, incidence of positive liquor or blood culture was collected when available.

Statistical analysis

The patients were separated into surgical and non-surgical groups and basic statistics was performed in order to better understand trends. Chi-square tests were performed with the aggregate data between groups. Bar graphs with binomial confidence intervals were performed. The Mann-Whitney U test was performed for continuous or ordinal variables. Values of $p<0.05$ were considered significant. GraphPad Prism version 9.0 was used for the analysis and graphic production.

RESULTS

A total of 90 unique publications were found using the search term. Thirty-six articles were read in full with 9 being excluded. Two of the articles were not available online in full and 7 articles did not report on culture results or existing brain lesions due to *Candida sp.* Twenty-three articles were included in the review. The summary of the results is presented in Table 2.

A total of 29 patients was included in the analysis with most articles consisting of case reports. A paper from Haruda et al.[29]. presented 2 patients and an article from Wang et al.[11] had 6 patients included. Fourteen patients were treated surgically and fifteen were treated clinically (Table 3).

The surgical group presented 50% of female patients while in the non-surgical group the female percentage was 56.6%.

Average age was 29.6 years for the surgical group and 19.4 years for the non-surgical group ($p=0.251$). The average hospital stay was 37.7 days for the surgical group and 112.4 days for the non-surgical group ($p=0.001$, Figure 5). The overall mortality was 13.8%, with 14.3% for the surgical group and 13.3% for the non-surgical group ($p=0.624$). The most common surgical approach was open drainage (35.7%), followed by stereotactic biopsy (28.6%), simple burr hole (7.14%) and endoscopic drainage (7.14%). In 14.3% of cases no drainage method was described. Four cases in the clinical treatment group presented a positive CSF culture, all for *C. albicans* while patients submitted to surgical approach presented different species obtained from surgical samples (Table 2).

DISCUSSION

Disseminated Candida infections tend to be extremely severe conditions. The mortality rate for a series of non-autopsy CNS *Candida sp.* ranges from 69-100%[1,30]. Our patient was clinically stable despite a complex medical history. There were no symptoms other than seizures and the surgical procedure was performed without complications, with minimal disability observed after the procedure.

Some studies suggest a decreasing role for open resection of these lesions, with preference for stereotactic and other minimally invasive techniques[26]. Our patient had a lesion in the left

Table 2. Study summary data.

Author	N	Age	Clinical presentation	Risk Factors	Surgical treatment	Mortality cases	CSF culture	Blood Culture
Black[8]	1	29	Seizures, decreased consciousness	Pregnancy, previous candida infection	Yes	1	C. albicans	Negative
Holyst[10]	1	51	Headache, vertigo, nausea, vomiting	Not reported	Yes	1	Negative	Negative
Haruda[11]	2	0	Sepsis	Premature, Premature rupture of membranes	No	1	Negative	Negative
Thron[12]	1	20	Headache, vomiting, left hemiparesis	Not reported	No	0	C. albicans	Not reported
Ilgren[13]	1	14	Headache, vomiting, decreased consciousness	No risk factors	Yes	0	Not reported	Not reported
Ikeda[14]	1	24	Headache, poor vision	Previous antibiotic	No	0	C. albicans	Negative
Burgert[15]	1	56	Hemiparesis	Alcohol, pancreatitis, central line, antibiotics	Yes	0	Negative	Positive
Kamitsuka[16]	1	1	Ultrasound hypoecoic areas	Premature, Premature rupture of membranes	No	0	C. albicans	Positive
Kaji[17]	1	49	Deafness	Diabetes, cirrhosis	No	0	Negative	Negative
Prabhu[18]	1	35	Fever, chills, delirium, headaches, diplopia	Prosthetic aortic valve/ fungal endocarditis	No	0	Not reported	Positive
Pham[19]	1	36	Headache, mild left hemiplegia	Traumatic brain injury and cerebral trombosis	Yes	0	Not reported	Not reported
Baradkar[20]	1	1	Fever, increased head circumference	Prematurity, low weight	Yes	0	Negative	Negative
Yampolsky et al.[9]	1	51	Headache, seizures, left arm paresis	Diabetes, previous candida infection, psoriasis	Yes	0	Not reported	Negative
Fennelly et al.[1]	1	57	Unresponsiveness,	Diabetes, I.V. drugs	Yes	0	Negative	Negative
Wang[21]	6	0	Fever, decreased responsiveness, and apnea in all, convulsion in only one case	Prematurity, low weight	No	1	Negative	Positive
Neves et al.[7]	1	46	Seizures, decreased consciousness	Hep C, I.V. drugs, alcoholism, pancreatitis, diabetes, antibiotics, sinusitis	No	0	Negative	Negative
Yoganathan et al.[22]	1	0	Vomiting, decreased feed intake	Administration of antibiotics through the peripheral line	Yes	0	Negative	Negative
Strickland[23]	1	33	Headache, vision loss, hypopituitarism, diabetic ketoacidosis	Diabetes, recent abscess drainage, antibiotics	Yes	0	Candida glabrata	Positive
Zhu[24]	1	25	Fever, cough, numbness in right hand, right hemiplegia, aphasia	Smoking, psoriasis, intestinal polyposis	Yes	0	Negative	Negative
Bilgin[25]	1	1	Discomfort and feeding difficulty	Previous operation (meningomyelocele + hydrocephalus), multiple ventriculoperitoneal shunts	Yes	0	Negative	Negative
Radhouane et al.[26]	1	32	Seizures, impaired consciousness, fever	No risk factors	Yes	0	Not performed	Negative
Zhu[27]	1	0	Lethargy and feeding intolerance	Prematurity, low weight	No	0	Candida albicans	Positive
Yoshida[28]	1	28	Fever, toracic tenderness, lumbar tenderness, left facial nerve palsy, and left upper limb paresis	Total parenteral nutrition, low BMI (anorexia nervosa)	Yes	0	Negative	Negative

Table 3. Comparison between surgical and non-surgical groups.

	Surgical	Non-surgical	p-value
N patients	14	15	0.182
Age (mean)	29.6	19.4	0.251
Hospital stay (mean)	37.7	112.4	0.001
Masculine (%)	50.0%	44.4%	0.795
Feminine (%)	50.0%	55.6%	0.795
Mortality (%)	14.3%	13.3%	0.624
Positive blood (%)	14.3%	26.7%	0.111
Positive CSF (%)	14.3%	26.7%	0.18

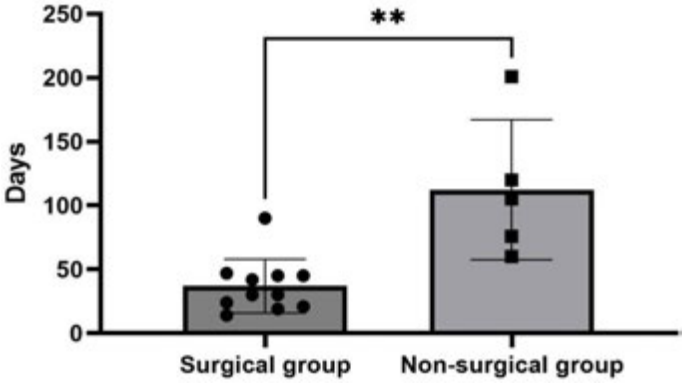

Figure 5. Review of reported cases about Candida Cerebral Abscess. Comparison between average hospital stay in patients with Candida Cerebral Abscess that were submitted to any surgical treatment versus those who only had clinical treatment. **p<0.05.

hemisphere, producing refractory seizures and vasogenic edema. We believe the open approach allowed for better identification of the anatomy, with an effective resection of the lesion. Ultimately, the patient presented a firm, non-cystic lesion, which would unlikely be removed only by draining approaches. The possibility of a highly viscous or even solid material presents an additional difficulty that needs to be considered in similar cases. The open resection allowed for complete removal of the infected material.

Several clinical conditions are crucial to understand the complexity of *Candida sp.* brain lesions. Specifically, diabetes is one of the most important comorbidities in relation to *Candida sp.* brain lesions[9,31]. In our review of patients who were surgically treated, 30% had diabetes.

It is mentioned that *Candida sp.* bloodstream infections represent 8–15% of all bloodstream infections, and systemic *Candida sp.* infection is one of the most important risk factors for Candida CNS infection[32]. A previous study reported 6% incidence of neurocandidiasis in patients with systemic Candida sp. infections[33]. However, blood and liquor cultures of our patient were negative for candidemia, which is consistent with about 80% of the cases reviewed (Table 2).

Immunosuppression and general poor health status of patients with invasive *Candida sp.* infections are associated with *Candida sp.* brain abscesses[1]. Other factors include history of malignancy, neutropenia, hematologic disorders, diabetes mellitus, thermal injuries, intravenous drug use, or central venous catheter, as well as prolonged antimicrobial therapy, particularly if there was a poor response to usual antibacterial agents[1,4].

Clinically, fungal infections affecting the CNS can present as abscesses and/or meningoencephalitis. When presenting as abscesses, there may be numerous associated focal neurological signs. The differential diagnoses in this group of patients include stroke, neoplastic lesions, multiple sclerosis, vasculitis, and many other conditions[34]. It is not rare for these patients to become dependent on intensive care unit support, using vasoactive or sedative drugs, and supported by diverse invasive devices. The most common clinical manifestation reported on previous studies is decreased level of consciousness[1].

A previous review of *Candida sp.* abscess cases revealed candidemia positive blood cultures in 55% of cases, and lumbar puncture yielded Candida sp. growth in only 23% of cases[1]. Of the cases presently reviewed, 20.7% had blood and liquor positive cultures.

CT and MRI findings cannot always differentiate between brain abscesses and neoplastic lesions. The magnetic resonance spectroscopy choline peak is correlated with neoplastic lesions and a Cho-Cr ratio greater than 1.6 is correlated with primary glial tumors[35]. Additionally, the edema observed in CNS infections is usually moderate compared to more pronounced findings observed for neoplastic lesions[36,37]. General MRI features of CNS fungal infections include: (1) early and heterogeneous punctate or ring-like reduced diffusion even before contrast enhancement due to high viscosity and cellularity of fungal pus; (2) variable contrast enhancement, which is proportional to the immune status and inflammatory capacities, commonly with weak ring-like enhancement in immunocompromised patients and possible robust enhancement in immunocompetent hosts. *Candida sp.*

CNS infections commonly produce microabscesses at the grey-white junction, basal ganglia, and cerebellum; meningitis and larger abscesses like that presently reported may also occur[38].

Amphotericin B is the standard therapy for *Candida sp.* brain abscesses. An alternative is fluconazole, which has better blood-brain-barrier penetration. The duration of therapy is typically 6–8 weeks, followed by oral therapy with no strict end point[39]. Intrathecal antibiotic delivery was reported in 2 of the presently reviewed studies[8,14]. In both cases the patients presented with critical clinical status, which resulted in a more invasive therapeutic regimen. Although there are some successful reports on the intrathecal application of antifungal agents, there is no formal indication of such antifungal therapy for *Candida sp.* lesions[40].

Indication of surgical drainage as a component of treatment is based on clinical and radiologic aspects of the case, including patient stability, neurologic features, location of the lesion, and lesion size. Previous studies have highlighted the applicability of drug treatment alone in abscesses smaller than 2.5 cm[7]. When the lesions are deep and surrounded by highly critical areas of the brain it is particularly necessary to exercise caution in recommending any type of surgery. However, lesions that are refractory to other treatments or that present with uncertain diagnosis are nonetheless recommended for surgical sample/removal[29]. Craniotomy with surgical resection is the ideal drainage route for larger superficial lesions and stereotactic drainage is a less invasive alternative that can be applied to deep lesions that are less accessible by an open route[22].

The review suggested a difference for hospital length of stay between groups (37.7 days for surgical and 112.4 days for non-surgical cases, p=0.001). To the best of our knowledge, this is the first time that this observation is described in medical literature. One hypothesis that can be drawn attempting to explain this finding is that surgical drainage could be associated with improved clearance of infected tissue, thus reducing the time of hospitalization needed to improve the patient's status. Variables such as age, gender distribution, mortality and rate of positive cultures were similar between surgical and non-surgical cases (Table 3).

Several limitations can be highlighted in this study. We performed a review of published studies that can present some kind of publication bias. Since this article is only pooling data from non-controlled studies no statistical conclusion should be drawn from these results, which should serve only as questions for future better designed investigations. More studies are needed in order to better understand the differences between cases treated with and without surgery.

CONCLUSION

We present a case of *Candida sp.* brain abscess that was successfully treated with open drainage. Surgical resection may alleviate local mass effect and provide definitive etiologic diagnosis. Additionally, the reviewed data support that fungal abscesses are rare conditions and frequently associated with poor prognosis. All treatment modalities must be individualized taking into consideration the patient's health condition, clinical presentation and imaging findings. We identified a trend suggesting that patients treated with surgery could have reduced lengths of hospital stay. More studies are needed to better investigate the trends identified in this review.

