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Supratentorial Anaplastic Ependymoma with Bilateral Papilledema

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Abstract

Ependymomas constitute the third most common histological type of CNS tumor in children. Compared to classic cellular ependymoma (WHO grade II), anaplastic ependymoma is a more aggressive and less common subtype of ependymal neoplasm. We report a case of a supratentorial anaplastic ependymoma in a child presenting with a right sixth nerve palsy with bilateral papilledema. To our knowledge, the ophthalmic findings presented herein have not been previously reported in the context of this tumor type.

Keywords

Ependymoma, Papilledema, Sixth nerve palsy

Case Report

An 11-year-old Caucasian male with no past medical history presented to his pediatrician with a three-week history of daily, morning headaches accompanied by vomiting. The patient was also noted to have asymmetric eye movements and began to hold books close to his face in order to read. The patient experienced diplopia when looking to the right and needed guidance to walk in unfamiliar places. His ocular history was remarkable for astigmatism that was corrected with spectacles. The patient was referred to an outside hospital for a CT of the head and was subsequently transferred to our facility for treatment.

On examination, his best corrected visual acuity was 20/80 and 20/100, and pupils were 8mm and largely unreactive without an afferent pupillary defect. Intraocular pressures were within normal limits. On extraocular motility testing, no abduction was noted in the right eye, while all other versions and ductions were full. Confrontation visual fields showed a right homonymous hemianopia. His refraction showed a hyperopic shift. The anterior chamber exam was within normal limits. On dilated fundoscopy, florid papilledema, peripapillary hemorrhages, cotton wool spots, and a macular star were noted bilaterally (Figure 1). All retinal veins were dilated and tortuous bilaterally.

An MRI of the brain with and without contrast showed a large 8.5 × 5.4 × 5.8cm heterogeneous, centrally necrotic mass. The space occupying lesion involved the majority of the right temporo-parieto-occipital lobes with significant surrounding edema (Figure 2) The posterior horn of the right lateral ventricle and the third ventricle were compressed, with anterior displacement of the corpus callosum and the adjacent midbrain. A 1.6 cm midline shift to the left was noted without evidence of overt herniation. The patient underwent occipital craniotomy with gross-total resection of the tumor followed by subsequent chemoradiation. Post-operative brain MRI with and without contrast showed post-operative changes with good decompression and improved midline shift and no evidence of residual tumor. Clinically, the patient's visual acuity improved to 20/20 and 20/30; however a persistent bitemporal hemianopsia was present (Figure 3).

