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REPORTE CASO CLÍNCO

Meningioma causado por meningioangiomatosis cerebral con diseminación neural y permeación nerviosa

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Resumen

La meningioangiomatosis (MA) es una rara patología hamartomatosa benigna originada de las leptomeninges y corteza cerebral. La asociación con meningiomas es rara. En este caso, presentamos a un hombre de 30 años de edad, sin historia previa de neurofibromatosis tipo 2, quien debutó con cefalea progresiva, disminución de agudeza visual, la cual progresó a amaurosis total del ojo izquierdo. En estudios de imagen revelaron una lesión homogénea localizada en la región frontotemporal izquierda originada de la apófisis clinoides anterior. Fue sometido a cirugía y se encontró un tumor rojizo con apariencia hemorrágica, correspondiente con vasos sanguíneos fibrosados con proliferación de células meningoteliales elongadas que formaban áreas sólidas, resemblantes de un meningioma meningotelial. Resultó ser positivo para EMA, vimentina y el factor VII demostró positividad en células perivasculares y negativo en áreas sólidas. Con la tinción de reticulina se observaron alteraciones en la pared de los vasos sanguíneos. Este caso se discute pues se presenta una masa cerebral formada por vasos sanguíneos anormales, así como con áreas sólidas correspondientes a meningioma.

Palabras claves: Hamartoma, leptomeninges, meningioangiomatosis, meningioma

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CLINICAL CASE REPORT

Meningioma caused by intense cerebral meningioangiomatosis with neural dissemination and nerve permeation

Abstract

Meningioangiomatosis (MA) is a rare benign hamartomatous lesion within the leptomeninges and cerebral cortex. The association with meningioma is very rare. We present a 30-year-old man, with no previous history of NF2, who started with progressive headache, decreased visual acuity, which progressed to total amaurosis of the left eye. Radiological studies showed a homogenous lesion located in the left frontotemporal region originating from the anterior clinoid process. He underwent surgery and a reddish tumor with a hemorrhagic spongy appearance that corresponded to numerous partially fibrous blood vessels, with proliferation of elongated meningothelial cells that formed solid areas with the appearance of a meningothelial meningioma. It was positive for EMA, vimentin, and Factor VIII showed positivity in the perivascular proliferating cells and negative in the solid areas. With the reticulin stain we observed alterations in the wall of the thick and large vessels. This case is discussed since it presents as a cerebral mass formed by abnormal vessels with solid areas that corresponds to meningioma.

Keywords: Hamartoma, leptomeninges, meningioangiomatosis, meningioma.

Introduction

Meningiomas are benign tumors that originate from the meninges and represent the most common primary central nervous system tumor, accounting for 24-30% of primary tumors[1]. Histologically they are classified in three grades: Grade I: meningothelial, fibrous, transitional, psammomatous, angiomatous, cystic, secreting, lymphoplasmocytic, and metaplastic. Grade II: atypical, chordoid, and clear-cell. Grade III: papillary, rhabdoid, and anaplastic.They can be unique or multiple, and be associated with type 2 neurofibromatosis[2].

Meningioangiomatosis (MA) is a rare, benign, hamartomatous lesion, typically described as a proliferation of fibroblastic or meningothelial cells around blood vessels[1]. Bassoe and Nuzum reported the first case in 1915[3,4]. The vast majority of cases are sporadic, but it has also been reported in association with NF2. The latter tend to be asymptomatic, while sporadic ones are unique and symptomatic, clinically presenting as epileptic crisis, usually in children and young adults[2]. Histologically, MA correspond to meningothelial cells proliferation disposed around cortical and meningeal blood vessels[3]. Meningiomas which arise from MA are rare, and tend to mimick

invasive meningiomas, being the most of them of the transitional type, however, their etiology and physiopathology remain still unclear[5,6]. We report the case of a non NF2 associated meningothelial meningioma arising from meningioangiomatosis areas in a 30 years-old patient.

Clinical summary

A 30 years-old male, with a three months history of headache and visual alterations. Neuro-ophtalmologic evaluation is performed, which reported bilateral papilledema in fundoscopic examination, as well as visual acuity and campimetric disturbances. Contrast enhanced magnetic resonance imaging (MRI) T1 weighted sequence and T2 sequence revealed a homogeneous lesion located on the left frontotemporal lobes, with dural attachment all along the lesser sphenoid wing, from the anterior clinoid process all the way to the pterion, with a homogeneous enhacement pattern and intense vasculature evidence on T2 sequence, with a suspicious diagnosis of sphenoidal meningioma. We performed a conventional pterional approach, achieving gross total resection (*Figure 1-2*).

