Optic Pathway Cavernous Malformations: a systematic review of clinical course and treatment outcomes

Malformações Cavernosas da Via Ótica: revisão sistemática dos resultados do curso clínico e do tratamento

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ABSTRACT
Cavernous malformations (CM) of the optic pathway are extremely rare and often can be forgotten when thinking about a differential diagnosis of lesions affecting the visual function. The authors reviewed the literature of 34 reported cases to investigate the clinical course, image studies, surgical approaches and outcomes. The review was performed on PubMed and Embase databases searching for case reports between 2000 and 2021. The most prevalent symptom was visual disturbances (94.1%) followed by headache (44.1%), and two patients were asymptomatic. Magnetic resonance imaging (MRI) is the exam of choice for cavernous malformation diagnosis, showing mostly mixed intensity signals. Some other exams can be used for helping to find the diagnosis, like computed tomography. In the analyzed cases 85.2% reported surgical treatment, but just 44.8% were total resections. About the outcome 41.3% of the patients reported improvement of the visual field defects and two developed diabetes insipidus after surgery. CM is an important differential diagnosis and should be considered. MRI is the most important exam to achieve the diagnosis and the surgical treatment can improve the outcome.

Keywords: Optic pathway; Cavernous malformation; Cavernoma; Cavernous angioma

RESUMO
As malformações cavernosas da via óptica são extremamente raras e muitas vezes podem ser esquecidas quando se pensa no diagnóstico diferencial de lesões que afetam a função visual. Os autores revisaram a literatura de 34 casos relatados para investigar a evolução clínica, estudos de imagens, abordagens cirúrgicas e resultados. A revisão foi realizada nos bancos de dados PubMed e Embase para relatos de casos entre 2000 e 2021. Em todos os casos, os sintomas mais prevalentes foram: distúrbios visuais (94,1%), seguido de cefaleia (44,1%) e dois pacientes eram assintomáticos. A ressonância magnética (RMI) foi o exame de escolha para o diagnóstico da malformação cavernosa, mostrando principalmente sinais de intensidade mista. Alguns outros exames podem ser utilizados para auxiliar no diagnóstico, como a tomografia computadorizada. Nos casos analisados 85,2% relataram tratamento cirúrgico, mas apenas 44,8% foram ressecções totais. Sobre o desfecho, 41,3% dos pacientes relataram melhora dos defeitos do campo visual e dois desenvolveram diabetes insípido após a cirurgia. A malformação cavernosa é um diagnóstico diferencial importante e deve ser considerado. A RMI é o exame mais importante para se chegar ao diagnóstico e o tratamento cirúrgico pode melhorar o resultado.

Palavras-Chave: Via óptica; Malformação cavernosa; Cavernoma; Angioma cavernoso
INTRODUCTION

Cavernous malformations (CMs) are well-circumscribed low flow vascular lesions also known as cavernomas, cavernous angiomas, cavernous hemangiomas, or vascular hamartomas. Histologically they are composed of immature, thin, irregular, and dilated endothelial lined vessels, packed together appearing like a “bunch of grapes” without intervening neural parenchyma. The walls of cavernous vessels are very delicate without elastic fibers and eventually get distended, forming a benign tumor. They are angiographically occult due to their slow circulation and are commonly delimited by reactive fibrillary gliosis.

Out of all vascular malformations of the central nervous system (CNS), approximately 10-15% are cavernous angiomas. These lesions exist in both sporadic and familial forms, and they have a prevalence of 0.5% and incidence of 0.3-0.7%, affecting females slightly more than males. These lesions can be found anywhere in the nervous system, as in the cerebrum, cerebellum, or spinal cord, and the most common locations are the frontal and temporal lobes. In some extremely rare cases, they can affect cranial nerves, specifically, the optic pathway, which is composed of the optic nerve, chiasm, and optic tract. Optic pathway cavernomas represent less than 1% of CNS cavernous malformations.

The clinical presentation of CMs is determined by their location, bleeding status and growth. While hemorrhage can cause an acute development of symptoms, tumor growth results in a progressive onset of symptoms. When the bleeding is extensive, patients can present with subarachnoid hemorrhage, hematoma or stroke symptoms. The annual bleeding rate associated with CMs ranges from 0.7% to 3.1%, while the rebleeding rate ranges from 4.5% to 22.9%.