Histopathological evaluation of the surgically excised lesional tissue revealed a poorly differentiated, highly cellular neuroepithelial neoplasm with perivascular pseudorosettes, lack of true rosettes,
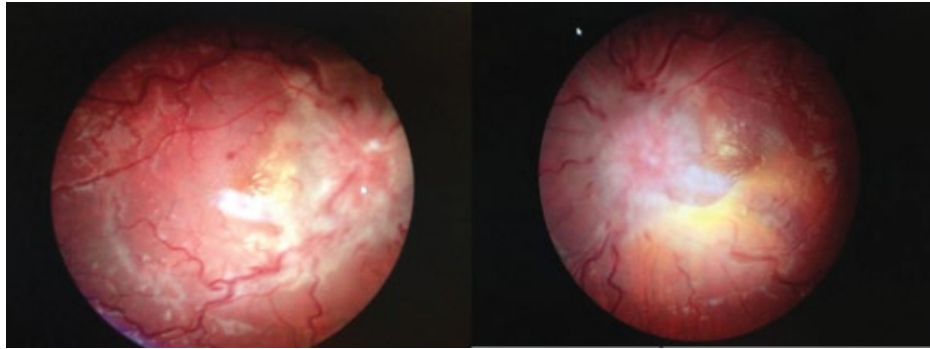
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Figure 1: Extensive bilateral papilledema due to mass effect. Note macular-star exudates and tortuous, dilated vessels due to elevated caval venous pressure.
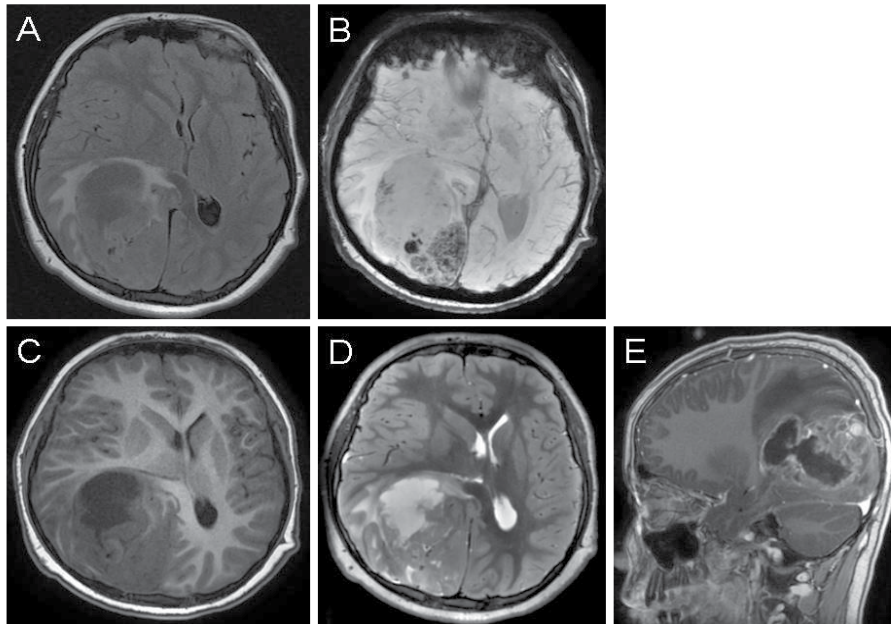

Figure 2: MRI of the brain showing 8.5 x 5.4 x 5.8 cm heterogeneous, centrally necrotic mass at the right temporo-parieto-occipital junction. Panel A depicts extensive vasogenic edema surrounding the mass, with resulting midline shift, seen on fluid-attenuated inversion recovery (FLAIR). Panel B depicts foci of susceptibility artifact seen within the posterior aspect of the lesion on susceptibility weighted imaging (SWI), which can be seen in the setting of hemorrhage or lesional mineralization. Panels C and D depict the centrally necrotic nature of the anterior aspect of the lesion on T1-weighted (C) and T2-weighted (D) imaging. Panel E depicts the rim enhancement of the centrally necrotic anterior aspect and diffuse, heterogeneous enhancement of the posterior aspect of the lesion on post-contrast T1-weighted imaging.
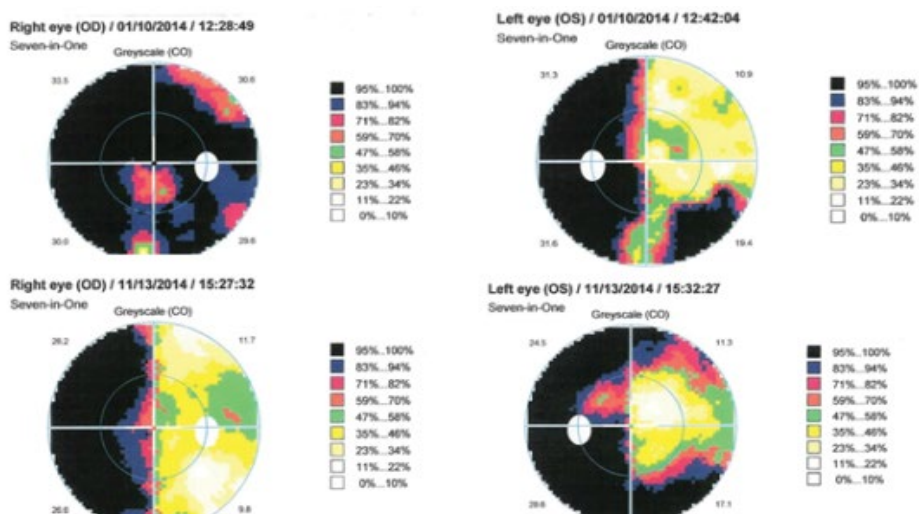