Axial magnetic resonance imaging

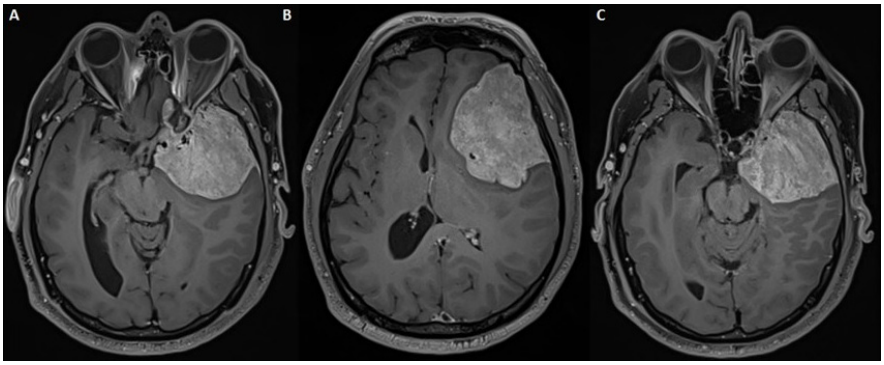

Figure 1. Magnetic resonance imaging: axial T1 contrast enhanced weighted sequence showing an extraxial lesion with dural attachment on the left sphenoid greater wing and pterion, compatible with a meningioma. (**A**) Optic chiasma severly displaced and left optic nerve completely embedded by the lesion. (**B**) and (**C**) Left pterional region and temporal pole involvement.

Sagittal magnetic resonance imaging

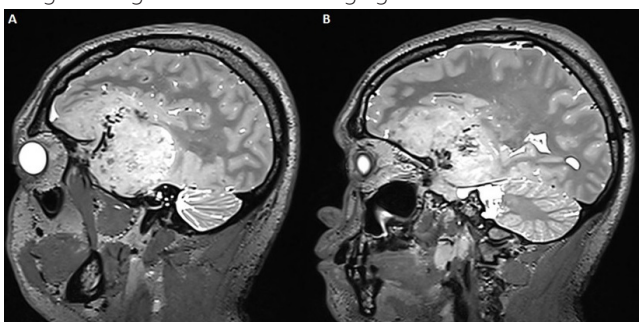

Figure 2. Magnetic resonance imaging: sagittal T2 enhanced weigthed sequence showing multiple vascular trajectories inside the lesion.

A 50x40mm reddish, spongy, and fragile sample was sent to our neuropathology laboratory; it presented multiple blood vessels all through its composition. A 40x30mm of duramater was also taken, which was described to have yellowish blood vessels adhered to it (*Figure 3A-B*). Histological examination revealed loose blood vessels surrounded by diffuse signs of hemorrhage (*Figure 3C*).

Theses vessels were variable in size (*Figure 3E*), covered by endothelial cells (*Figure 3D*). The muscular layer showed intense fibrosis (*Figure 3F*). Meningothelial-like cells proliferation could be observed in the vasa vasorum, tending to form a solid pattern of growth with an aspect similar to meningothelial meningioma (*Figure 3G*). No atypical cells nor mitosis were evidenced (*Figure 3H*).

Macro and microscopic findings

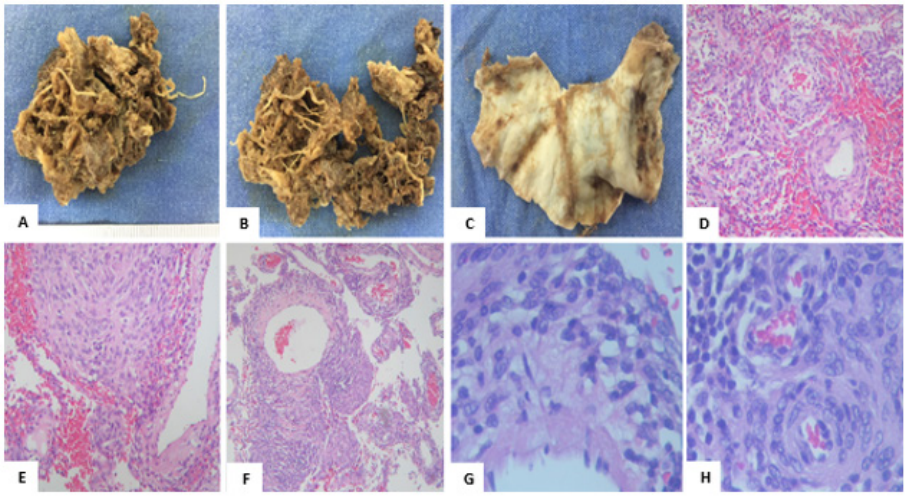

Figure 3. Macro and microscopic findings. (**A-B**) Macroscopic apperance of the tumor; 50x40mm. (**C**) 40x30mm. duramater fragment with evidente attachment of lesion. (**D-E**) Multiple loose blood vessels can be visualized, in a diffuse hemorrhage background (H&E x200). (**F-G**) Blood vessels´walls present diffuse thickening secondary to meningothelial cells wich form irregular clusters and cause muscular layer intense fibrosis (H6E x200;x400). (**H**) Meningothelial cells prolifetation around vasa vasorum with a solid growth pattern, which resembles that of meningiomas (H&E x400).