In general, seizures are the most common presentation of symptomatic CMs, but the manifestations of optochiasmatic CMs can vary, and many patients can be asymptomatic. In most cases, patients have suffered an acute or subacute onset of symptoms, typically manifesting optic nerve, chiasmal or junctional visual field defects, associated with retro-orbital or frontal headache. Conditions such as alcohol ingestion, pregnancy and labor can precipitate these symptoms. Although less frequent, progressive loss of vision, often accompanied or preceded by headaches, nausea and focal deficits may occur. Furthermore, neurological deficits such as vomiting, cranial nerve palsies, or mental deterioration are rarely observed. An important manifestation to be mentioned is the “chiasmal apoplexy”, known as a set of symptoms already mentioned, such as loss of vision and reduction of the visual field predominantly associated with retro-orbital or frontal headache.

The clinical presentation of cavernomas is unspecific, and the differential diagnosis includes aneurysms, pituitary apoplexy, infiltrative and inflammatory conditions, craniopharyngioma, and tumors in the optic chiasm. It is important not to initially dismiss them as a possible diagnosis and to become acquainted with the possible clinical presentations of cavernous angiomas and treatment options in order to identify this lesion early and provide the best possible care to patients. Therefore, the objectives of this systematic review are analyzing the clinical course and treatment outcomes related to cavernous malformations of the optic pathway.

MATERIALS AND METHODS

This systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA).

Search sources
The MedLine/PubMed and Embase databases were searched on June 4, 2021 using as keywords: “cavernoma”, “cavernous angioma”, “cerebral cavernous malformation”, “cavernous malformation”, “cavernous hemangioma”, “optic nerve”, “optic chiasm”, “optic pathway”, and “optic tract”. All articles published in English between 2000 and 2021 were included.

Exclusion criteria
As exclusion criteria the following items were considered: (1) articles that did not report clinic course and treatment outcomes, (2) systematic reviews, letters, comments, manuscripts, incomplete unpublished articles, research protocols, guidelines, animal experiments, and editorials, (3) articles that did not confirm the diagnosis with imaging studies, (4) patients that did not have a cavernous malformation on the optic pathway, and (5)
articles with insufficient data or those in which neuroprotective approaches were not observed.

**Data extraction**
The information of each study was obtained independently by the four authors. All studies were evaluated according to their title and abstract in agreement with inclusion and exclusion criteria. If these studies matched the eligibility criteria, the full text was selected. Disagreements were solved by consensus. All articles with full text analyzed are described in the “Results” section.

**RESULTS**

**Search flow**
The electronic search found 541 results for the keywords used. After removing 108 duplicates, 433 potentially eligible studies were identified. Of these, 405 studies did not fulfill the inclusion and exclusion criteria. Only 28 studies were included in qualitative synthesis (Figure 1).

**Clinical course**
Thirty-four cases of CMs involving the optical pathways were reported (Table 1). The average patient age was 39-year-old, consistent with the epidemiology of CMs. Headaches were present in 15 patients (44.1%), visual disturbances were common in 32 patients (94.1%), and two patients were asymptomatic. Among the 34 reported cases, four were not specific regarding visual disturbances. In the remaining 30 cases, 18 (60%) suffered visual field defects, 17 (56.6%) suffered loss of visual acuity, and six (20%) suffered blurred vision, being these the most common visual symptoms. In some cases, there were additional symptoms such as, left retro-orbital pain, and less frequently, confusion, headache and mild fever. In 16 (45.7%) cases the symptoms appeared suddenly, 14 (40%) appeared progressively, three (8.5%) were not specified, and in only two (5.7%) cases the patients were asymptomatic33,34.

![Figure 1. PRISMA 2009 Flow Diagram.](image-url)
Table 1. Main characteristics of the 34 case reports analyzed.