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Hemorragia Subaracnoidea Perimesencefálica Não Aneurismática Após Ressecção Endoscópica de Adenoma Hipofisário Não Funcionante: relato de caso e revisão da literatura

Non-Aneurysmal Perimesencephalic Subarachnoid Hemorrhage After Endoscopic Resection of a Non-Functioning Pituitary Adenoma: case report and literature review

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RESUMO

A hemorragia subaracnoidea perimesencefálica não aneurismática é um tipo relativamente raro de sangramento subaracnoideo espontâneo, definido pelo acúmulo de sangue em topografias específicas do sistema nervoso central, a saber, cisternas da base (interpeduncular, crural, ambiens e quadrigêmea) podendo se estender para parte posterior da fissura inter-hemisférica anterior e parte basal da fissura sylviana, não associados a sangramento intraventricular franco ou hematoma intraparenquimatoso. É uma condição clínica de curso benigno, mostrando melhor prognóstico que sangramento aneurismático sendo, na maioria das vezes, tratamento conservador. O presente artigo visa descrever o relato de um caso com características de uma hemorragia perimesencefálica na evolução pós-operatória de um adenoma hipofisário não produtor, abordado por via endoscópica assim como revisar epidemiologia, diagnóstico, prognóstico e considerações na literatura sobre a patologia hemorrágica.

Palavras-Chave: *Hemorragia subaracnoidea perimesencefálica não aneurismática; Cisterna interpeduncular; Vasoespasmo; Adenoma hipofisário; Revisão*

ABSTRACT

Non-aneurysmal perimesencephalic subarachnoid hemorrhage is a relatively rare type of spontaneous subarachnoid bleeding defined by the accumulation of blood in specific topographies of the central nervous system, namely basal cisterns (interpeduncular, crural, ambient and quadrigeminal), which may extend to the posterior part of the fissure. anterior interhemispheric artery and basal part of the sylvian fissure, not associated with frank intraventricular bleeding or intraparenchymal hematoma. It is a clinical condition with benign course, with better prognosis than aneurysmal bleeding and being most often conservative treatment. This article aims to describe a case report with characteristics of a perimesencephalic hemorrhage in the postoperative evolution of a non-producing pituitary adenoma, approached endoscopically, as well as to review epidemiology, diagnosis, prognosis and considerations in the literature on the hemorrhagic pathology.

Keywords: *Non-aneurysmal perimesencephalic subarachnoid hemorrhage; Interpeduncular cistern, Vasospasm; Pituitary adenoma; Review*

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INTRODUÇÃO

A hemorragia subaracnoide (HSA) espontânea é uma forma de acidente vascular encefálico hemorrágico que acomete, em sua maioria, indivíduos jovens e está associada a altas taxas de morbimortalidade[1]. Na ausência de traumatismo craniano, a maioria dos casos de HSA decorre da ruptura de um aneurisma intracraniano ou outras malformações vasculares cerebrais que podem ser identificadas ou não na angiografia cerebral[2].

A HSA perimesencefálica (HSA-PM) apresenta uma distribuição do sangramento nas cisternas perimesencefálicas anteriores ao tronco cerebral, que pode se estender até a cisterna ambiens e partes basais das fissuras sylvianas[3]. É responsável por cerca de 5 a 10% das HSA e mais de 30% de todas as hemorragias subaracnoideas não aneurismáticas[4]. Em comparação com o padrão aneurismático de sangramento subaracnoideo, está associada a um resultado encorajador, muitas vezes autolimitado[5].

O presente artigo descreve um relato de caso com características de uma hemorragia perimesencefálica na evolução pós-operatória de um adenoma hipofisário não produtor, abordado por via endoscópica, assim como, apresenta uma revisão da epidemiologia, diagnóstico, prognóstico e considerações na literatura sobre a patologia hemorrágica.

RELATO DE CASO

Paciente do sexo feminino, 39 anos, parda. Internada no Hospital Getúlio Vargas com história de tonturas, visão turva e alteração menstrual há cerca de 2 anos. Submetida a investigação da acuidade visual, campimetria óptica e fundoscopia, foi documentado uma hemianopsia bitemporal. Na avaliação endocrinológica, apresentou perfil hormonal compatível com adenoma hipofisário não produtor.

A ressonância magnética de crânio mostrou lesão expansiva sólida intrasselar com extensão suprasselar apresentando áreas de degeneração cística, bem delimitada, medindo 2,7 × 2,4 × 2,2 cm, rechaçando superiormente o quiasma óptico e com insinuação para seio cavernoso direito, mantendo contato com a porção intracavernosa da artéria carótida interna direita, sem redução de seu calibre (Figura 1).

Em 25/11/2022, a paciente foi submetida à ressecção endoscópica por via transesfenoidal, abordagem endonasal, abertura do seio esfenoidal, drilagem do assoalho da sela com abertura do endosteum, seguido de enucleação intacavitária tumoral, com preservação do diafragma selar sem visualização de sangramentos anormais. No 8º dia pós-operatório, apresentou cefaleia holocraniana de forte intensidade, associada a náuseas, vômitos, fotofobia e sinais de irritação meníngea, sem apresentar

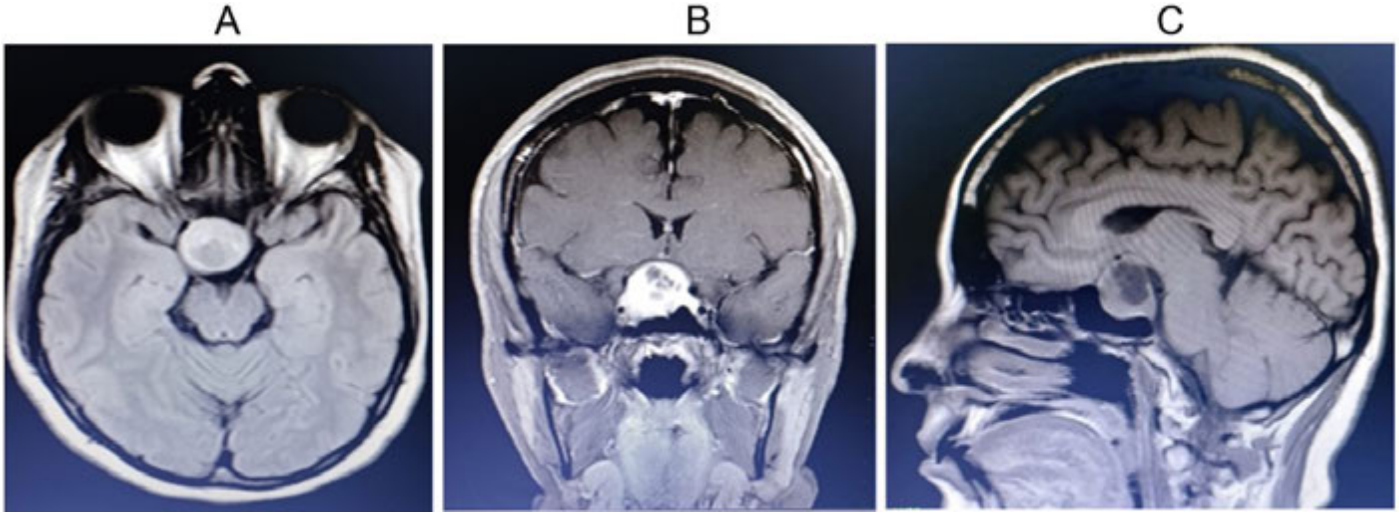

Figura 1. Ressonância magnética de encéfalo. **A**. Sequência T1 sem contraste corte axial. **B**. Sequência T1 com contraste corte coronal. **C**. Sequência T1 sem contraste corte sagital. Acervo da Radiologia, Hospital Getúlio Vargas (HGV).

déficits neurológicos focais (Hunt-Hess II). TC de crânio mostrou hemorragia subaracnoidea aguda ocupando apenas as cisternas interpenduncular e pré-pontina (Figura 2).

Realizada angiorressonância arterial cerebral que não mostrou aneurismas ou outras malformações arteriovenosas, porém com sinais sugestivos de vasoespasmo na artéria basilar (Figura 3).

Considerando os exames clínicos e radiológicos pós-operatórios, a paciente foi conduzida de forma conservadora com repouso no leito, analgésicos, antieméticos e nimodipina oral. Evoluiu sem sequelas neurológicas, recebendo alta hospitalar no 14º dia do pós-operatório.

DISCUSSÃO

A hemorragia subaracnoidea espontânea (HSAE) é uma forma de acidente vascular encefálico hemorrágico que acomete, em sua maioria, indivíduos jovens e está associada a altas taxas de morbimortalidade[1]. Afastada a hipótese de traumatismo, na grande maioria dos casos, a HSAE está frequentemente relacionada a aneurismas intracranianos rotos (70-80%) e malformações arteriovenosas (4%), os quais podem ser identificados na angiografia cerebral[6]. Entretanto, em cerca de 15% dos pacientes, a angiografia inicial é normal e a origem do sangramento é desconhecida[7,8].

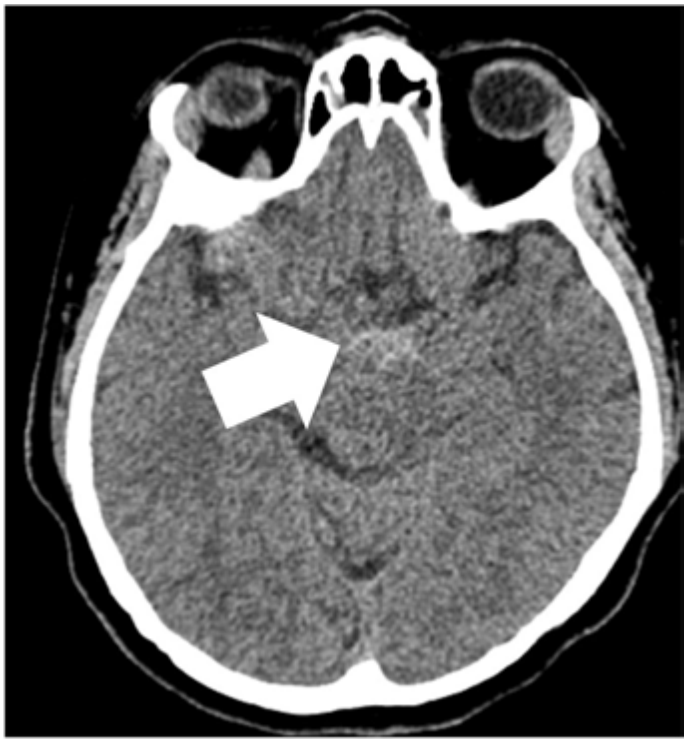

Figura 2. Tomografia computadorizada de encéfalo. Seta branca mostrando o sangramento agudo (seta cor branca). Acervo da Radiologia, Hospital Getúlio Vargas (HGV).

A hemorragia subaracnoidea perimesencefálica (HSAPM) é um tipo relativamente raro de sangramento subaracnoideo, caracterizado pelo acúmulo de sangue anteriormente ao mesencéfalo, próximo à cisterna interpeduncular, ou à ponte, com ou sem extensão ao redor do tronco encefálico, cisterna suprasselar ou fissuras silvyanas proximais[3-5,9-11]. A cisterna interpenducular é uma região anatomicamente específica que abriga várias estruturas importantes, incluindo a artéria cerebral posterior, a artéria cerebelar superior e o nervo oculomotor (III NC)[3]. Esse padrão de sangramento foi descrito pela primeira vez por Van et al., em 1985[12].

Com uma incidência de 0,3-0,5 casos por 100.000 pessoas, a HSAPM é responsável por aproximadamente 5 a 10% das hemorragias subaracnoideas e mais de 30% de todos os casos de HSA não aneurismáticas[4,9].

A etiologia da HSAPM ainda não foi completamente elucidada[13]. Distúrbios no fluxo sanguíneo cerebral profundo parecem ser fator causal válido para HSAPM, pois existe um sistema venoso complexo envolvendo o mesencéfalo, incluindo veias cerebrais internas, a veia basal de Rosenthal e os seios durais[14]. O aumento da pressão na circulação venosa intracerebral, bem como anomalias na mesma, incluindo o seio reto, a veia jugular ou a veia de Galeno, podem estar associados à HSAPM[15-17].

O quadro clínico da HSAPM normalmente apresenta sintomas menos intensos em comparação com uma hemorragia subaracnoidea aneurismática convencional. Os sintomas mais frequentemente mencionados incluem cefaleia de início abrupto, sensibilidade meníngea (presença de rigidez de nuca), sinais de Kernig e Brudzinski, fotofobia, além de náuseas e vômitos[1]. Şahin et al. demonstraram que a vasta maioria dos pacientes que receberam o diagnóstico de NAPMSAH (especificamente 93%), foi categorizada como pertencente aos Graus I ou II na escala de Hunt-Hess, enquanto que apenas cerca de 7% dos pacientes se

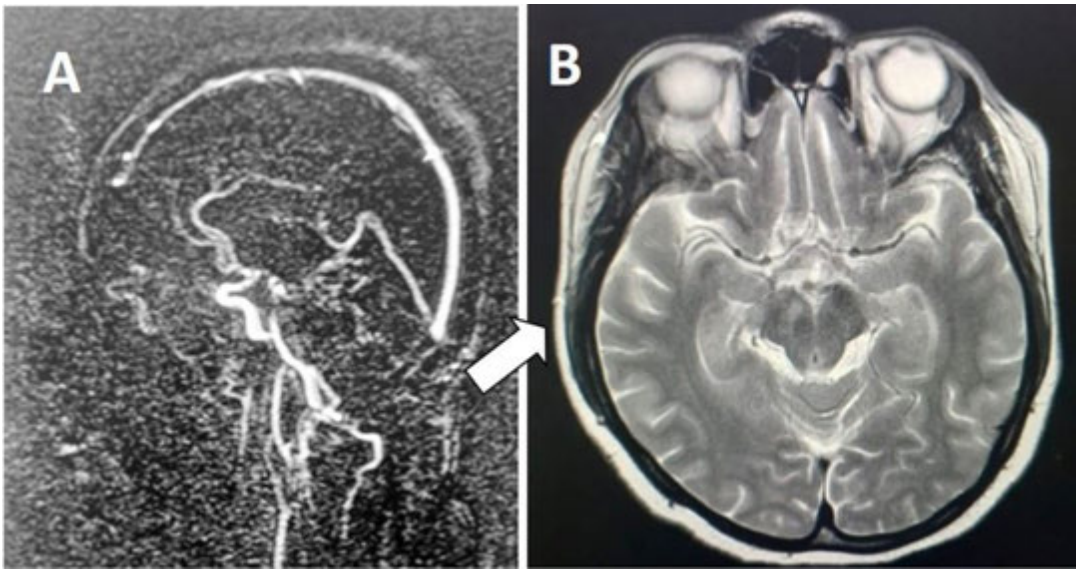

Figura 3. Angiorressonância cerebral fase arterial, corte sagital (A), corte axial (B), sem malformações arteriovenosas, porém com sinais sugestivos de vasoespasmo na artéria basilar. Acervo da Radiologia, Hospital Getúlio Vargas (HGV).

enquadrou nos Graus III ou acima, ressaltando a menor gravidade associada a essa forma de hemorragia[18].