Masson´s trichromic stain showed dense blue proliferated thickened vessels (*Figure 4A*). With reticular fibers stain, irregular vessels with fragmented fibers are observed (*Figure 4B*), which tend to form irregular tangles along the vessel wall (*Figure 4C-D*). Vimentin stain is positive all along the vessel´s wall and meningothelial cells (*Figure 4E*). Epithelial membrane antigen (EMA) showed an intense perivascular expression (*Figure 4F*). CD34 was negative and Factor VIII shows an intense positivity in the endothelial and meningothelial cells growing from the vasa vasorum in its nuclear and cytoplasmic form (*Figure 4G*) and was negative in the solid meningothelial cells´ proliferation foci. Ki-67 expression was low (*Figure 4H*). Duramater showed significant fibrosis, thickened blood vessels with proliferation of meningothelial cells (*Figure 4I*). Infiltration of elongated meningothelial cells was observed (*Figure 4J*). S-100 protein showed infiltration and nerve permeation (*Figure 4K-L*).

Vimentin was strongly positive in meningothelial proliferation and nerves fibers (*Figure 4M*). With all of these histological and immunohistochemistry findings, diagnosis of meningothelial meningioma caused by intense meningioangiomatosis, with infiltration and nerve permeation was concluded.

Microphotographs of histological findings

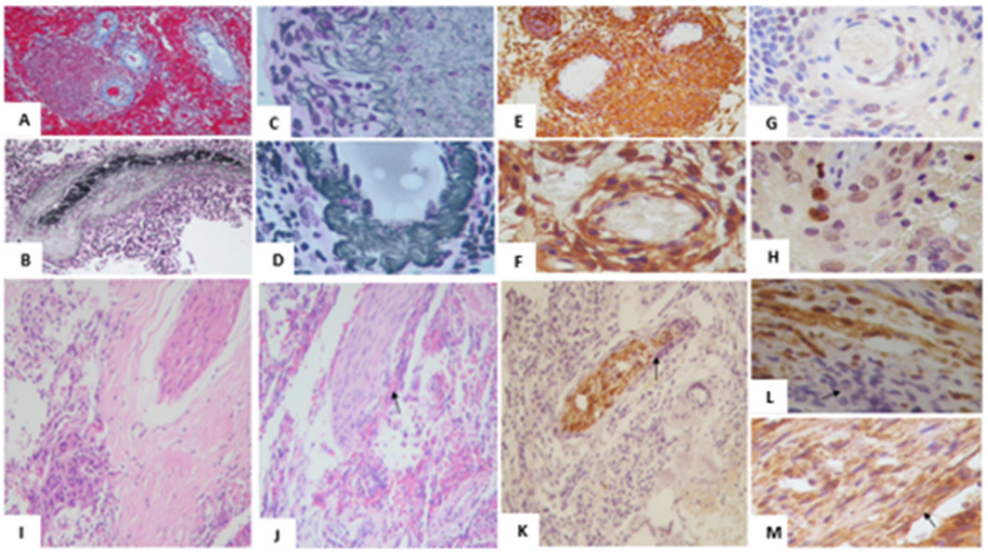

Figure 4. Microphotographs of histological findings. (**A**) Masson´s trichromic stain shows thickened proliferated vessels with a blue vall (x200). (**B**) Reticular fibers stain shows irregular vessels (x200). (**C-D**) Figure 5B with x400 augmentation shows reticular fibers fragmentation and thickening of internal lamina, forming tangles of irregular blood vessels. (**E**) Positivity for vimentin in blood vessels´valls and meningothelial cells (x200). (**F**) EMA shows intense perivascular expression (x400). (**G**) Factor VIII shows intense positivity in endothelial and meningothelial cells growing concentrically around the vessel wall, both in nuclear and cytiplasmic form (x400). (**H**) Low ki-67 expression. (**I-J**) Duramater shows fiborosis and infiltration by meningothelial cells, signaled by arrow (H&E x200). (**K-L**) S-100 protein positive immunorection with nerve infiltration and permeation by neoplatic cells, signaled by arrow (x400). (**M**) Vimentin strongly positive in meningothelial cells, singnaled by arrow (x400).