<table>
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<tr>
<th>Reference</th>
<th>Age (years) / Sex</th>
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<tbody>
<tr>
<td>Paladino et al.⁴</td>
<td>58/F</td>
<td>Headache, visual deficits</td>
<td>OC</td>
<td>Solid homogeneous enhancing suprasellar mass with greater projection to the right</td>
<td>Eyebrow keyhole; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Shaikh et al.¹⁵</td>
<td>42/M</td>
<td>Visual déficits</td>
<td>RON, OC</td>
<td>NR</td>
<td>Right pterional craniotomy; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Deshmukh et al.²⁵</td>
<td>28/F</td>
<td>Visual déficits</td>
<td>OC</td>
<td>Hyperintense lesion involving the optic chiasm, with suprachiasmatic and posterior extension</td>
<td>Orbitozygomatic; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Giastonburry et al.²⁶</td>
<td>29/F</td>
<td>Visual déficits, headache</td>
<td>RON</td>
<td>Enlargement and a hyperintensity on T2 of the prechiasmal RON and right half of the chiasm</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Kehagias²³</td>
<td>27/M</td>
<td>Headache, Visual déficits</td>
<td>RON, OC</td>
<td>Mass isointense on T2-weighted images and heterogeneous on T1-W images with minimal enhancement after intravenous contrast medium</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Ozer et al.¹⁵</td>
<td>15/M</td>
<td>Visual deficit</td>
<td>OC, LON</td>
<td>Suprasellar mass causing enlargement of the optic chiasm and left optic nerve</td>
<td>Left pterional craniotomy</td>
<td>Improved</td>
</tr>
<tr>
<td>Hempelmann et al.¹¹</td>
<td>38/M</td>
<td>Headache, visual deficit, confusion, lethargy and somnolence</td>
<td>LON, OC, optical tract</td>
<td>Partial cystic and hemorrhagic mass with slight peripheral enhancement in the suprasellar region and the dorsal part of the gyrus rectus, expanding into the right perimesencephalic cistern and the adjacent parts of the temporal lobe and displacing both carotid arteries and the anterior cerebral artery. Additional frontal haemorrhage beside a second minor bleeding in the same gyrus and several small hypointense lesions in both temporal lobes</td>
<td>Pterional; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Son et al.²⁷</td>
<td>39/F</td>
<td>Visual deficit, headache, nausea</td>
<td>OC</td>
<td>1.5 sized mass involving OC with intrachiasmatic and posterior extension. T1-W images showed a hyperintensity and T2 a markedly hypointense peripheral rim of hemosiderin</td>
<td>Pterional craniotomy; total resection</td>
<td>Stable</td>
</tr>
<tr>
<td>Newman et al.⁶</td>
<td>16/M</td>
<td>Visual deficit, headache</td>
<td>OC</td>
<td>Chiasmal apoplexy</td>
<td>Left frontotemporal craniotomy</td>
<td>Improved</td>
</tr>
<tr>
<td>Cerase et al.²⁸</td>
<td>30/M</td>
<td>Fluctuating visual loss</td>
<td>LON</td>
<td>Heterogeneous CMs in both T1 and T2 sequences, showing a crosslinked mixed signal nucleus (‘popcorn’) in the right frontal lobe. In the left temporal lobe hypointense to isointense MCs were found on T1 images, hypointense on T2 images and markedly hypointense on T2 images due to the predominance of hemosiderin</td>
<td>No surgery was mentioned</td>
<td>Worsened</td>
</tr>
<tr>
<td>Panczykowski et al.¹⁸</td>
<td>78/F</td>
<td>Visual deficit</td>
<td>LON</td>
<td>Enlarged lesion with heterogeneous enhancement</td>
<td>Orbitozygomatic; total resection</td>
<td>Stable</td>
</tr>
</tbody>
</table>