Quanto ao diagnóstico por imagem, a angiografia por subtração digital (ASD), a despeito de ser um exame invasivo, segue sendo método gold standard para exclusão de aneurismas intracranianos, o que é fundamental para o diagnóstico de HSAPM, uma vez que o diagnóstico dessa doença é classicamente de exclusão[19,20].

Ainda que a ASD seja reconhecida como o método de maior precisão disponível para descartar origens aneurismáticas, a utilização da angiotomografia de alta resolução tem sido aceita devido à sua utilidade como uma ferramenta de investigação específica, visto que proporciona tanto um estudo das artérias intracranianas quanto das veias profundas, apresentando alta sensibilidade e especificidade para confirmar ou descartar aneurismas intracranianos, além de ser não invasivo[5,21,22].

A ressonância magnética de controle no pós- operatório da paciente do presente relato de caso mostrou hipersinal T2/FLAIR, restrição a difusão e realce predominantemente periférico após gadolíneo, localizado no tálamo e pedúnculo cerebral direitos, achados relacionados a alteração isquêmica subaguda. A angiorressonância de vasos intracranianos na fase arterial mostrou redução do calibre da artéria basilar no seu terço médio em cerca de 50% de sua espessura, sugerindo vasoespasmo.

A vascularização do tálamo é realizada através de quatro fontes arteriais, a saber: a) artérias perfurantes póstero-mediais, ramos ascendentes da artéria cerebral posterior; b) artérias tálamo-perfurantes, ramos das artérias comunicantes posteriores direita e esquerda; c) artérias tálamo-geniculadas, ramos ascendentes da artéria cerebral posterior, responsáveis pela vascularização dos núcleos ou corpos geniculados lateral e medial; e d) artérias coroideas posteriores, ramos da artéria cerebral posterior, que se dirigem ao tálamo, glândula pineal e plexo coroide do III ventrículo. Os ramos das artérias cerebral posterior e comunicante posterior irrigam não apenas o tálamo, mas também estruturas diencefálicas, cápsula interna, núcleos septais e núcleos da base[23].

Apesar do vasoespasmo provocado pela HSA aneurismática ser uma complicação bem documentada, no contexto da HSAPM, esse evento é raro, com poucos relatos presentes na literatura[24]. O padrão de vasoespasmo na HSAPM é tipicamente confinado à circulação posterior[25], tendo como principais fatores de risco idade mais jovem, sexo feminino e escores de Hunt-Hess mais altos e menor risco em pacientes tratados com estatinas ($p < 0,05$)[26]. O tempo médio de início do vasoespasmo cerebral na HSAPM ocorre no 4º dia do sangramento subaracnoideo, com cessação média no 15º após a hemorragia[26].

A gravidade do vasoespasmo pode ser quantificada pelo grau de estreitamento vascular à angiografia: leve, se comprometimento

> 33% do lúmen arterial; moderado entre 33 e 66%; e grave, se superior a 66% do diâmetro do vaso acometido[27].

O Doppler transcraniano é um método não invasivo que também desempenha um importante papel na avaliação do envolvimento de vasos cerebrais maiores[28]. Esse exame leva em consideração a velocidade do fluxo, a qual é inversamente proporcional à área da secção transversal do lúmen do vaso[29]. A velocidade média do sangue é medida constantemente, pois pode ser considerada significativa caso o valor médio exceda 120 cm/s ou haja um aumento do valor basal de mais de 50 cm/s[28].

Correlacionando o achado de imagem com a irrigação do polígono de Willis, observa-se que o vasoespasmo, comprometendo o território da artéria basilar, provocou redução do fluxo sanguíneo regional em torno dos ramos distais deste vaso, ou seja, as artérias cerebrais posteriores, em especial à direita. A despeito dessa alteração, a paciente evoluiu sem déficits focais específicos.

As demais complicações possíveis, a saber, hiponatremia e crises convulsivas são bem menos frequentes no contexto da HSAPM em comparação às hemorragias não-perimesencefálicas[30,31]. Hidrocefalia e convulsões associam-se diretamente ao padrão de sangramento e à quantidade do volume hemorrágico, avaliada pela escala tomográfica de Fisher[32,33].

Kim et al. realizaram uma análise retrospectiva que incluiu 51 casos de hemorragia subaracnoidea perimesencefálica, sem relação com aneurismas. Utilizando a escala de Rankin modificada (mRS) para avaliação de desfecho funcional de médio a longo prazo na HSAPM, 80,3% dos pacientes demonstraram melhora notável em até 6 meses após o diagnóstico. Além desse aspecto, a pesquisa identificou diversos fatores relacionados a um prognóstico mais favorável, tais como um baixo escore inicial no mRS, ausência de hidrocefalia precoce e hemorragia não classificada como tipo 3 ou superior pelo sistema de classificação de Fisher[34].

Diversas pesquisas apontam que até 97% dos pacientes com HSAPM apresentam recuperação clínica favorável e retorno rápido às atividades após a alta hospitalar[35]. Todavia, devido à proximidade do mesencéfalo em relação a estruturas cruciais da substância branca, tais como as vias de ligação tálamo-límbicas, quaisquer danos potenciais a essas partes da substância branca têm a possibilidade de resultar em prejuízos cognitivos e declínio na capacidade de memória[36]. Godefroy et al. utilizaram a Escala de Estado Mental Modificada para evidenciar que há mínimo ou nenhum déficit cognitivo observado durante o acompanhamento a longo prazo para esses pacientes[37].

Na maioria dos casos, o tratamento da HSAPM é conservador, consistindo em monitoramento do equilíbrio eletrolítico, hidrocefalia, vasoespasmo e convulsão, conforme apropriado, na unidade de terapia intensiva, diante do prognóstico benigno dessa condição, com os pacientes permanecendo na unidade por 2 a 4 dias até que a cefaleia melhore e/ou a hidrocefalia aguda seja resolvida[29,38]. O uso de shunt intraventricular pode ser necessário no manejo da hidrocefalia aguda sintomática; nos casos de vasoespasmo sintomático, é possível a adoção de medidas clínicas visando aumento permissivo da pressão arterial média e vasodilatação vascular cerebral seletiva para melhorar a perfusão do parênquima[39].

CONCLUSÃO

A HSAPM não aneurismática é uma condição relativamente rara, com etiologia não completamente elucidada, que acontece em uma região nobre cerebral, com curso clínico benigno, em sua grande maioria excelente prognóstico, menor incidência de complicações e podem normalmente exigir unicamente tratamento conservador, como no caso descrito.

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Spinal Cord Stimulation for Postherpetic Neuralgia and Parkinson's Disease: literature review

Estimulação da Medula Espinhal para Neuralgia Pós-Herpética e Doença de Parkinson: revisão da literatura

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ABSTRACT

Background: *Spinal Cord Stimulation (SCS) has long been studied for the treatment of chronic neuropathic pain. Nevertheless, studies have associated SCS with improvement of axial manifestations of Parkinson's Disease (PD), which are often refractory to conservative treatment and Deep Brain Stimulation (DBS). We report a case of clinical improvement of PD's freezing of gait (FoG) after spinal cord stimulation.* **Case presentation:** *Male patient, 82-year-old with a 10-year history of PD under a pharmacological treatment that provided resolution of tremor, but was unable to improve gait disturbance. The patient presented with severe refractory postherpetic neuralgia. A cervical epidural lead for SCS was implanted, resulting not only in improvement of neuropathic pain but also in parkinson's posture and FoG. with an increase in gait speed.* **Discussion:** *SCS is a promising therapeutic alternative in the management of axial manifestations of PD refractory to pharmacological therapy. SCS has been thoroughly studied in the management of chronic pain, but this report and other published studies suggest that the spinal cord could also be an interesting target in the treatment of PD.* **Conclusion***: In this report, SCS was responsible for improvement of gait and posture in a patient with refractory PD with postherpetic neuralgia.*

Keywords: *Parkinson's disease; Spinal cord stimulation; Postherpetic neuralgia; Neuromodulation*

RESUMO

Introdução*: A estimulação da medula espinhal (EME) tem sido estudada há muito tempo para tratamento da dor neuropática crônica. Estudos também têm associado a EME à melhora das manifestações axiais da Doença de Parkinson (DP), muitas vezes refratárias ao tratamento conservador e à Estimulação Cerebral Profunda. Relatamos um caso de melhora clínica do congelamento da marcha (FoG) da DP após estimulação medular.* **Relato do caso:** *Paciente do sexo masculino de 82 anos com história de 10 anos de DP sob tratamento farmacológico que proporcionou resolução do tremor, mas não do distúrbio da marcha. O paciente apresentou neuralgia pós-herpética refratária grave. Foi implantado um eletrodo epidural cervical para EME, resultando não apenas na melhora da dor neuropática, mas também na postura em DPe FoG, com o aumento da velocidade da marcha.* **Discussão:** *A EME é uma alternativa promissora no manejo das manifestações axiais da DP refratária à terapia farmacológica. A EME tem sido amplamente estudada no manejo da dor crônica, mas este relato e outros estudos publicados sugerem que a medula espinhal também pode ser um alvo interessante no tratamento da DP. Neste relato, o EME foi responsável pela melhora da marcha e postura em DP refratária com neuralgia pós-herpética.*

Palavras-Chave: *Doença de Parkinson; Estimulação da medula espinhal; Neuralgia pós-herpética; Neuromodulação*

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INTRODUCTION

Postherpetic neuralgia (PHN) is classified in the ICD-11 as a chronic peripheral neuropathic pain that persists for three months or more after acute Herpes-Zoster (HZ) cure and develops in 9% to 14% of cases. It is estimated that there are around 1 million cases in the United States. The disease is more common in white, immunocompromised and elderly people. The involvement generally follows one or two dermatomes and predominates at the thoracic, cervical and ophthalmic trigeminal levels[1-3]. Due to the refractoriness of conservative therapy, injections, percutaneous and peripheral nerve stimulation, radiofrequency, dorsal ganglion neuroablation and Spinal Cord Stimulation (SCS) are possibilities for interventional treatment[4].

Parkinson's Disease (PD) is among the most common degenerative diseases of the central nervous system. The prevalence of PD increases with age, reaching its peak incidence between 70-79 years[5]. Its pathophysiology involves the degeneration of nigrostriatal dopaminergic neurons in the compact portion of the midbrain and impairs the movement regulation exerted by the basal ganglia[6]. The main symptoms are bradykinesia, plastic hypertonia and resting tremor. Secondary motor symptoms also occur, such as freezing of gait (FoG) and, finally, non-motor symptoms, such as cognitive deficits[7]. The best evaluated and established surgical treatment is Deep Brain Stimulation (DBS) of the internal globus pallidus or the subthalamic nucleus of Luys. SCS has been studied as a therapeutic alternative for motor and gait dysfunction in patients with PD, especially gait freezing, with promising results. There are still several questions to be clarified about this type of treatment[8].

This is the case of a patient with PD who presented with improvement of gait and posture after SCS. We also review the literature for case reports, case series and clinical trials reporting the effect of SCS on PD symptoms.

CASE PRESENTATION

We present the case of an 82-year-old man with a 10-year history of PD. The patient had a history of coronary artery disease, had undergone drug-eluting stent for 2 years, was taking Acetylsalicylic Acid (ASA) and presented a narrowing of the L4/L5 lumbar canal, and no dementia.

The patient was under pharmacological treatment for PD with high-dose dopamine agonist (Levodopa) and an anticholinergic agent (Amantadine). While the tremor was well controlled, he still presented with persistent stiffness, bradykinesia, flexed posture and gait disturbance.

The patient developed burning pain in the right flank, intensity 8/10 on the Numeric Pain Rating Scale (NPRS), in the path between the fourth and twelfth ribs, characteristic of the previous vesicular phase of Herpes-Zoster. He started treatment with Acyclovir, but did not observe any pain relief. After pain management therapy with the use of analgesics, pregabalin, multiple infiltrations, dorsal ganglion rhizotomy and physiotherapy for PD for a period of 6 months, pain intensity decreased to 6/10 on the NPRS scale.

