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Case report

Optic pathway gliosarcoma: A very rare location for a rare disease ☆☆☆

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ABSTRACT

Gliosarcoma, a variant of glioblastoma, is a rare and aggressive tumor of the central nervous system (CNS) composed of glial and sarcomatous tissues. Up to now, there are only 2 reported cases of gliosarcoma of the optical pathway. We report a case from March 2018 of a 53-year-old male patient presented with 6 months' of right fronto-orbital pulsatile headache, behavior changes, and visual loss. The MRI study showed an expansile optic pathway lesion involving the chiasm and right optic nerve. The diagnosis of gliosarcoma was obtained by open brain biopsy and immunohistochemical analysis. Although gliosarcoma is rare, it should be considered a differential diagnosis even in optic pathway tumors in older patients. The experience of the neuropathologist with a trained eye can be the differential in the accurate diagnostic process.

Optic pathway, Gliosarcoma, Glioblastoma, Magnetic resonance imaging

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Introduction

Gliosarcoma (GS) is an aggressive primary CNS tumor classified as grade IV by the World Health Organization (WHO). Considered a glioblastoma (GBM) variant, GS is composed of a glial (anaplastic astrocytes) associated with mixed areas of malignant mesenchymal elements [1]. It affects adults with a median age over 60 years, predominantly by male sex (63.1%) [1]. The prognosis is dismal, with median overall survival ranging from 6–18 months' and a 5-year survival rate of 5.6%. GS in-

cidence varies between 1% and 8% in all gliomas, making it extremely rare [2]. The temporal lobe is usually the most affected place [1]. To our knowledge, it will be the third case report of optic pathway gliosarcoma, after Crimino et al. [3] and Tuna et al. [4].

Case report

We report a case of a 53-year-old male patient who presented with 6 months' of right fronto-orbital pulsatile headache,

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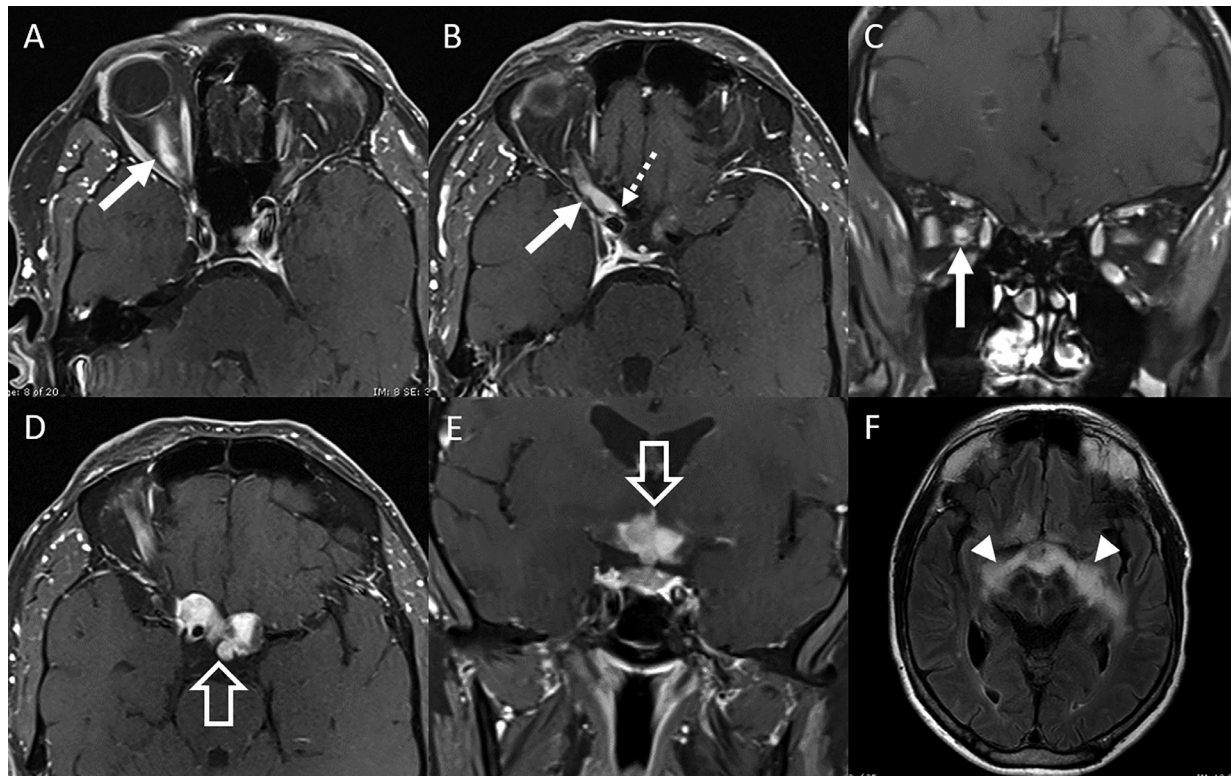


Fig. 1 – Brain MRI. Axial (A, B) and coronal (C) T1 post-contrast sequences show the lesional involvement of the entire optic nerve, which is thickened and widens the optic canal. Axial (D) and coronal (E) depict an expansive lesion with intense enhancement by the paramagnetic contrast affecting the optic chiasma. Axial FLAIR sequence demonstrates hyperintensity sign in both optical radiations, indicating lesional involvement.

which worsened during this period. He also complained of visual loss, worse on the right. The family claimed that the patient had behavior changes with increasing irritability.