ON = optic nerve; OC = optic chiasm; NR = not reported; RON = right optic nerve; LON = Left optic nerve; T1-W = T1-weighted; T2-W = T2-weighted; 3D = three-dimensional; F = Female  M = Male; OP = optic pathway.
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<tr>
<td>Jo et al.29</td>
<td>31/F</td>
<td>Visual deficit</td>
<td>Both optic nerves</td>
<td>Fluid-fluid level well demarcated mass in the suprasellar subchiasmatic area displacing both optic nerves</td>
<td>Supraorbital; partial resection</td>
<td>Worsened</td>
</tr>
<tr>
<td>Murai et al.30</td>
<td>23/M</td>
<td>Visual deficit</td>
<td>OC</td>
<td>T1-W MRI with gadolinium revealed a partially enhanced lesion in contact with the OC</td>
<td>Right pterional</td>
<td>Stable</td>
</tr>
<tr>
<td>Ning et al.16</td>
<td>28/M</td>
<td>Visual deficit, headache</td>
<td>Right side of the OC</td>
<td>A 1.8 mm x 1.7 mm mass located in the right suprasellar cistern and the right side of the OC. The mass lesion had clear boundaries and no edema around the lesion T1- and T2-W images showed mixed signal intensity surrounded by a peripheral rim of low signal on the T2-weighted images</td>
<td>Right pterional craniotomy; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Ramina et al.31</td>
<td>19/M</td>
<td>Acute visual loss, headache</td>
<td>RON</td>
<td>T1-W MRI scan showed a mixed-intensity mass of the dorsal region near the OC, regularly and slightly enhanced after gadolinium. T2-weighted scan showed a high-intensity area with hypointensity surrounded area</td>
<td>Right fronto-lateral (supraorbital) craniotomy</td>
<td>Improved</td>
</tr>
<tr>
<td>Uppal et al.12</td>
<td>48/M</td>
<td>Visual deficit</td>
<td>OC</td>
<td>Hemorrhagic mass lesion arising from the chiasm</td>
<td>NR</td>
<td>Stable</td>
</tr>
<tr>
<td>Sun and Yu20</td>
<td>12/F</td>
<td>Visual deficit, headache</td>
<td>ROC</td>
<td>Round mass with a mild and uneven contrast enhancement in the suprasellar cistern, a lesion in the right OC complex</td>
<td>Right-sided pterional; total resection</td>
<td>Stable</td>
</tr>
<tr>
<td>Takeda et al.12</td>
<td>58/F</td>
<td>Progressive blurred vision, visual loss</td>
<td>LON, OC</td>
<td>Multilocular lesion at the left optic nerve to the optic chiasm with mixed intense signals</td>
<td>Left pterional craniotomy; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Gonçalves and Gonçalves9</td>
<td>40/F</td>
<td>Visual deficit</td>
<td>RON</td>
<td>Focal solitary well-defined rounded lesion involving the RON in its intracranial prechiasmatic segment, sparing the chiasm. Spontaneously hyperintense lesion on T1-W noncontrasted sequence showed a. On T2-W MRI, lesion with heterogeneous signal intensity and peripheral hypointense rim</td>
<td>Right pterional craniotomy</td>
<td>Improved</td>
</tr>
<tr>
<td>Mano et al.13</td>
<td>20/M</td>
<td>Acute visual loss</td>
<td>LON, OC</td>
<td>Left optic nerve edema with peripheral enhancement followed by hemorrhagic after two weeks. After two more weeks increase in bleeding and hemosiderin border and popcorn-like lesion</td>
<td>Left frontal osteoplastic craniotomy and a subfrontal approach.</td>
<td>Improved</td>
</tr>
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<tr>
<td>Alafaci et al.³</td>
<td>48/F</td>
<td>Visual deficit</td>
<td>OC</td>
<td>T2: hypointense lesion inside the optic chiasm in the suprasellar region.</td>
<td>Right pterional</td>
<td>Improved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T1: intraaxial lesion inside the optic chiasm, without enhancement after gadolinium injection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grob et al.⁵</td>
<td>49/F</td>
<td>Visual deficit</td>
<td>RON</td>
<td>Two loculated foci with fluid-fluid levels in the optic nerve with a posterior area of signal dropout</td>
<td>No surgery was mentioned</td>
<td>NR</td>
</tr>
<tr>
<td>Mamat et al.²²</td>
<td>43/M</td>
<td>Headache, Visual deficit</td>
<td>OC</td>