Due to the presence of refractory neuropathic pain, he underwent Spinal Cord Stimulation (SCS), with implantation of an epidural cervical lead over C4 to C8 levels. The Precision Artisan™ Spinal Stimulation Electrode Kit, 16 contacts (Boston Scientific, Valencia, CA, USA) and a Precision Montage MRI rechargeable pulse generator were used. During hospitalization, the following initial settings were reached: amplitude (i) of 1.6 mA, frequency (f) of 180 Hz and pulse width (pw) of 250 ms. After one month, the settings were readjusted to i = 0.9 mA, pw = 200 ms and f = 180 Hz.

Significant improvement in pain was achieved and a considerable increase in gait speed was observed. He also presented a progressive reversal of flexed posture. Even with lower dosages of PD drugs, the improvement of gait and posture was maintained.

DISCUSSION

PHN is a painful manifestation of Varicella Zoster virus reactivation. After the initial infection, the virus may remain quiescent in the sensory ganglia of the spinal nerves, where it can initiate a process of demyelination, wallerian degeneration and

deafferentation. Such aggression manifests as neuropathic pain, characterized by burning, stabbing pain, electric or dysesthetic shock. The pain can be continuous or intermittent and is located, in most cases, in one or two dermatomes, especially in the thoracic or lumbar levels[2,4].

In this report, a patient with PD underwent SCS for the treatment of postherpetic neuralgia pain and observed improvement of posture and gait. SCS has been demonstrated to act on suprasegmental circuits through stimulation of ascending fibers that project to the brainstem, cerebellum, basal ganglia, thalamus, and cortical areas, which could explain the improvement of SCS in PD patients. SCS can also interrupt the inhibition of the internal globus pallidus over the thalamus and the supplementary motor area (SMA), influencing the neuronal firing in this region, which is a key center for the control of the onset of gait[8-10].

Furthermore, SCS affects two postural control mechanisms differently – the reactive and the anticipatory. The cortical circuits that depend on cortical participation are more sensitive to SCS, given the increase in cortical input to the striatum, reaching the structures involved in the planning of movement, necessary during the anticipatory postural control, but not the reactive. Anticipatory Postural Adjustment (APA) mechanisms depend on thalamus-cortico-striatal loops, highly influenced by changes in attention and the environment. As part of the circuit that controls the APA, the SMA has cortical projections to the pedunculopontine nuclei (PPN), a region particularly involved in gait initiation. Since the activity of the SMA, globus pallidus and PPN are impaired in patients with FoG, SCS could be able to modulate this circuit and improve APA and gait initiation. On the other hand, the reactive mechanism of postural control to unpredictable external triggers depends on neuronal circuits involving the brainstem and spinal cord with less participation of the cerebral cortex[8-10].

Although DBS can be an effective treatment of PD, it presents limitations regarding the improvement of axial manifestations (posture and gait). Therefore, SCS could be another promising approach in patients with refractory axial symptoms of PD[8].

Some authors have used SCS as an alternative therapeutic option to manage motor and non-motor symptoms of PD (Table 1)[10-23]. Although there are few and heterogeneous studies, they present promising data that indicate SCS as an effective and safe treatment. In our literature review, we identified 14 studies, comprising a total of 76 patients with PD treated with SCS. Only one study reported a postoperative complication caused by SCS, which was lead migration, a common occurrence in epidural lead neurostimulation[10].

SCS is an effective therapeutic option in the treatment of pain refractory to conservative therapies. It has been available for more than 50 years and has robust evidence supporting its efficacy and safety in the management of pain[24,25]. An important component of PD, that directly affects the quality of life, is pain. Pain is one of the most common non-motor symptoms of PD and is divided by the King's Parkinson's Disease Pain Scale in the following domains: musculoskeletal pain, radicular pain, chronic pain, fluctuation-related pain, nocturnal pain, orofacial pain, and pain with discolouration/oedema/swelling[26,27]. SCS in PD has been associated with a consistent improvement of pain, including significant reduction on the visual analogue scale of pain in patients with advanced PD and pain refractory to conservative treatment and deep brain stimulation[11,13,14,16-19,21-23].

In this case report, the patient underwent SCS for the treatment of postherpetic neuralgia. Besides the improvement in pain intensity, the patient also experienced an important improvement in motor symptoms of PD, including posture and gait. These results are consistent with other published studies, which have also associated SCS in PD with improvement in abnormal posture and improvement of gait[16,17,21]. In a study with five patients with PD experiencing gait disturbance and FoG, SCS was able to improve step length, stride velocity, sit-to-stand test and FoG[12].

In our literature review, only one study did not identify an improvement in motor symptoms of PD. It was, nevertheless, a case series of two patients with a follow-up of 10 days and, hence, no definite conclusion can be drawn from these findings[20].

Some authors have successfully used SCS as salvage therapy in patients who failed DBS[10,12,15,17,18]. In these patients, SCS is a particularly interesting therapy that could enhance the quality of life and improve refractory motor and non-motor symptoms.

Table 1. Literature review of spinal cord stimulation in Parkinson's Disease.

Author	Study design	Numberof Patients	Symptoms treated and assessed	Outcome	Complications	Follow-up	Previous DBS/ Location	Spinal level of stimulation	Frequency	Pulse width (µs)	Pulse amplitude
Lima-Pardini et al.[10]	Clinical trial	4	FoG	Significant improvement of FoG and anticipatory postural adjustment. SCS failed to improve reactive postural responses.	None	N/A	Yes/STN	T2-T4	300 Hz	90	N/A
Lai et al.[11]	Case Report	1	Gait disturbance and pain	Improvement to gait and pain. Quality of life improvement (40% improvement in PDQ-8). VAS decreased from 7 to 3. KPPS decreased from 12 to 4.	Dislocation of percutaneous lead. After reoperation, symptoms improved.	2 months	Yes/STN	T8-T10	60 Hz	270-390	3.6-4.0 V
Samotus et al.[12]	Clinical trial	5	Gait disturbance and FoG	Improvement of mean UPDRS (33.5%), step length (38.8%), stride velocity (42.3%), sit-to-stand (50.3%) and of FoG.	None	6 months	N/A	T8-T10	30-130 Hz	200-500	N/A
Furusawa et al.[13]	Case series	5	Intractable lower back pain and gait disturbance	Improvement of affective pain and severity of motor symptoms.	None	6 months	No	T8-T9	Burst stimulation inter-burst rate = 40 Hz/intra-burst rate = 500 Hz	1000	N/A

DBS: Deep Brain Stimulation; FoG: Freezing of Gait; KPPS: King's Parkinson's Disease Pain Scale; MDS: Movement Disorders Society; N/A: Not Available; NPRS: Numeric Pain Rating Scale; PDQ-8: Parkinson's Disease Questionnaire; SCS: Spinal Cord Stimulation; STN: Subthalamic Nucleus; TUG: Timed Up and Go; UPDRS: Unified Parkinson's Disease Rating Scale; VAS: Visual Analogue Scale.

Table 1. Continued...

Author	Study design	Numberof Patients	Symptoms treated and assessed	Outcome	Complications	Follow-up	Previous DBS/ Location	Spinal level of stimulation	Frequency	Pulse width (µs)	Pulse amplitude
Mazzone et al.[14]	Prospective case series	18	Pain and motor symptoms	Improvement in pain and motor symptoms. Patients who underwent burst stimulation presented with a more acute response to treatment	None	12 months	Yes (1 patient)/ DBS	High cervical	Tonic stimulation group: 130-185 Hz; Burst stimulation group: inter-burst rate = 40 Hz/intra-burst rate = 500 Hz	Tonic stimulation group: 60-210; Burst stimulation group: 1000	Tonic stimulation group: 1.3-3.6 V; Burst stimulation group: 0.2-0.9 mA
Pinto de Souza et al.[15]	Clinical trial	4	Postural instability and gait disturbance	50 to 65% improvement in gait measurements and 35 to 45% in UPDRS III	None	6 months	Yes/STN	T2-T4	300 Hz	90	N/A
Agari et al.[16]	Prospective case series	15	Abnormal posture, gait disturbance and pain	Mean VAS decreased from 8.9 to 2.3. There was no significant improvement of total UPDRS motor score, but among motor subscores, there was significant improvement of gait. Improvement of posture	None	12 months	Yes (7 patients)/ N/A	T7-T12	5-20 Hz	210-330	0-4 V
Akiyama et al.[17]	Case report	1	Painful camptocormia with Pisa syndrome	Improvement of pain and posture. UPDRS improved from 48 to 34 points and TUG test improved from 15 s to 7 s	None	6 months	Yes/STN	T8-L3	7 Hz	250-450	2.5-3.5 V

DBS: Deep Brain Stimulation; FoG: Freezing of Gait; KPPS: King's Parkinson's Disease Pain Scale; MDS: Movement Disorders Society; N/A: Not Available; NPRS: Numeric Pain Rating Scale; PDQ-8: Parkinson's Disease Questionnaire; SCS: Spinal Cord Stimulation; STN: Subthalamic Nucleus; TUG: Timed Up and Go; UPDRS: Unified Parkinson's Disease Rating Scale; VAS: Visual Analogue Scale.

Table 1. Continued...

Author	Study design	Numberof Patients	Symptoms treated and assessed	Outcome	Complications	Follow-up	Previous DBS/ Location	Spinal level of stimulation	Frequency	Pulse width (µs)	Pulse amplitude
Chakravarthy et al.[18]	Prospective case series	15	Pain and motor symptoms	59% reduction in VAS. 73% of patients presented with improvement in the 10-meter walk test and 64% experienced improvement in the TUG test	None	4-33 months (mean: 22)	Yes (8 patients)/ STN	C2-T12	Burst stimulation: inter-burst rate = 40 Hz/ intra-burst rate = 500 Hz; Tonic stimulation: 10-40 Hz	1000	0.15-4.5 mA
Nishioka and Nakajima[19]	Case series	3	Intractable chronic pain, motor symptoms	There was significant improvement in VAS score and UPDRS III	None	12 months	No	T8-L1	5-65 Hz	60-450	0.45-5.8 V
Thevathasan et al.[20]	Case series	2	Motor impairment	There was no improvement in UPDRS motor score	None	10 days	No	High cervical	130-300 Hz	200-240	2-4 V
Hassan et al.[21]	Case Report	1	Resting tremors, bradykinesia and shuffling gait. Abdominal tremors and neuropathic pain.	VAS decreased from 8 or 9 to 0 or 1. Relief from motor symptons and gait in UPDRS and 10-meter walk test. The tremors largely disappeared. Rigidity decreased. Shuffling gait and posture at baseline improved. Masked facies improved	None	24 months	No	C2	40 Hz	500	0.3-1.1 mA

DBS: Deep Brain Stimulation; FoG: Freezing of Gait; KPPS: King's Parkinson's Disease Pain Scale; MDS: Movement Disorders Society; N/A: Not Available; NPRS: Numeric Pain Rating Scale; PDQ-8: Parkinson's Disease Questionnaire; SCS: Spinal Cord Stimulation; STN: Subthalamic Nucleus; TUG: Timed Up and Go; UPDRS: Unified Parkinson's Disease Rating Scale; VAS: Visual Analogue Scale.

Table 1. Continued...

Author	Study design	Numberof Patients	Symptoms treated and assessed	Outcome	Complications	Follow-up	Previous DBS/ Location	Spinal level of stimulation	Frequency	Pulse width (µs)	Pulse amplitude
Landi et al.[22]	Case Report	1	Pain, dysesthesia, and paresthesia. Motor impairment	VAS decreasead 70%. Improvemente in gait, postural stability, bladder control, incontinence and dysesthesias. Subjective evaluation of quality of life (EQ-VAS) improved 60%. UPDRS unchanged.	None	16 months	Yes/STN	T9-T10	30Hz	250	1.8-2.5 V
Fénelon et al.[23]	Case Report	1	Lower limb neuropathic pain, motor symptoms	Motor score and UPDRS were reduced by 50%. Amplitude reduction of tremor. Pain relief. Rigidity and bradykinesia improved	None	24 months	No	T9-T10	70-130 Hz	410	3.5 V

DBS: Deep Brain Stimulation; FoG: Freezing of Gait; KPPS: King's Parkinson's Disease Pain Scale; MDS: Movement Disorders Society; N/A: Not Available; NPRS: Numeric Pain Rating Scale; PDQ-8: Parkinson's Disease Questionnaire; SCS: Spinal Cord Stimulation; STN: Subthalamic Nucleus; TUG: Timed Up and Go; UPDRS: Unified Parkinson's Disease Rating Scale; VAS: Visual Analogue Scale.

CONCLUSION

In this case report, spinal cord stimulation was able to provide improvement of gait and posture in a patient with PD. Other studies have also published results that support the spinal cord as a potential neurostimulation target for the management of refractory PD.

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Pituitary Carcinoma with Cerebral Spinal Fluid Dissemination Presenting with Spinal Cord Compression

Carcinoma de Hipófise com Disseminação Liquórica Apresentando-se com Compressão Medular

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ABSTRACT

Pituitary carcinoma is a rare tumor of the anterior pituitary, and by definition occurs in the presence of distant metastasis. Treatment involves surgical resection, radiotherapy and adjuvant chemotherapy. The authors report the case of a patient with pituitary carcinoma that evolved with spinal cord compression.