The patient had mydriatic pupils on physical exam, with photo motor reflex absent on the right side. Muscle strength and other reflexes were normal. Prior medical history was positive for major depression.

The magnetic resonance imaging (MRI) showed an expansive, solid lesion affecting the optic chiasma, with regular, and macrolobulated outlines. It also affected the entire right optic nerve, which was presented with increased caliber, determining the optic canal's enlargement and intimate contact with the neural sheath. Optic radiation showed signal hyperintensity in the fluid attenuated inversion recovery (FLAIR) sequence, suggesting a posterior extension of the lesion. In post-contrast sequences, the entire lesion had avid enhancement.

An open brain biopsy was performed 15 days later, through right frontal craniotomy. Hematoxylin and eosin (HE) microscopy showed a spindle cell component with intense pleomorphism and mitosis (Figs. 2A and B). The immunohistochemistry study showed diffuse expression of Verhoeff stain (VEG), indicating the reticulin component's presence, which is characteristic of the mesenchymal tissue. It was also positive for glial fibrillary acid protein (GFAP), S-100, and SOX2 (Fig. 2E and F). The antigens EMA and 1A4 were negatives, excluding other CNS neoplasms with similar morphology. The antibody Ki-67 determined the proliferative index, which was positive

in about 30% of cells (Fig. 2D). The overall histomorphologic and immunohistochemical were diagnostic of optic pathway gliosarcoma.

At first, the patient was treated with 6 chemotherapy sessions with temozolomide, a similar treatment used on glioblastoma tumors, and after, was discharged to follow up. He returned 3 months' later complaining of cough and asthenia. Chest CT showed pulmonary embolism. He was admitted to the ICU but died 22 days later from hospital pneumonia.

The standard genetic panel for primary grade IV CNS tumors includes mutation analysis of the IDH1 and TP53 genes and epigenetic alterations of the O⁶-methylguanine DNA methyltransferase (MGMT) methylation promoter. Considering the histomorphological and immunohistochemical findings, we advise having collagen gene signature analysis, despite the patient's additional cost. The genetic study was not performed because the patient died before the analysis, and the relatives did not want to bear the costs of the examination.

Discussion

First described in 1895, gliosarcoma, an uncommon variant of glioblastoma, is a grade IV primary tumor of the SNC by WHO classification in 2016 [1]. It accounts for approximately 2% of