Figure 3: Panels A and B show the preoperative automated visual fields, while panels C and D show the residual post-operative visual field defects.

high mitotic rate, microvascular proliferation, and geographic areas of necrosis consistent with an anaplastic ependymoma (WHO grade III, ICD-O 9392/3) (Figure 4). The Ki-67 proliferative index was high (≥ 30%) (Figure 4C). Ependymal tumor phenotype was confirmed immunohistochemically by intra-cytoplasmic dot-like staining for epithelial membrane antigen (Figure 4D) [1]. Collectively, immunohistochemical studies did not support the diagnosis of a CNS primitive neuroectodermal tumor (CNS-PNET), an embryonal
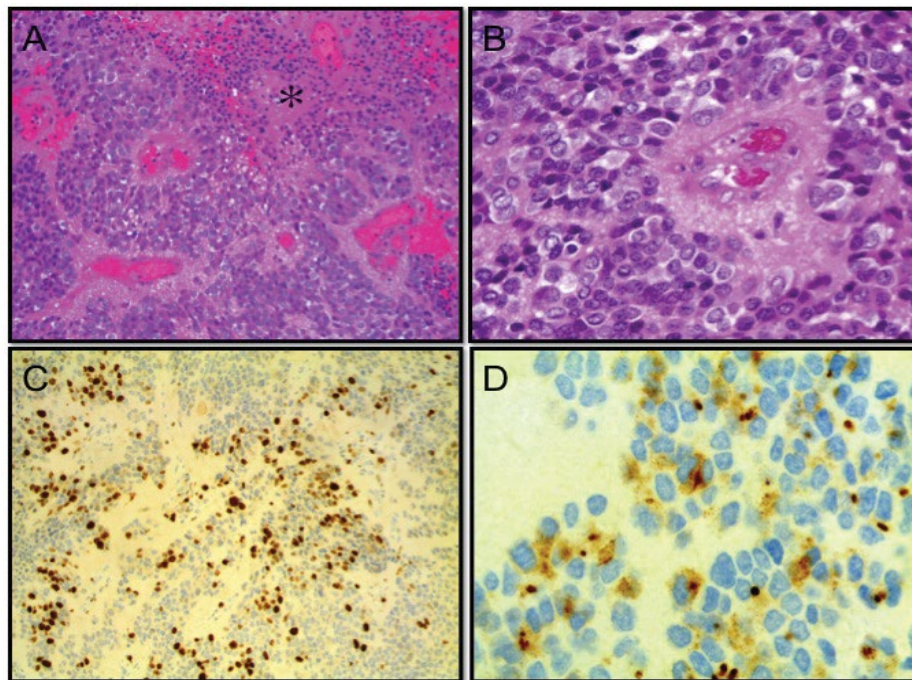
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Figure 4: Panels A and B depict low and high power fields featuring poorly differentiated, highly cellular tumor with perivascular pseudorosettes, vascular proliferation, and geographic necrosis (asterisk in panel A). Panel C shows widespread Ki-67 labeling (brown) of tumor cell nuclei (Ki-67 proliferative index ≥ 30%). Panel D depicts cytoplasmic dot-like staining (brown) for epithelial membrane antigen consistent with an ependymal tumor cell phenotype. A, B: Hematoxylin and eosin staining. C, D: Avdin-biotin comple peroxidase with hematoxylin counterstain. Images in panels A and C were taken with a 20x objective and images in panels B and D were obtained using 40x and 100x objectives respectively.

tumor with abundant neuropil and true rosettes (ETANTR), or an atypical teratoid/rhabdoid tumor (AT/RT) [1]. Genetic evaluation revealed genomic changes XX[cp12] similar to those previously reported in three anaplastic ependymoma cases (two infratentorial and one supratentorial) [2].