Keywords: *Pituitary neoplasms; Pituitary tumors; Pituitary adenoma; Spinal cord compression*

RESUMO

O carcinoma de hipófise é um tumor raro da hipófise anterior e, por definição, ocorre na presença de metástase à distância. O tratamento envolve a ressecção cirúrgica, radioterapia e quimioterapia adjuvante. Os autores relatam o caso de um paciente com carcinoma de hipófise que evoluiu com compressão medular.

Palavras-chave: *Neoplasias de hipófise; Tumores de hipófise; Adenoma hipofisário; Compressão da medula espinhal*

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INTRODUCTION

Despite the relatively high prevalence of pituitary tumors, only a minority evolute to carcinoma. Pituitary carcinomas originate from the anterior pituitary, and by definition occur in the presence of metastases, which may be systemic or in the central nervous system. The vast majority are hormone producers, especially ACTH, prolactin and GH[1]. The authors report in the present work the case of a patient with pituitary carcinoma that evolved with spinal cord compression after leptomeningeal dissemination of the disease.

CASE PRESENTATION

A 54-year-old female patient, with no known previous pathologies, presented progressive visual deterioration and ptosis of the right eye with 4 months of evolution, which subsequently evolved with low bilateral visual acuity. She investigated the condition with magnetic resonance imaging (MRI), which showed an expansive lesion with an intra and suprasellar component, suggestive of a pituitary macroadenoma (Figure 1). She underwent surgery for resection via the transphenoidal route, with partial removal of the tumor, which was complemented with a transcranial route during the same hospital stay. She presented partial improvement of vision after the procedure.

The anatomopathological and immunohistochemical results showed pituitary carcinoma without hormone suppression as the final diagnosis, and the patient was then referred for complementary treatment with radiotherapy, since it was not possible to perform a complete resection of the tumor due to invasion of parasellar structures. Systemic screening for metastasis at the time was negative.

Outpatient follow-up with the neurosurgical team continued for another 2 years, with sella MRI demonstrating an excellent response to radiotherapy and stability of the condition during the follow-up period (Figure 2).

In the third year of follow-up, the patient was hospitalized again due to subacute paraparesis and urinary retention. On admission, she already had paraplegia with a week of evolution. Spine MRI identified two intradural and extramedullary expansive lesions at the level of T10-T11 and L2-L3, causing medullary and radicular compression(Figure 3). New systemic screening with computed tomography (CT) scans of the chest and abdomen was negative for other metastatic lesions.

Given the time course of the neurological symptoms and the lack of new benefits from surgical therapy, the patient was referred to the oncology team, where she underwent a new radiotherapy cycle, supplemented with temozolamide.

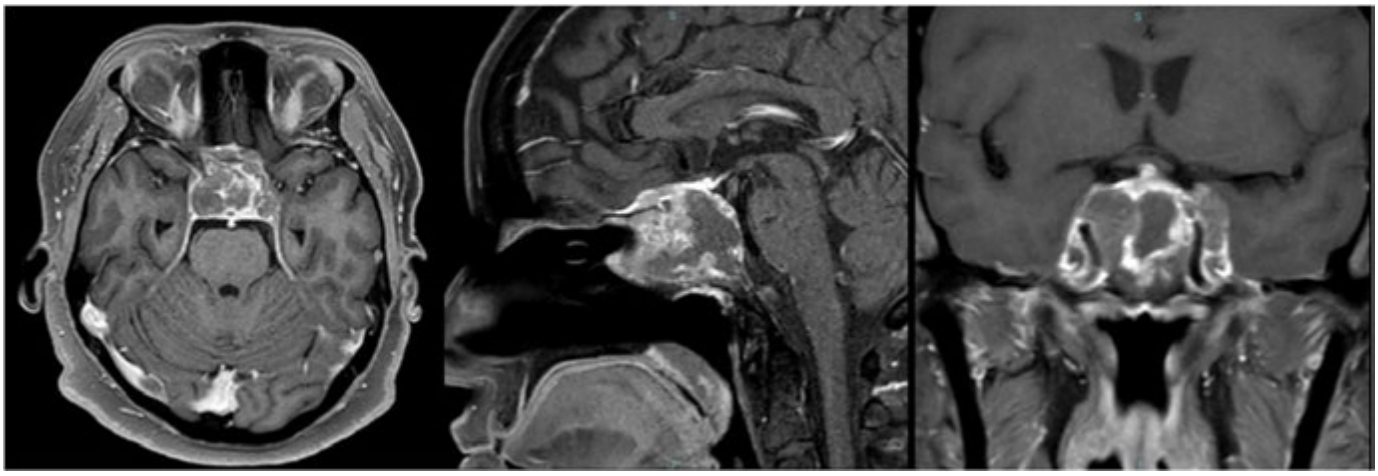

Figure 1. Expansive lesion with solid aspect and necrotic component, intra and suprasellar, which extends to the middle fossa and involves the cavernous segments of the internal carotid arteries and presents homogeneous enhancement after the use of gadolinium.

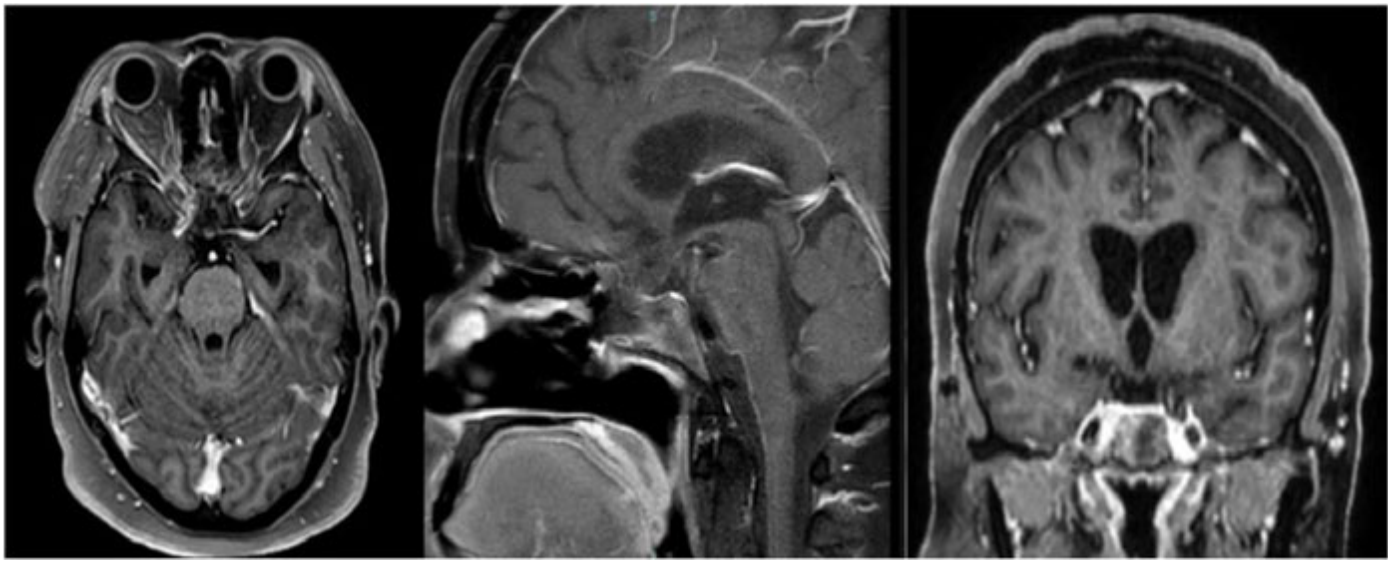

Figure 2. Post-surgical alterations related to the right frontotemporal craniotomy, as well as the heterogeneous enhancement in the surgical bed in the sellar / suprasellar / parasellar region, which remain with similar characteristics, with no significant alterations in the extension and relationship with adjacent structures.

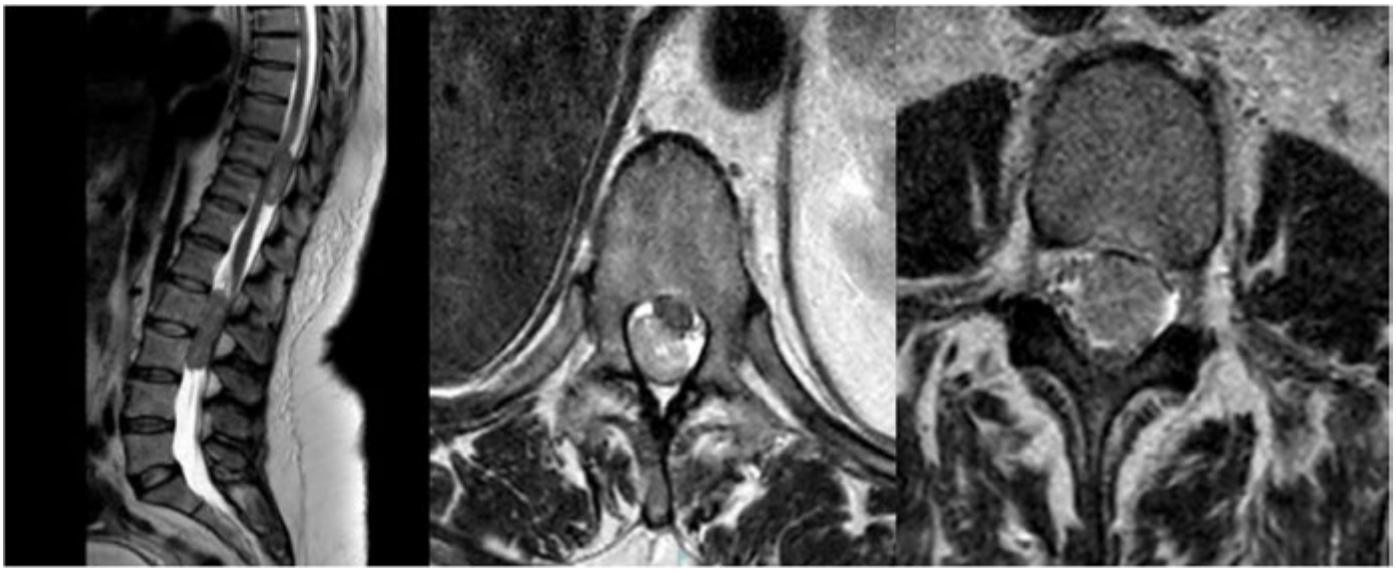

Figure 3. Intradural and extramedullary expansive lesions are identified at the level of T10-T11 and L2-L3, the first one is located posteriorly to the spinal cord, causing compression on its right posterolateral face and anterior deviation of the same, with apparent hypersignal intramedullary T2 at this level. The other, more caudal, is located anteriorly to the roots of the cauda equina.

DISCUSSION

Pituitary tumors are neoplasms that originate from the adenohypophysis, represented mostly by adenomas. Despite having the potential to invade bone, meningeal and neural structures adjacent to the sella, it is considered a benign disease.

Unlike pituitary adenomas, pituitary carcinoma is defined as a malignant neoplasm of the adenohypophysis, being mandatory

for the presence of systemic dissemination of the disease or dissemination in the central nervous system for its characterization. It is a rare disease, representing 0.5% of pituitary tumors and 0.2% of sellar tumors, with its peak prevalence in the fourth and fifth decade of life, being an even rarer disease in the pediatric population[2,3].

In addition to the presence of metastases, other criteria are necessary to characterize a pituitary carcinoma, such as histology and markers compatible with pituitary tumors and the absence of another primary tumor, since other systemic neoplasms can affect the sellar area[4]. Such criteria are necessary since it is impossible to distinguish adenoma from carcinoma based only on histological criteria, since hypercellularity, nuclear pleomorphism and necrosis may also be present in ACTH and GH producing adenomas.

The symptoms of pituitary carcinoma are identical to other tumors of the sellar region, and occur due to direct compression of brain structures or hormonal changes, such as visual loss, diplopia, hypopituitarism, diabetes insipidus or hormone hypersecretion syndromes, since the vast majority of carcinomas are hormonally active, and most commonly produce ACTH, prolactin and GH[4,5].

Interestingly, systemic metastases are more common than dissemination in the central nervous system, with the liver, bones and lungs being the most common metastatic sites, and they occur due to hematogenous and lymphatic dissemination of the tumor[5]. In the central nervous system, dissemination occurs via CSF, and affects mainly the brain, cerebellum and region of the cerebellopontine angle. In the case presented above, the patient had only intraspinal metastases, with no evidence of systemic disease or disease elsewhere in the nervous system.

In four cases of pituitary carcinoma described by Alshaikh et al.[2], three of them presented dissemination to the spine, but with no description of intraspinal involvement[2]. In the case described by Guzel et al.[5], the patient had intramedullary lesions, in addition to concomitant intracranial involvement[5]. Despite the possibility of CSF dissemination in this type of tumor, neuraxial examination is not routinely performed, being guided by the clinical symptoms of the patient[6]. Intraspinal metastatic spread of pituitary carcinoma represents an exceptionally rare disease, with few cases reported so far, and there is usually a long interval between the diagnosis of the primary tumor and the clinical presentation of the intraspinal metastasis[7,8].

Treatment of pituitary carcinoma involves surgical resection, radiotherapy and adjuvant chemotherapy. Radiotherapy has been shown to be effective in the local control of the disease, without showing any benefit in terms of increased survival, and is also used in the management of bone and visceral metastases for temporary control and pain management[4,6].

Several different chemotherapy schemes have been used as adjuvant therapy, with good response, however with short and temporary duration. Based on currently available data from ACTH and prolactin-secreting carcinomas, temozolamide has been shown to be an effective therapy[6,9,10].