<td>Heterogeneous suprasellar mass with surrounding hyposignal in T2-W sequence without enhancement after gadolinium injection. After 2 months the mass developed at the expanse of the optic chiasm and had mixed hyper-hyposignal with a typical 'popcorn' aspect</td>
<td>Surgery was not performed</td>
<td>NR</td>
</tr>
<tr>
<td>Abou-Al-Shaar et al.³</td>
<td>33/F</td>
<td>Acute vision loss, headache</td>
<td>OC</td>
<td>Large heterogeneous, hyperintense, hemorrhagic right suprasellar extra-axial complex cystic structure on T1-W images</td>
<td>Right frontal craniotomy; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Katta et al.³³</td>
<td>60/F</td>
<td>Asymptomatic</td>
<td>Optic disk</td>
<td>NR</td>
<td>Surgery was not performed</td>
<td>NR</td>
</tr>
<tr>
<td>Muta et al.¹⁰</td>
<td>14/M</td>
<td>Visual deficit</td>
<td>OC, RON</td>
<td>Mass located in the suprasellar region displacing the optic nerves caudally and the infundibulum posteriorly. The lesion produced mixed intensity signals on T1- and T2-W images</td>
<td>Anterior basal interhemispheric approach; partial resection</td>
<td>Worsened</td>
</tr>
<tr>
<td>Rani et al.³⁴</td>
<td>57/M</td>
<td>Visual loss in the upper field</td>
<td>ON, head on both eyes</td>
<td>NR</td>
<td>No surgery was mentioned</td>
<td>NR</td>
</tr>
<tr>
<td>Trentadue et al.⁷</td>
<td>49/M</td>
<td>Asymptomatic</td>
<td>OC, left optic tract</td>
<td>1 cm lobulated lesion, On T2 images a hypo-intense 'blooming' spot with a 'black dot-like'</td>
<td>Surgery was not performed</td>
<td>NR</td>
</tr>
<tr>
<td>Ribeiro et al.²⁵</td>
<td>63/F</td>
<td>Acute visual loss</td>
<td>LON, OC</td>
<td>Mass with mixed signal intensity at the LON and OC</td>
<td>Left frontotemporal craniotomy using the pterional approach; total resection</td>
<td>Improved</td>
</tr>
<tr>
<td>Algoet et al.²</td>
<td>38/M</td>
<td>Progressive visual loss</td>
<td>LON</td>
<td>Oval-shaped hyperintense zone on T2-W sequence. Axial 3D fluid attenuated inversion recovery images revealed an oval-shaped T2 hyperintense zone along the course and at the ventral side of the LON, with some compression on it, starting from the optic foramen inward toward the optic canal</td>
<td>A left frontolateral craniotomy with extradural skull base approach with neuronavigation</td>
<td>Improved</td>
</tr>
</tbody>
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<td>Tomita et al.14</td>
<td>27/F</td>
<td>Acute visual loss, headache</td>
<td>OC</td>
<td>Hemorrhagic lesion in the OC. Initial MRI showed oval mass in the suprasellar region, mainly in the OC. Both T1- and T2-W images showed the center of the mass as hypointense</td>
</tr>
<tr>
<td>Kakuta et al.26</td>
<td>59/M</td>
<td>Visual disturbance</td>
<td>OC</td>
<td>Heterogeneous signal intensity mass at OP with a low signal intensity on T2</td>
</tr>
<tr>
<td>Zoia et al.37</td>
<td>53/F</td>
<td>Mild fever, headache, acute visual loss</td>
<td>Both ON and chiasm</td>
<td>Hemorrhagic mass in the suprasellar region that affected both the pituitary stalk and the hypothalamus while reaching cranially the left Monro foramen and compressing the optic nerves and chiasm</td>
</tr>
<tr>
<td>Sbeih et al.</td>
<td>44/F</td>
<td>Visual deficit, headache</td>
<td>OC</td>
<td>Suprasellar mass lesion involving the optic chiasm. Heterogeneous mass in appearance with areas that were isointense and hyperintense on T1-W images, isointense and hypointense on T2-W images</td>
</tr>
</tbody>
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A slight female predominance was found, with 17 male patients and 18 female. Tomita et al.14 reported a case in which a woman developed symptoms during pregnancy. Abou-Al-Shaar et al.1, reported a woman who had visual symptoms 3 months after delivery and Cerase et al.28 reported a case in which a 30-year-old woman woke up with visual impairment one week after an 8-month period of nursing her second child. In the same case, the patient’s father also had a biopsy-confirmed CM.