Discussion

This case report illustrates an instance of a supratentorial anaplastic ependymoma in a pre-adolescent male presenting with a right sixth nerve palsy with bilateral papilledema. To our knowledge, this ophthalmological presentation has not been previously reported in this clinicopathological setting.

Ependymomas account for 5-12% of primary CNS tumors and are the third most common CNS tumor in children [3,4]. The World Health Organization (WHO) grading scale for ependymal tumors is based on histological features corresponding to WHO grades I through III), with higher stages showing less differentiation, higher mitotic activity, and a tendency to recur after excision [5]. Anaplastic ependymoma is the least common and most aggressive ependymal neoplasm, being considered as high grade (WHO Grade III) [5]. The diagnosis of anaplastic ependymoma (WHO grade III) in the index case was made with the caveat that (a) necrosis of the non-palisading type is also common in grade II ependymomas and that the distinction between non-palisading and palisading necrosis may be subjective; (b) microvascular proliferation is not a required criterion for grade III tumors; and (c) there is no precise cut-off of mitotic counts that would distinguish grade II from grade III tumors of the ependymoma group [1]. Unlike the present case, most anaplastic ependymomas involve the posterior fossa.

Ependymomas comprise multiple genetically distinct disease phenotypes and it is thought that supratentorial ependymomas are largely driven by *EPHB2* gene amplification [6]. Presenting symptoms are secondary to obstructive hydrocephalus. Treatment focuses on achieving near total gross surgical excision and on adjuvant radiation [3,7]. Approximately 65% of patients with ependymoma are cured by surgical resection and adjuvant radiotherapy [8]. Conversely, recurrent disease is not curable in most cases, but prolonged survival

disease-free intervals can be achieved following repeat surgical resection and chemotherapy and/or radiotherapy [9,10].

A recent Children's Oncology Group (COG) study based on a large prospective trial for newly diagnosed ependymoma demonstrated that the extent of surgical resection is a crucial and independent determinant of disease control [11]. Patients who underwent either a near-total resection (i.e., <5mm² residual tumor) or macroscopic gross total resection had a significantly longer 3-year event-free survival compared to those who had only partial surgical resection, irrespective of tumor histological grade or anatomical location [11].

Pathophysiology of Ophthalmic Findings

To the best of our knowledge, the ophthalmic findings have not been previously reported in the context of this tumor type. Our patient displayed signs of increased intracranial pressure, namely an abducens palsy, due to the predominantly right-sided intracranial pressure elevation leading to compression of the homolateral VIth cranial nerve. Concomitantly, the increased intracranial pressure also lead to a decrease in caval venous drainage, causing stasis retinopathy in the retinal vasculature. With the increased resistance, Starling forces reverse with hydrostatic pressure forcing fluid out of capillaries. Clinically, this results in a macular scar and dot-blot hemorrhages. A final consequence of outflow resistance is papilledema. Cerebrospinal fluid egress into the arachnoid villi, and subsequently into dural veins is also limited. Our current understanding of papilledema is that it represents a transfer of intracranial pressure to the optic nerve through the subarachnoid space in the surrounding meningeal coverings [12]. This causes decreased axoplasmic flow and nerve distention. An alternative theory to explain unilateral papilledema in cases of increased intracranial pressure is a compartment-like syndrome that develops in the meninges [12]. On fundoscopic examination, this translates into flame shaped hemorrhages in the nerve fiber layer, optic nerve head elevation, and cotton-wool spots representing nerve fiber layer infarcts.

This report raises awareness of the ophthalmic manifestations and sequelae incurred in the setting of supratentorial ependymomas. It further calls attention to the importance of recognizing the

potential effects of intracranial space-occupying lesions and increased intracranial pressure on ocular structures, most commonly papilledema with an ipsilateral sixth nerve palsy.

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