Despite advances in treatment, it remains an extremely aggressive disease, with average survival of 12 months after diagnosis. The obstacles to the advancement of studies on the subject are due to the rarity of the disease, making it difficult to carry out large-scale studies[6].

CONCLUSION

Pituitary carcinoma is a rare and aggressive neoplasm. To be considered a pituitary carcinoma, it is mandatory that there is dissemination of the disease, either systemic or in the central nervous system. The treatment for this disease is multidisciplinary and involves surgical resection of the tumor, complemented with radiotherapy and adjuvant chemotherapy. Currently, it is difficult to distinguish which pituitary neoplasms can evolve into carcinoma, when based only on their histological characteristics.

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Benign Metastasizing Leiomyoma with Multiple Metastasis of Lungs and Bones

Leiomioma Benigno Metastático con Múltiples Metástasis en Pulmones y Huesos

Marcel Sincari[1]
Francisco José Oliveira Cabrita[2]
Francisco Manuel Calheiros Nogueira Martins[3]

ABSTRACT

Background: *benign metastasizing leiomyomas (BML) represents a rare disease consisting of the extra-uterine metastasizing of smooth muscle cells with similar histological, immunological, and molecular patterns to those of benign uterine leiomyomas. They are characterized by low mitotic activity, lack of anaplasia or necrosis and bad vascularization. BML is a rarely found entity with few documented cases in the literature, usually occurring in women of reproductive age with a history of myomectomy or hysterectomy. The leiomyomas can metastasize to several organs, the lungs being the most commonly affected.* **Case presentation:** *we present a case of a 40 year old infertile woman, with BML with multiple metastasis (lungs and bony: lumbar spine, pelvis, knee, and humerus), firstly she presented low back complaints, refractory to medical treatment, and was submitted to percutaneous L3-L5 fixation and transpedicular biopsy. Later on she was submitted to hysterectomy and bilateral ovariectomy with 7 years follow up. Good resolution of pain after surgery, 5 years after surgery she had SARS-Cov2 pneumonia, associated with coinfection with Aspergillus niger and Cryptococcus laurenti with 37 days of hospitalization, including 13 days in Intensive Care Unit (ICU) with good evolution.*

Keywords: *Leiomyoma; Benign; Hysterectomy*

RESUMEN

Introducción: *la BML representa una enfermedad rara (trastorno) que consiste en la diseminación extrauterina de las células del músculo liso. Estas lesiones exhiben patrones histológicos, inmunológicos y moleculares similares a los observados en los leiomiomas uterinos benignos. Las BML se caracterizan por una baja actividad mitótica, ausencia de anaplasia o necrosis y vascularización inadecuada. A pesar de su rareza, las BML se han documentado en un número limitado de casos, afectando principalmente a mujeres en edad reproductiva con antecedentes de miomectomía o histerectomía. Entre los órganos susceptibles de metástasis, los pulmones son el sitio más comúnmente afectado.* **Reporte de caso:** *presentamos el caso de una mujer infértil de 40 años diagnosticada de LMB con múltiples metástasis en ambos pulmones y en varias localizaciones óseas, entre ellas columna lumbar, pelvis, rodilla y húmero. Inicialmente la paciente presentaba dolencias lumbares refractarias al tratamiento médico. La biopsia transpedicular se obtuvo durante la fijación percutánea de L3-L5, seguida de histerectomía y oforectomía bilateral. La paciente ha estado en seguimiento durante 7 años. La paciente experimentó una reducción significativa del dolor después de la cirugía y no se observaron metástasis adicionales. Sin embargo, cinco años después de la cirugía, desarrolló neumonía por SARS-Cov2, asociada a coinfección por Aspergillus niger y Cryptococcus laurenti, que requirió 37 días de hospitalización, incluidos 13 días en Unidad de Cuidados Intensivos (UCI). Alentadoramente, la paciente demostró una evolución favorable durante este período difícil.*

Palabras-Clave: *Leiomioma; Benigno; Histerectomía*

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INTRODUCTION

BML is an infrequent condition that consists of metastatic dissemination of uterine leiomyomas to distant sites while maintaining benign pathologic characteristics. BML primarily affects menopausal or postmenopausal women who have previously undergone hysterectomy for leiomyomas, often several years after initial surgery[1-5]. While spinal involvement is uncommon[1], the occurrence of multiple leiomyomas in BML patients is exceedingly rare[6]. BML is a rare cause of extra pelvic metastasis, predominantly to the lungs, often associated with prior gynecological instrumentation[7]. According to some authors, BML presents itself in extra-uterine sites, namely lungs (79.5%), lymph nodes, abdominal and pelvic cavity, nervous system, and bone[8]. Although it is relatively uncommon, BML accounts for approximately 4.4% of all benign soft tissue tumors[9].

CASE PRESENTATION

A 40 years old woman, married, no children, previously healthy, presented with severe lumbar pain, unresponsive to analgesics. No localizing neurological deficit was detected. Radiological investigations, including X-Ray, CT scan and MRI of lumbar spine, revealed tumoral infiltration of L4 vertebral body with canal stenosis (Figure 1). Further examinations detected tumours on additional sites, namely on the knee (Figure 2A), pelvis and uterus (Figure 2B), lung (Figure 2C), and humerus (Figure 2D).

The patient underwent percutaneous fixation after transpedicular biopsy, accompanied by an attempted of anterior and posterior cementation procedure, which was aborted due to leakage (Figure 3). Under the same anesthesia, a biopsy of the pelvic tumoral mass of the pelvis was also performed. Histopathological examination confirmed metastasizing benign leiomyoma. Hysterectomy and bilateral oophorectomy followed after 2-month recovery.

The patient has been closely monitored for 7 years and has displayed excellent overall outcome. Adequate pain control has been achieved, requiring only occasional analgesics. The remaining tumoral mass have remained stable throughout the follow-up period.

Additionally, the patient overcame a challenging infection 5 years after surgery, when she developed SARS-Cov2 pneumonia, complicated by coinfection with Aspergillus niger and Cryptococcus laurenti. At this juncture, she required a 37-day of hospitalization, including 13 days in the IUC, and exhibited favorable evolution.

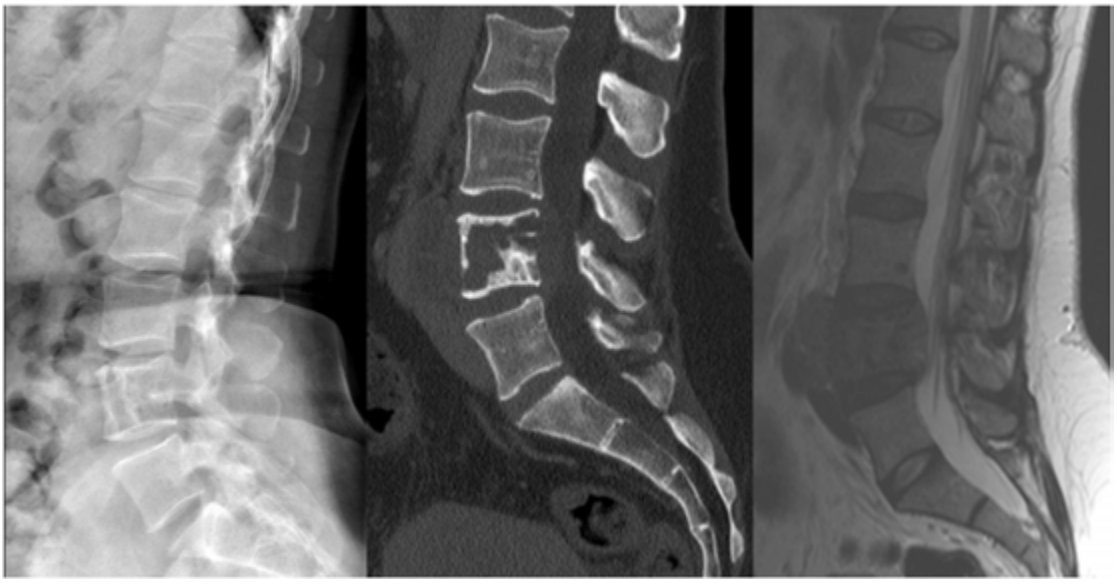

Figure 1. X-Ray, CT scan and MRI revealing mass involving L4 vertebra.

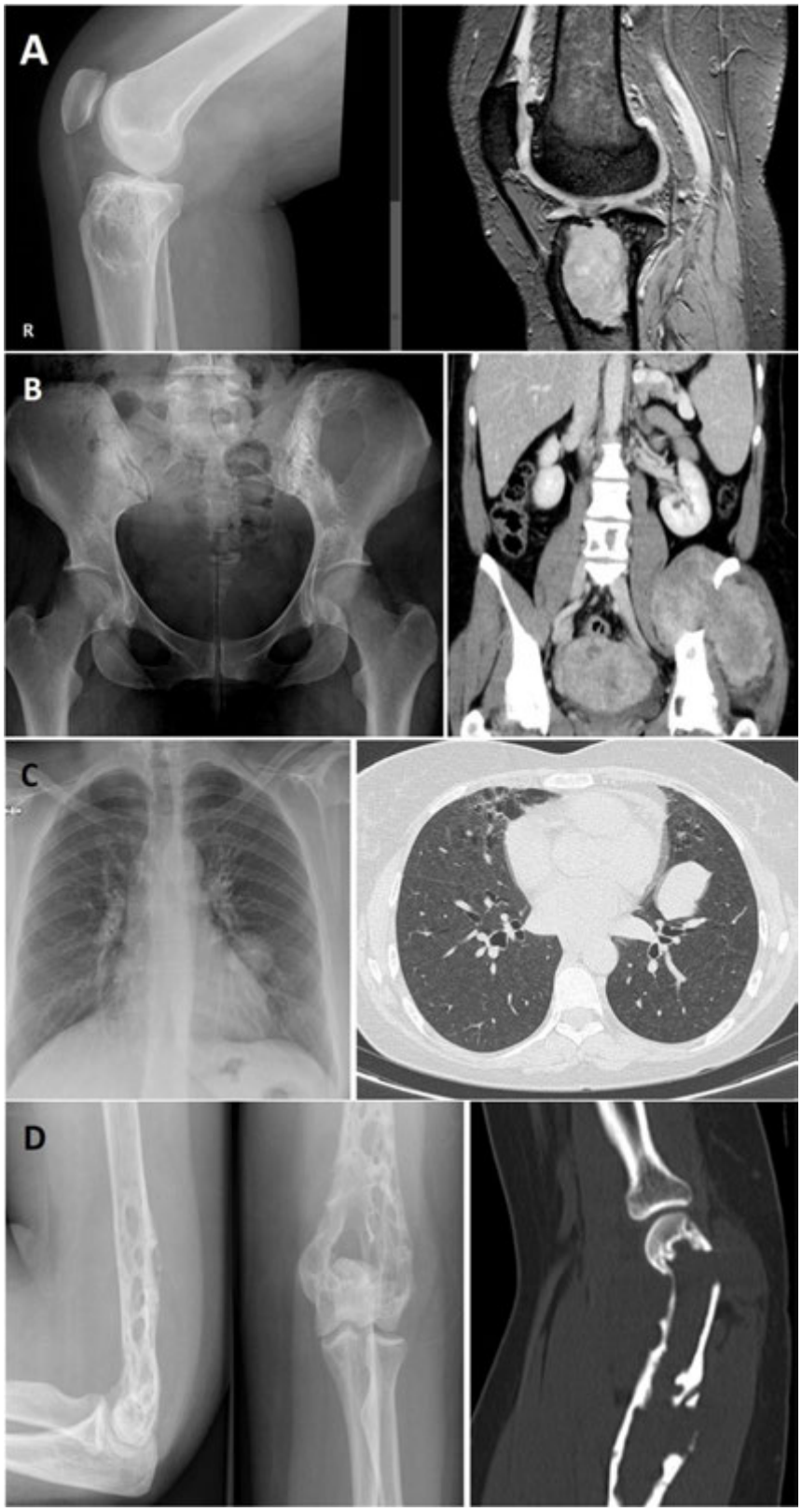

Figure 2. A. Left, X-ray; Right, MRI: tumor involving tibia. **B.** Left, X-ray - tumor of left iliac crest; Right, CT scan: tumor of iliac crest and uterus. **C.** Left pumonary nodule. **D.** Humerus tumor.