From ten cases in which CT was used, in nine hypodense masses were found, three had a hemorrhage, three had calcifications and one was isodense. Regarding angiography, five cases were normal and three had reported modifications (Table 1). On the MRI we can see the exact location of the CMs, 41.1% of the cases were located just at the optic chiasm, 26.4% were located just at the optic nerve, and in 37.1% of the cases, cavernous angiomas were located in more than one spot of the optic pathway, being 23.5% located at the optic chiasm and optic nerve and 8.8% in other combinations (Table 1).

Diagnostic
The test that is most used to confirm the diagnosis of cavernoma is the magnetic resonance imaging (MRI). In 10 cases both MRI and CT were analyzed, in four cases MRI, CT and angiography were performed, in three cases MRI and angiography were used, and in only one case only angiography was performed. To help the diagnosis, color fundus photographs can be used showing a “cluster of grapes’ appearance in the case of CMs, as seen in three of the 34 cases5,10,33.

Katta et al.33 reported the use of gadolinium-enhanced MRI to exclude extra-scleral and intracranial involvement in one case. In the other cases, 44.4% showed no significant contrast enhancement after gadolinium was injected, and 44.4% showed an enhancement.

In the cases in which MRI was described, a mixed signal intensity on T1 and T2 weighted images was found, and in most of the
cases the reported findings corresponded to hemorrhages, such as popcorn-like lesions and hemosiderin rings. Besides that there were some studies that showed peripheral hyperintensity and a central hypointensity mass on T2 and four showed hyperintensity on T1.

**Treatment and outcomes**

Out of the 34 cases analyzed, 85.2% reported surgical treatment, 7.4% did not mention whether surgery was performed, and 7.4% did not perform surgery. Regarding the reported surgeries, 44.8% were gross total resection, 6.8% partial resections, and 48.4% did not specify whether the tumour was fully resected or not. Visual acuity improvement was observed in 41.3% of the patients who were surgically treated. Visual field defects were improved in 48.2%, headaches in 13.7%, and non-specified visual symptoms in 10.3%. Two patients developed diabetes insipidus after surgery.

Both of the patients who had a partial resection presented tumoral hemorrhage and growth after surgery. reported the case of a patient who suffered sudden blurred vision in the right eye, temporal defect in the right visual field, and severe occipital and bitemporal headache two days after surgery, due to intratumoral hemorrhage. Even though the visual field defect progressed to complete bitemporal hemianopsia, conservative therapy was preferred to surgery in order to avoid further damage of the optic pathway structures. The headache eventually disappeared, but the visual symptoms persisted.

In the case described by Jo et al., nine months post-surgery the patient presented sudden loss of vision in the left eye due to repeated bleeding and mass growth, but refused surgery and, therefore, underwent conservative treatment. Initially, there was improvement of the visual loss, but the mass continued to grow and there was another episode of bleeding, and after which the patient underwent fractionated radiation therapy. In the next five years loss of vision in both eyes and development of gait disturbance and dementia were developed. MRI showed hydrocephalus and a multilobulated, multistage parasellar hematoma with calcification extending to the third ventricle and midbrain. Since there was progressive worsening of symptoms and no response to radiation treatment, a second surgery was performed to remove the mass. The visual symptoms were unchanged, but the dementia and gait disturbance improved.

Two of the three patients who were not treated with surgery received regular close monitoring. The patient mentioned by Katta et al., showed no worsening nor improvement of the symptoms, while the patient mentioned by Marnat et al. initially showed a spontaneous partial recovery soon after the onset of the symptoms. The other patient who did not undergo surgery, had a family history of CM and initially received 1g/day (intravenous) bolus of prednisone for 3 days and 50mg/day oral prednisolone with gradual tapering for one month. This treatment was repeated twice later with the addition of 250mg/day of acetazolamide, administered orally also for a month. The first round of treatment resulted in the improvement of the visual acuity and reduction of the blind spot lesion size, with regression of the symptoms and thickening of the affected optic nerve after 4 months. The second round resulted in initial complete visual recovery and further regression of the symptoms, and the third and last round mentioned was not effective, showing declined visual acuity after 1 month.