Discussion

MA is a rare benign hamartomatous lesion within the leptomeninges and cerebral cortex that tends to be unique but can become multiple when associated with NF type 2. Sporadic MA generally presents in children and young adults. Clinical presentation varies from asymptomatic, to headache and epileptic crisis being the most frequent symptoms[7]. Demographic distribution favors its presentation in males[7,9]. Kim, et al.[8] reported allelic losses in chromosomes 1p32, 9p21, 13q14, and 16q22 in angiomatosis, and 22q12 in meningioangiomatosis associated meningiomas. The most common locations are the frontal and temporal lobes, but growth can achieve both compartments[6,7].

However, sites such as thalamus, third ventricle, and cerebral peduncles have been reported to be affected[9]. Radiologically, MA appears as a benign lesion with no apparent brain parenchyma invasion, that is usually diagnosed as meningioma, however due to its high vascularization, it can be sometimes mistaken for an arteriovenous malformation[8]. A calcified mass in CT or MRI in T2 weighted images can suggest MA[9].

Histologically, it is conformed by a proliferation of meningothelial cells which are immunorreactive to vimentin and EMA, expressing as a focal thickening of the meninges which no not invade the cerebral cortex, or as an exclusively intracortical lesion with no relationship with the meninges. The magnitude of theses intracortical lesions is variable, from perivascular fascicles to authentic nodules, with reactive gliosis and neural dysplasia[10,11]. Wide ranges of histologic features have been previously described[12]. Fibrosis, hyalinization, calcium deposition, mineralization, psammoma bodies, and even hemosiderophagous have been reported[10].

With immunohistochemistry, vimentin and EMA were intensely positive in perivascular and meningothelial cells, and as the lesions turns to a more solid pattern, this stains become weakly positive to negative[10,11]. CD 34 turned weakly positive, however, factor VIII was intensely positive in perivascular cells, both cytoplasmic as nuclear components. Some of these tumors present estrogenic receptors.

Some MA cases have been associated with arteriovenous malformations, enkephalocele[12], oligodendroglioma[13,] and Sturge-Weber syndrome, which is a congenital neurocutaneous disease that is characterized by facial capillary malformations with ipsilateral cerebral and ocular, vascular malformations[14,16]. Nevertheless, its most common association is with meningiomas[15].

Besides, meningiomas are the main differential diagnosis, and MA can simulate invasive or high grade ones[6-9]. Angioblastic and clear cell meningiomas present with abundant hyalinized vessels, which can be mistaken for perivascular meningothelial cells, characteristic of MA but not present in other entities[1]. Endothelial cells must be observed as well, as they do not tend to have mitotic figures nor cellular atypia, suggesting a benign nature.

Discussion arises when it comes to determine whether lesions like the one we describe is of primary neoplastic origin which could lead to invasion, or whether it originates from meningioangiomatosis areas secondary to meningothelial hyperplasia[5]. Ki-67 tends to be reported below 3% in both conditions, and an increase could be related to invasion or recurrence[1]. Cortical "invasion" by meningiomas, which occurs through Virchow-Robin spaces does not represent a real parenchymal invasion, but can predict a major probability of recurrence. Real invasion occur when tumoral cells break through piamater to involve underlying cerebral cortex[2]. Recent studies show that a chromosome 22q12 and heterozigozity losses have been found in pure Ma and meningioma associated MA, which suggests a MA´s neoplastic origin[8]. Perry, et al.[4] suggest that the majority of meningioma associated MA have a neoplastic source which gives its exuberating perivascular dissemination pattern, instead of a underlying hamartoma. Wiebe, et al.[6] suggest that MA originates from a pluripotential cell that would differentiate into the components of this lesion. Despite all that has been written, further studies shall be performed in order to answer these questions.

Surgical treatment has become the first therapeutical option, and a gross total resection is associated with favorable long-term outcomes. However, it is not technically easy to achieve these

results, as surgical risks are considerable and serious complications have been reported[17,18]. Chemo and radiotherapy must be considered but must not be overused, as this diagnosis tends to be mistaken for malignant meningiomas. Gamma Knife radiosurgery has recently turned into an important weapon in the wide therapeutic arsenal available[18].

Conclusions

Meningioangiomatosis is a rare disease, historically described as hamartomatous, however, due to recent studies and histological findings, this has been questioned, and neoplastic origins have been proposed. It tends to present clinically as epileptic crisis, tipically in the frontal or temporal lobes. Imaging findings are similar to meningioma´s, which can accompany MA, and is the main differential diagnosis. Histological and immunohistochemistry observations are the cornerstone elements to reach a correct diagnosis.

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Disclosure

The authors have no conflict of interest associated with this article.

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