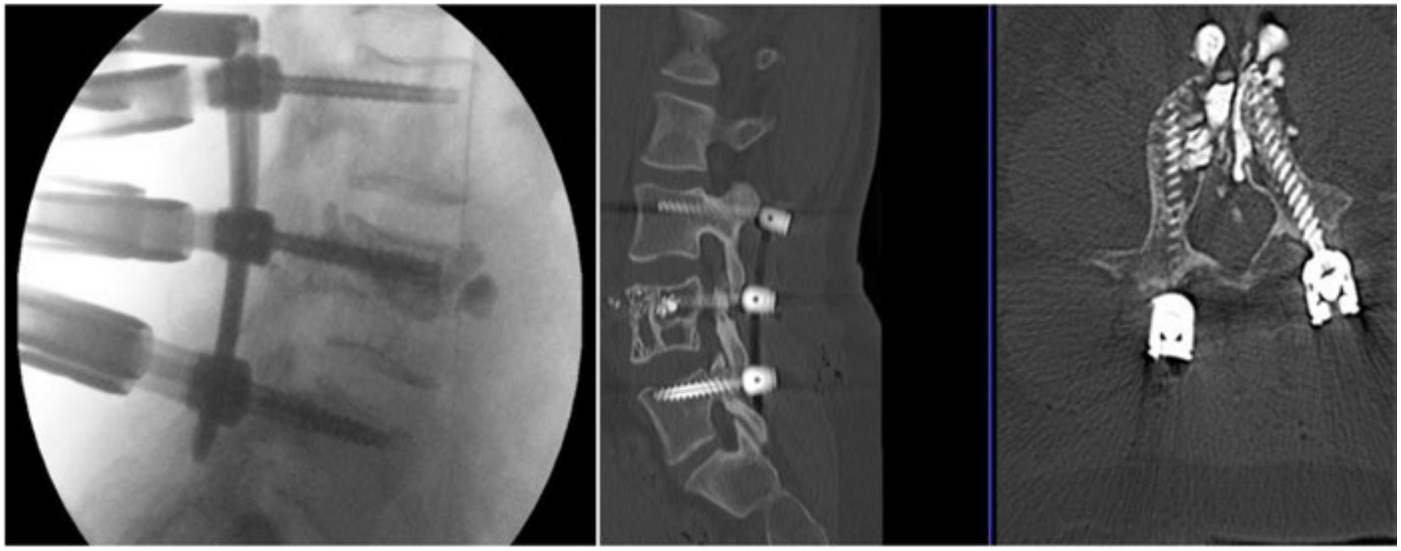

Figure 3. Percutaneous fixation after transpedicular biopsy and attempt of cementation with cement anterior and posterior leak.

CONCLUSION

Our case report highlights the diagnostic and therapeutic intricacies and challenges associated with BML, which is an exceptionally rare condition. Despite some literature suggesting an indolent nature[10], our patient debuting symptom was severe lumbar pain, refractory to analgesic treatment. Unlike the majority of reported cases, which involve patients who have undergone hysterectomy and partial oophorectomy, our case was presented with symptomatic spine metastasis. Successfully management, required lumbar spine fixation, followed by hysterectomy and oophorectomy, radiotherapy and long-term hormonal therapy.

The diagnosis of BML relies on meticulous medical history evaluation, (appropriate radiology) along with histopathologic and immunohistochemical analysis of metastatic lesions or primary tumor. To date, no standard treatment approach has been established. The clinical course of BML varies depending on the number and sites of metastases, emphasizing the need for an individualized (tailored) approach. Furthermore, our case underscores the importance of multidisciplinary collaboration and long-term follow-up in effectively managing BML patients.

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An Uncommon Case of Orbital Myofibroma in Adult: case report

Um Caso Incomum de Miofibroma de Órbita em Adulto: relato de caso

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Rafael Reis do Espírito Santos[2]
Tiago Miranda Dias[3]

ABSTRACT

Introduction: *Myofibroma was initially described by Williams Schrum in 1951 as Congenital Fibrosarcoma. This is an uncommon benign tumor of mesenchymal cells exhibiting myofibroblastic differentiation that occurs mainly in the first decade of life.* **Case Presentation:** *A 44-year-old male patient presented to the neurosurgery clinics with a history of diplopia and bulging of his left eyeball, his visual acuity was normal, and no other abnormalities were found on ophthalmological examination. The Magnetic Resonance Imaging of the head was performed with intravenous contrast. It showed a well-defined lesion measuring 3.3 × 2.4 cm in T2-weighted sequence in the left orbital and intracranial region involving the left eyeball and extending to the ethmoid sinus, frontal bone, medial rectus muscle and optic nerve. Subsequently, the patient underwent a left fronto-orbital craniotomy for tumor resection. The microscopy and immunohistochemistry study are most consistent with the diagnosis of an orbital myofibroma/myopericytoma.* **Discussion and Conclusion:** *We reported a rare occurrence of adult myofibroma in the orbital region. The patient had excellent postoperative recovery and is under ambulatory follow-up.*

Keywords: *Myofibroma; Myofibromatosis; Eye; Neoplasms; Adult*

RESUMO

Introdução: *O miofibroma foi descrito inicialmente por Williams Schrum em 1951 como fibrossarcoma congênito. É um tumor benigno incomum de células mesenquimais exibindo diferenciação miofibroblástica que ocorre principalmente na primeira década de vida.* **Relato do caso***: Paciente do sexo masculino, 44 anos, apresentado ao ambulatório de neurocirurgia com histórico de diplopia e abaulamento do globo ocular esquerdo, acuidade visual normal e nenhuma outra anormalidade foi encontrada no exame oftalmológico. A ressonância magnética da cabeça foi realizada com contraste intravenoso, apresentando lesão bem definida medindo 3,3 × 2,4 cm em sequência ponderada em T2 na região orbitária esquerda e intracraniana envolvendo o globo ocular esquerdo e estendendo-se até o seio etmoidal, osso frontal, músculo reto medial e nervo óptico. Posteriormente, o paciente foi submetido à craniotomia fronto-orbitária esquerda para ressecção tumoral. Foi realizada uma orbitotomia da borda orbitária superior esquerda para a excisão tumoral. O estudo de microscopia e imuno-histoquímica é mais consistente com o diagnóstico de miofibroma/miopericitoma orbital.* **Discussão e Conclusão***: Relatamos uma ocorrência rara de miofibroma adulto na região orbital. O paciente apresentou excelente recuperação pós-operatória e está em acompanhamento ambulatorial.*

Palavras-chave: *Miofibroma; Miofibromatose; Olho; Neoplasia; Adulto*

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INTRODUCTION

Myofibroma was initially described by Williams Schrum in 1951 as Congenital Fibrosarcoma[1]. This is an uncommon benign tumor of mesenchymal cells exhibiting myofibroblastic differentiation that occurs mainly in the first decade of life. It can be classified as solitary, multicentric or generalized. However, myofibroma in adulthood is usually solitary and superficial[2,3]. Though the most common site of occurrence is the head and neck region, myofibroma of the orbit is a very rare site of involvement and its solitary occurrence in adult patients is even more rare[4]. In our report we presented an adult patient who had a solitary myofibroma with cranial and orbital involvement. The presentation of this disorder as shown here has few cases described in the literature.

CASE PRESENTATION

A 44-year-old male patient presented to the neurosurgery clinics with a history of diplopia and bulging of his left eyeball (proptosis), his visual acuity was normal, and no other abnormalities were found on ophthalmological examination. There was no significant family or past medical history.

The Magnetic Resonance Imaging (MRI) of the head was performed with intravenous contrast. It showed a well-defined lesion measuring 3.3 × 2.4 cm in T2-weighted sequence in the left orbital and intracranial region involving the left eyeball and extending to the ethmoid sinus, frontal bone, medial rectus muscle and optic nerve (Figure 1).

Subsequently, the patient underwent a left fronto-orbital craniotomy for tumor resection. A left superior orbital rim orbitotomy for the tumor excision was performed. No significant postoperative complication was observed (Figure 2). Mild headache and enophthalmos were seen on postoperative follow-up.

On immunohistochemistry, the spindle cells were positive for smooth muscle Actin and Ki 67, however, it was negative for CD 34, Desmin, PGR 636, Cytokeratin 18, and E29.

Microscopy study showed a mesenchymal neoplasm with proliferation of spindle cells containing slightly irregular nuclei and ill-defined eosinophilic cytoplasm. There were areas of calcifications and fibroblastic star-shaped cells. There were no areas of necrosis and rarely mitotic activity was identified (Figures 3-6).

The microscopy and immunohistochemistry study are most consistent with the diagnosis of an orbital myofibroma/myopericytoma.

DISCUSSION

According to the World Health Organization (WHO) classification of tumors of soft tissue and bone, the myofibroma was classified

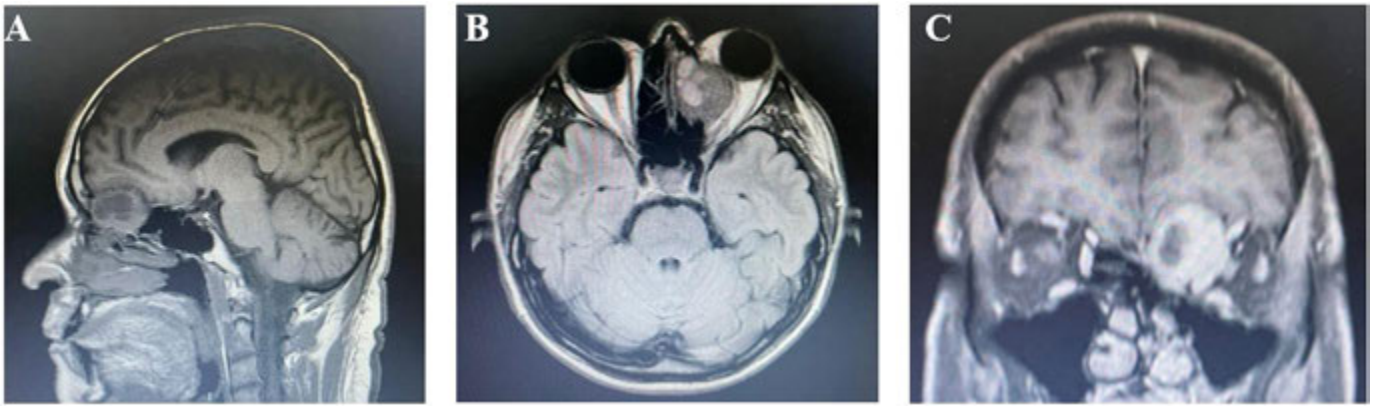

Figure 1. MRI. **A**. sagittal. **B**. axial. **C**. coronal planes showing a large contrast enhancing mass in the superior portion of the orbit associated with compression of adjacent structures.

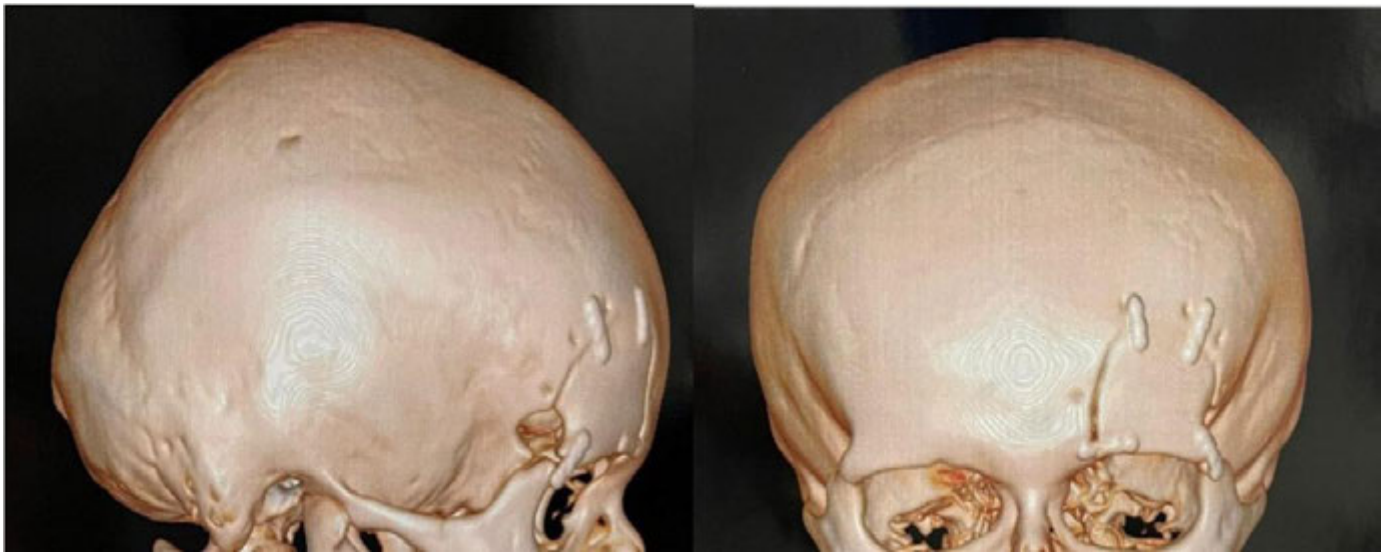

Figure 2. Postoperative CT-scan.

as a perivascular tumor[5]. Myofibroma of the ocular region (which includes the orbits and the eyelids) is very rare in the literature with majority of cases reported occurring in children[6,7]. There are few cases reported in the literature of orbital myofibroma in adults with comprehensive immunohistochemical and microscopy study.

Immunohistochemistry is extremely important in diagnosis of a myofibroma. It generally shows positivity for actin and vimentin, but desmin, EMA, S100 and CK, are usually negative.

Myofibroma can be localized or generalized self-limiting benign processes represented by cells with characteristics of myofibroblasts and sometimes pericytes[8,9]. Furthermore, myofibroma has other characteristics as plump spindled cells in a moderately cellular distribution dispersed amidst prominent intratumoral vascular channels. Although some mitoses can be seen, features of malignancy such as increased mitotic activity, atypical mitotic figures, necrosis, vascular invasion, or locally infiltrative growth are not identified. In some cases, it can be observed numerous mitoses as well as areas of necrosis[2]. The differential diagnosis of myofibroma include leiomyoma, neurofibroma, nodular fasciitis, hemangiopericytoma, and fibrosarcoma due to their histopathologic similarities[10,11].