Cavernous malformations are well-circumscribed low flow vascular lesions also known as cavernomas, cavernous angiomas, cavernous hemangiomas or vascular hamartomas. Out of all vascular malformations of the central nervous system (CNS), approximately 10-15% are cavernous angiomas. In some extremely rare cases, they can affect cranial nerves or the optic pathway, which is composed of the optic nerve, chiasm, and optic tract, usually with extra-chiasmal involvement. Optic pathway cavernomas represent less than 1% of CNS cavernous malformations. In most cases, patients have suffered an acute or subacute onset of symptoms, typically manifested as loss of vision and reduction of the visual field predominantly associated with retro-orbital or frontal headache (‘chiasmal apoplexy’). The clinical presentation of cavernomas is nonspecific. Therefore, it is important not to initially dismiss them as a possible diagnosis.

**Natural history**

The natural history of cavernous malformations of the optic pathway (OPCM) is not clear, partly because there is a small amount of data regarding it. However, an understanding of this history is essential in order to formulate a rational management plan for these patients. In our study, we reviewed only 34 case reports of OPCMs, in patients between 12 and 78 years of age and with female predominance. OPCH can lead to distinct and
unspecific symptoms. In most cases, patients have suffered an abrupt onset of symptoms typically manifesting as loss of visual acuity, visual field defects, and frontal or retro-orbital headache. In addition to these events, a significant portion of patients suffered subacute clinical symptoms for many years, due to progressive tumor enlargement and repeated hemorrhage.

The incidence of OPCM appears to have a familial component. Whereas cavernous malformations may be observed in either sporadic or familial form, patients with the last form tend to have multiple lesions in the central nervous system. Cerase et al. reported a case in which the patient’s father had a biopsy-confirmed cavernous hemangioma in the right leg associated with multiple MCCs in the brain evidenced by MRI.

It is thought that OPCMs have a higher tendency to bleed than cerebral CMs because of the eloquence of the optic pathway region in OPCM hemorrhage is higher in females. Although the natural history of cavernous malformations of the optic chiasm remains unclear, the incidence of recurrent hemorrhage tends to be much higher than the 0.7% per year reported for intracranial cavernous malformations. Cavernous malformations are more likely to enlarge and have a higher incidence of bleeding during pregnancy. Cerase et al. reported a case of cavernous malformation in which one week after a period of 8 months of breastfeeding her second son, a 30-year-old woman awoke with visual impairment of the left eye.

**Imaging studies**

Magnetic resonance imaging is the most specific and sensitive exam for identifying cavernous malformations, and is especially sensitive to see small anatomical structures such as cranial nerves. The combination of T1- and T2-weighted images has superior efficiency to show acute and subacute hemorrhages, and they can also demonstrate blood deposits of different ages. On T1 images, a hypointense to isointense appearance is usually demonstrated, while on T2 images, it is possible to see a dark signal known as the blooming effect of hemosiderin.

The ‘popcorn-like’ lesions, which are rounded with mixed hyperintensity and hypointensity signals, are a typical alteration that can be seen in MRIs. The MRI appearance is usually related to hemorrhage in evolution, suggesting the diagnosis of CMs, which can be seen as hyperintense areas. Both T1- and T2-weighted images show a hypointense hemosiderin rim also known as the ‘iron ring sign’ deposited around the CM. When intravenous gadolinium was administered, minimal or no enhancement occurred. In one of the cases, the MRI was not able to find any abnormality and a 3-Tesla scanner was used.

Computed tomography can demonstrate well-marginated and hyperdense masses that often can reveal calcification. Although common, these findings are non-specific and may lead to an incorrect diagnosis. According to Sbeiha et al., several studies reported that postoperative-visual-outcome can be predicted by preoperative retinal nerve fiber layer (RNFL) thickness that can be evaluated by the Optical Coherence Tomography. CMs are hardly detected in angiography because of their low flow and high incidence of internal thrombosis.

**Differential diagnosis**

Cavernous malformations of the optic pathway are extremely rare. Since the clinical presentation can mimic other diagnoses, CM is usually excluded from the differential diagnosis of lesions affecting the visual pathway.