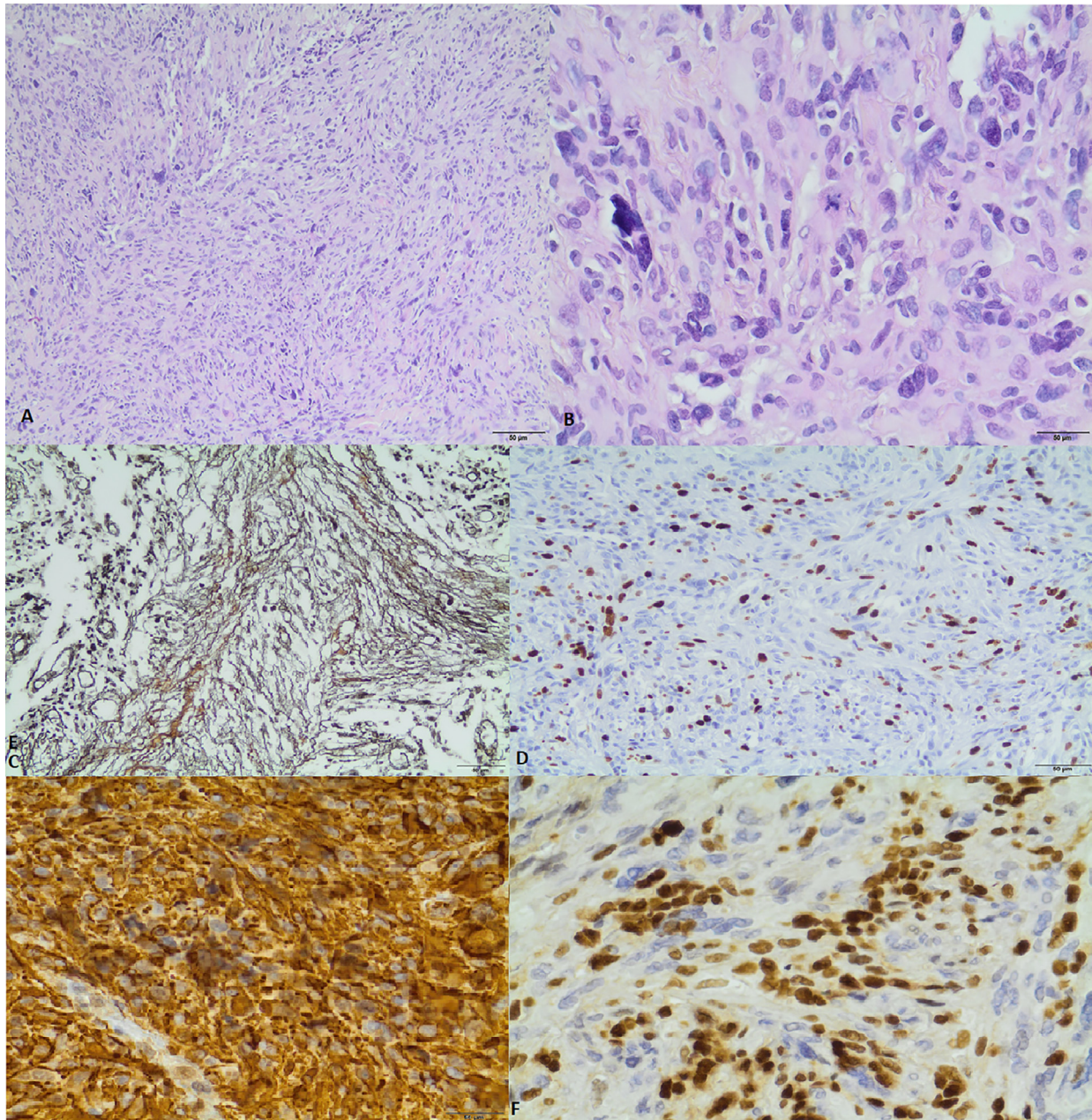


Fig. 2 - Biopsy A (100x original magnification) and B (400x original magnification) and immunohistochemistry C to F (200x original magnification). (A and B) show spindle cell neoplasia, with intense pleomorphism and mitosis. (C) Verhoeff, showing reticulin component. (D) Ki-67, showing intense mitosis (30% positive). (E and F) Positivity for GFAP (E) and SOX2 (F), proving glial components.

all cases of glioblastoma [4]. High-grade optic nerve glioma is more common in adulthood and almost always sporadic [4]. The GS treatment protocol is the same used in GBM (Stupp protocol) since there is no GS-specific protocol management [1].

Histologically, GS has a biphasic pattern with mixed glial and mesenchymal elements [3,4,5]. The mesenchymal tissue is mainly fibrosarcomatous, but other elements like chondromatous liposarcomatous, melanocytic and muscular, have been described [6]. The immunohistochemistry study usually identifies GFAP antigens in the lesion's glial portion [3,5,6], like

in our case. The lesion's mesenchymal part shows intensely positive staining for vimentin [3,6]. We have opted to use the VEG antigen because we do not have access to vimentin stain in the public health service. The S-100 antigen usually stains the entire tumor [3].

GS is generally wild-type - lacks mutations in the genes *IDH1/2* [3,5,6,7]. They have some genetic alterations similar to glioblastomas, such as Phosphatase and tensin homolog (*PTEN* and *PIK3*) mutations [7]. However, collagen gene signature (*COL1A1*, *COL1A2*, *COL3A1*, *COL6A@*, and *COL6A3*) are the gliosarcomas' main

biomarkers, differentiating them from glioblastomas [7]. Another group of genes that can determine GS from GBM encompasses genes coding for zinc finger proteins [7].

The MRI characteristics of primary GS are similar to those of GBM [5]. The brain MRI morphology is a single expansive and superficial lesion located in one of the cerebral hemispheres, with irregular contours, and heterogeneous enhancement by the paramagnetic contrast medium. It may have liquefaction and/or necrosis central area and involves the dura-mater. However, our case involves the optical pathways, and the imaging characteristic resembles a primary optical pathway glioblastoma. Our case's tumor morphology is very similar to that reported by Tuna et al. [4].

GS usually affects the cerebral hemispheres, with the temporal lobe being the most involved, representing approximately 39% of the cases [1,4]. However, there were reported cases involving the posterior fossa, spinal cord [1,4], and metastasize disease through the body, the lung, and liver being the most common sites [2]. Since then, there have only been 2 reported primary optic nerve GS cases, one in 2016 by Crimino et al. [3] and the other in 2020 by Tuna et al. [4]. To our knowledge, it will be the third case report of primary GS of the optical pathways.

Conclusion

Gliosarcoma of the optic pathways is an aggressive and extremely rare tumor, and this article is the third report in the literature. MRI of the brain and orbits is essential in staging the disease. However, the definitive diagnosis is only possible through immunohistochemical studies demonstrating biphasic tissue patterns with glial and mesenchymal components of specific stains. Therefore the trained eyes of the experienced neuropathologist are crucial for the correct diagnosis.

Patient consent

Written informed consent was obtained from the patient's mother for publication of this case report and the use of the accompanying images.

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