Soft tissue lesions are difficult to distinguish from other mesenchymal tumors and the findings of radiologic imaging can differ depending on the location of the lesion. Nevertheless, MRI and CT-scans represent imaging modalities that has proven

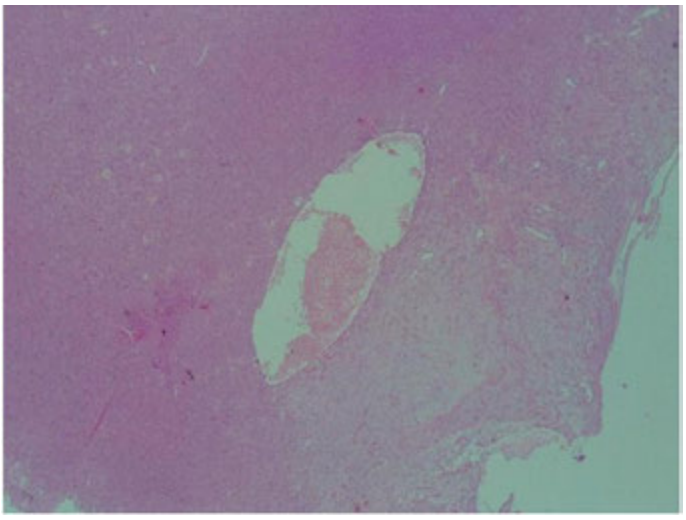

Figure 3. Classic zonation pattern showing a hypercellular area (left) and a myxoid, edematous, less cellular area (right). Vessels are prominent, sometimes dilated and often in a hemangiopericytomatous (staghorn) pattern (4x magnification).

useful in the diagnosis of myofibroma, because it typically shows non-homogeneous well-circumscribed masses, with moderate vascularity. Contrast-enhanced scans show variability in the enhancement pattern. On T1-weighted MRI, myofibromas appear as moderately low to low intensity images. On T2-weighted MRI, the lesions tend to appear as high intensity lesions. Ultrasonography, when performed, may yield a well-circumscribed lesion, which exhibits low internal reflectivity and

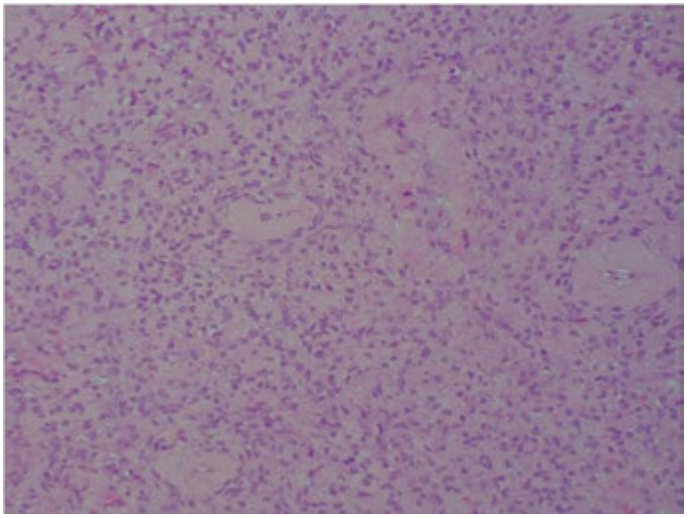

Figure 4. Myoid appearing ovoid to spindle cells showing bland nuclei and a frequent concentric growth around hyalinized small vessels, the so-called myopericytomatous pattern (10x magnification).

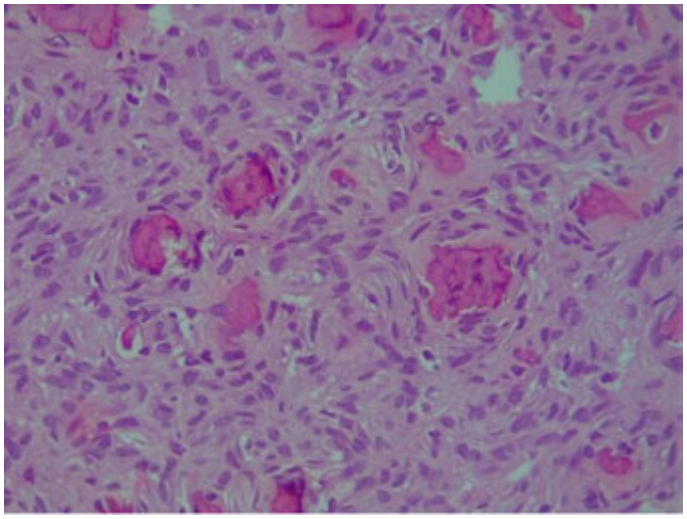

Figure 5. Cellular zones show foci of calcification (40x magnification).

a heterogeneous internal structure. Additionally, myofibromas with increased vascularity enhance with gadolinium[12]. Even with sophisticated imaging techniques, differential diagnosis can still be difficult hence histopathology is ultimately necessary to make a definitive diagnosis and to rule out a more aggressive neoplasm[13].

Albeit it's more common in infants and childhood, it is important to remember myofibroma occurrence when a spindle cell lesion

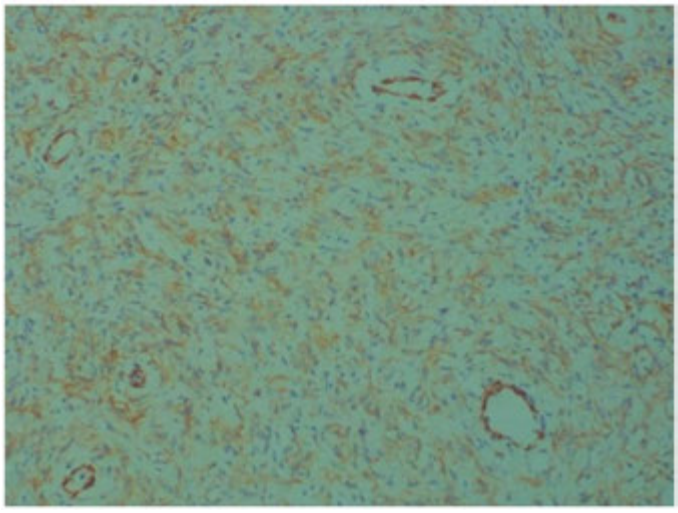

Figure 6. Tumor cells and vessels stains for Smooth Muscle Actin (AML) immunohistochemistry marker, which confirms its myoid/pericytic differentiation (10x magnification).

with a nodular, fascicular or whirling growth patterns and areas of hyalinization, which are admixed with blood vessels, is seen. Complete resection of the solitary orbital myofibroma is the preferred treatment modality[12,14]. The recurrence rates for myofibromas are quite low, ranging from 0% to 12.5%. Recurrences can be attributed to tumors with difficult surgical access or incomplete removal[15].

CONCLUSION

A rare occurrence of adult myofibroma in the orbital region was reported. Surgical excision was the treatment of choice, once its recurrence is known to be uncommon after complete resection. The patient had excellent postoperative recovery and is under ambulatory follow-up.

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Large Asymptomatic Arachnoid Cyst With Normal Neurological Examination

Grande Cisto Aracnoide Assintomático Com Exame Neurológico Normal

Aldo Jose Ferreira da Silva[1]
Bianca Ramalho dos Santos Silva[2]

ABSTRACT

Arachnoid Cyst (AC) is formed by the division of the arachnoid membrane that contains cerebrospinal fluid. Rarely, patients have neurological symptoms related to the cyst. The case presented is of a large asymptomatic AC. A male child presented large AC on magnetic resonance imaging of the skull, with mass effect on the right hemisphere and midline shift. The child was asymptomatic with normal neurological examination. The chosen treatment was conservative. The decision for surgical treatment is still a matter of debate. Even in the image described with a large AC, the type of treatment remains controversial.

Keywords: *Arachnoid cysts; Magnetic resonance imaging; Neurologic examination; Child*

RESUMO

O cisto aracnoide (CA) é formado pela divisão da membrana aracnoide contendo líquido cefalorraquidiano. Raramente, os pacientes apresentam sintomas neurológicos relacionados ao cisto. O caso apresentado é de um grande CA assintomático. Criança do sexo masculino apresentando na ressonância magnética do crânio grande CA, com efeito de massa no hemisfério direito e desvio da linha média. A criança encontrava-se assintomática com exame neurológico normal. A conduta foi conservadora. A decisão pelo tratamento cirúrgico ainda é motivo de debate. Mesmo na imagem descrita com um grande cisto aracnoide, continua sendo controverso o tipo de tratamento.

Palavras-Chave: *Cistos aracnoides; Ressonância magnética; Exame neurológico; Criança*

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CLINICAL IMAGES

A male child of healthy and non-consanguineous parents was delivered at term (40 weeks) with a weight of 4100 g, height of 49 cm, head circumference of 37 cm, and Apgar 9 and 10 at the first and fifth minutes, respectively, by vaginal delivery. At the age of 6 years, he fell off a playground equipment at school. He underwent computed tomography of the skull, which revealed no traumatic lesions, but a large arachnoid cyst (AC) was noted in the right middle cranial fossa. Until then, the patient presented with no changes in developmental milestones and no history of headache or epilepsy. His neurological examination was normal. Moreover, magnetic resonance imaging of the skull was performed, which revealed a large AC, with a clear mass effect on the right hemisphere, including a midline shift (Figure 1). Furthermore, for better investigation, a neuropsychological study was conducted, and the results indicated an above-average intelligence quotient, with no changes in cognitive, behavioral, or emotional functions. Subsequently, conservative treatment and follow-up with a specialist were decided.

The pathophysiology of ACs remains controversial. Most of these cysts are congenital, but they can also be secondary to trauma or infection. ACs are often incidental findings on imaging studies investigating head trauma, seizures, and developmental delay. Most of them located in the middle fossa and more commonly occurring in males[1,2].

ACs were classified by Galassi in 1982 according to their size, as follows: 1) type I: small ACs located anterior to the middle cranial fossa; 2) type II: ACs located along the Sylvian fissure and displacing the temporal lobe; 3) type III: large ACs occupying the

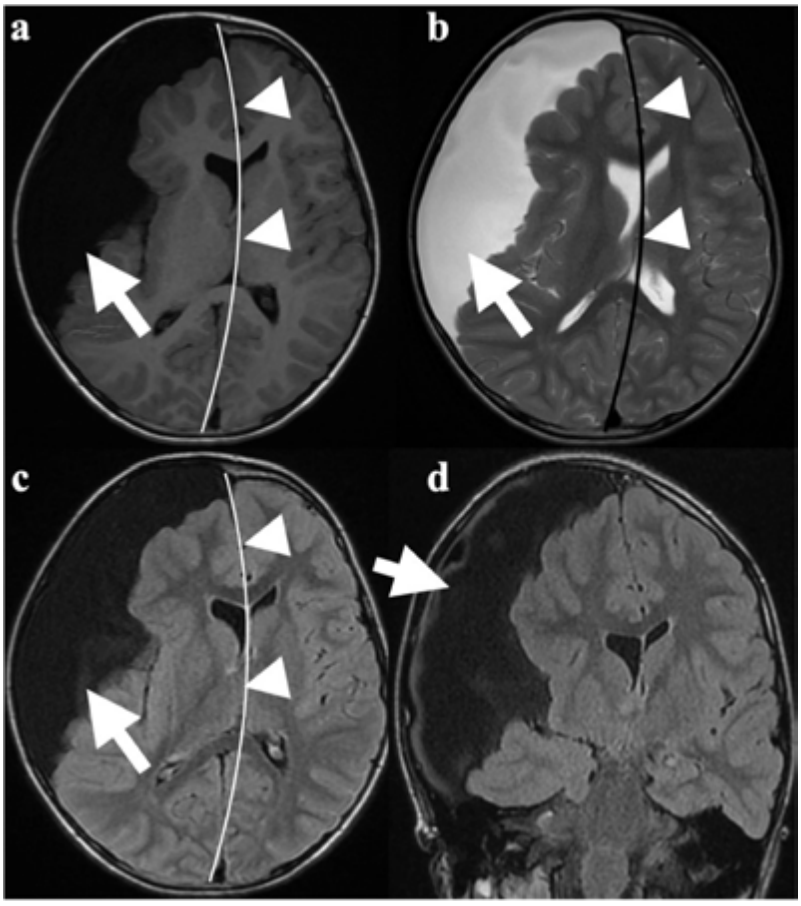

Figure 1. Magnetic Resonance Imaging (MRI): **A.** Axial T1. **B.** Axial T2. **C.** Axial FLAIR. **D.** Coronal FLAIR. Coronal fluid-attenuated inversion recovery (FLAIR) showing a large arachnoid cyst (white arrow) on the right, with displacement of the frontal, temporal, and parietal lobes, resulting in midline shift (white arrowhead).

entire middle cranial fossa and displacing the temporal, parietal, and frontal lobes. For Galassi type I ACs, the treatment is usually conservative, whereas for type II and III ACs, the ideal treatment is very controversial[2,3].

In such cases, surgery may be considered in patients with headache, seizures, developmental delay, and neurological deficits, especially hydrocephalus with signs of intracranial hypertension[1]. However, the correlation of these symptoms with the presence of the cyst (including Galassi type III cysts) is still questionable. Even in the investigation of epilepsy, electroencephalograms do not show a reliable correlation between seizures and the location of the cyst. In addition, a neuropsychological study can be performed to decide the treatment of cases of large cysts[2,4]. Therefore, as reported in this case, the treatment of large ACs of the Sylvian fissure remains a challenge, especially in asymptomatic cases.

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