In literature review, eleven other diagnoses were mentioned, being cranioopharyngioma cited in all the studies. Meningioma, aneurysm, optic glioma, arteriovenous malformation, pituitary adenoma, leukemia, lymphoma, multiple sclerosis, optic neuritis, and metastasis were also mentioned. It is difficult to distinguish CMs in differential diagnosis, and the answer often depends on characteristic MRI findings, clinical presentation, and evolution.

According to Ibrahim Sbeiha et al., Fluorodeoxyglucose positron emission tomography (FDG-PET) might be useful to differentiate optic chiasmal cavernoma from other chiasmal tumors. In these images, OCC does not show an increase in the fluorodeoxyglucose (FDG) accumulation, while malignant tumors such as multiform glioblastoma will demonstrate it.

The lack of endocrine dysfunction, ophthalmoplegia and diplopia can help to discriminate a chiasmal malformation from pituitary apoplexy because the acute expansion of the hypophysis can compress the third cranial nerve (oculomotor), which would not be expected in a case of cavernous malformation. To differentiate...
CMs from gliomas, granulomas, metastatic tumors and germ cell tumors, neuroimaging is necessary due to the signals of hemorrhage and the ‘iron ring’ that can be found in CMs MRI.6

Surgical treatment and outcomes
In asymptomatic patients, conservative treatment with cautious observation and annual follow-up is acceptable.8,13. However, surgical resection is the gold standard for symptomatic patients, and, in case of chiasmal apoplexy due to hemorrhage, emergency surgery should be performed to avoid permanent visual impairment.8,10,14,27. In addition, surgery is also indicated in case of recurrent hemorrhage, progressive visual and/or neurological deterioration, and asymptomatic patients without unacceptably high surgical risk with a growing CM shown in follow-up MRIs.8

The risks of performing biopsy alone, without total resection of the tumour, outweigh the benefits since they might be inconclusive, can induce accelerated growth of the cavernoma, and increase the likelihood of symptom worsening and CM bleeding. Partial resection of these lesions carries the possibility of recurrence and shares the same risks as biopsy alone, and therefore not recommended.3,4,13,15,17,25. Total resection is crucial to prevent growth and bleeding from residual parts of the tumour, relieve optic compression and preserve or improve visual function, providing a better outcome.3,8,13,18,29

Surgery on the optic pathway carries a high risk of damage to the surrounding structures, and permanent visual loss is a possible outcome.4. Parenchyma stained by hemosiderin around the cavernoma is a part of the optic pathway, and not part of the lesion, therefore, its resection should be avoided. Well-circumscribed lesions and demarcation of the optic nerve or chiasm by reactive fibrillary gliosis facilitates total resection.10

The sensitivity of CMs tissue makes radiation therapy a risky and controversial option, since there is a significant risk of progressive neuronal insult and higher risk of bleeding.5,14. According to Panczykowski et al., this option represents an unacceptable morbidity rate and has not been curative in previous studies. However, there is not enough data about the efficacy of radiation therapy to reach definitive conclusions.

Surgical approaches
The surgical resection of cavernomas is challenging because of their deep location and eloquence, besides the fact that few neurosurgeons have experience with this type of tumour due to its low incidence.3,20. In order to choose the appropriate surgical approach, the surgeon must evaluate the size of the lesion and the development of the disease, taking into account which approach is more familiar to the surgeon. The pterional approach was the most observed surgical approach during this review, being used on 41.3% of the patients who received surgery. Other approaches were used, such as frontotemporal, supraorbital, orbitozygomatic, eyebrow keyhole, subfrontal, anterior basal interhemispheric, extradural skull base, and extended endoscopic endonasal transsphenoidal.

CONCLUSION
Cavernous malformations of the optic pathways are extremely rare. This pathology must always be considered in the differential diagnosis of optic neuropathy and visual loss despite its low incidence. Magnetic resonance imaging is the modality of choice for diagnosing these lesions, which often appear as ‘pop-corn like’ lesions. The gold standard treatment of cerebral cavernous malformation is gross total resection. Further studies on the natural history of these specific lesions are needed to assess the role of surgery in cases of OPCMs.

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