

Case Report

A case of astroblastoma: Radiological and histopathological characteristics and a review of current treatment options

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Abstract

Background: Astroblastoma is a rare neuroepithelial tumor that often originates in the cerebral hemisphere of children and young adults. Diagnosis of this obscure neoplasm can be difficult because these tumors are so infrequently encountered and share common radiological and neuropathological features of other glial neoplasms. As such, it should be included in the differential diagnosis of astrocytoma and ependymoma if the clinical and radiographic features suggest it. Standardized treatment of astroblastomas remains under dispute because of the lack of knowledge regarding the tumor and a paucity of studies in the literature.

Case Description: We present a case of a low-grade astroblastoma diagnosed in a 30-year-old female with seizures, headache, and vision changes. She underwent gross total resection and, without evidence of high-grade features, adjuvant therapy was not planned postoperatively. Post-operative surveillance suggested early recurrence, warranting referral to radiation therapy. Patient ended up expiring despite adjuvant therapy secondary to extensive recurrence and tumor metastasis.

Conclusions: Astroblastoma must be considered in the differential of supratentorial tumors in children and young adults. Treatment of such, as suggested by most recent literature, includes gross total resection and adjuvant radiotherapy for lesions exhibiting high-grade features.

Key Words: Adjuvant radiotherapy, astroblastoma, brain edema, case report, cerebrum

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INTRODUCTION

First described by Bailey and Cushing in 1926, astroblastomas are rare glial tumors, accounting for approximately 0.4–2.8% of primary brain tumors.^[1] Although classically considered as pediatric brain tumors, astroblastomas tend to display a bimodal incidence with many cases occurring in young adults and some in older patients.^[8] This tumor is commonly found in the frontoparietal hemispheres, although other locations, such as brainstem, cerebellum, hypothalamus,

and intraventricular, have been documented.^[5,7,15,16,20] The clinical presentation is often related to signs of

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elevated intracranial pressure including headaches, nausea, and vomiting. Focal neurological deficits, seizures, and hemorrhage may also exist at the time of presentation. Much confusion has centered on the cell of origin as well as histopathologic criteria for diagnosis because they share features of both astrocytomas and ependymomas.^[17] Recently, it has been determined that these tumors represent a distinct disease entity. Initially, in the 2000 edition of the World Health Organization (WHO) classification, it was considered premature to establish a WHO grade due to the absence of sufficient clinicopathological data. Since then, multiple articles have been published showcasing a variable biological behavior of astroblastoma tumors.^[11,12,19] The 2007 update of the WHO classification describes astroblastoma as a neuroepithelial tumor of unknown origin, but was again unable to assign a proper grade.^[13] The most recent revision describes astroblastoma as a high-grade (grade 4) neuroepithelial tumor of unknown origin.^[9] Despite this, controversy persists as more recent works analyzing long-term data demonstrate a 95% survival rate following gross total resection.^[3,12,20] There are no established guidelines for the treatment of astroblastomas, and therapy has ranged from radiotherapy alone to subtotal resection to gross total resection with or without adjuvant chemo/radiation. The lack of knowledge and consensus regarding therapeutic modalities create problems when attempting to provide timely and appropriate treatment for these rare tumors. We present a case of an astroblastoma in a young woman, focusing on neuroimaging and neuropathological features in comparison to other central nervous system (CNS) tumors, while also reviewing the most recent management options.

CASE REPORT

A 30-year-old woman presented with a seizure, right scalp paresthesias, a right-sided headache, blurred vision, and nausea. Her neurological examination was unremarkable, however, formal ophthalmological testing demonstrated left homonymous quadrantanopsia. She underwent a non-contrast computed tomography (CT), with results indicating an intracranial neoplasm. Subsequently, magnetic resonance imaging (MRI) of the brain with intravenous (IV) gadolinium was obtained, which demonstrated a 6.1 cm heterogeneously enhancing mass in the posteromedial aspect of the right temporoparietal lobes protruding into the right atrium. It displayed mixed T1 and T2 signal intensity with regions of restricted diffusion. There was mild peritumoral T2 hyperintensity, signifying peritumoral edema. A large area of gradient susceptibility along the posterior aspect of the lesion represented calcifications [Figure 1]. The patient underwent a diagnostic cerebral angiogram to rule out a vascular abnormality and to delineate blood supply to

the lesion. The angiogram was negative for aneurysm or arteriovenous malformation (AVM) and demonstrated a contrast blush in the region of the lesion.

The patient subsequently underwent a right craniotomy for biopsy and partial resection, with initial pathology described as a low-grade astrocytic tumor. She continued to be symptomatic with headaches and underwent complete resection 2 months later; the macrocalcification was left behind due to tethering of normal brain tissue. Postoperatively, she had persistent resection cavity fluid collections, as well as a trapped right temporal horn. She subsequently underwent cystoperitoneal shunt placement. Postoperatively, she required one proximal revision of her shunt secondary to malfunction, but otherwise remained clinically stable with resolution of her headaches and no additional neurological deficits. Three months after the resection, imaging follow-up demonstrated interval enhancement of the surgical cavity, suggestive of local recurrence. Histologically, the tumor demonstrated epithelioid cells with short cytoplasmic processes arranged in perivascular pseudorosettes. Minimal mitotic activity was observed with PHH3, and no high-grade features were identified. The neoplasm was positive for glial fibrillary acidic protein (GFAP), synaptophysin, and Olig2; IDH1 was negative, similar to the staining profiles reported in recent literature [Figure 2]. Taken together, the imaging and pathology findings were most consistent with a low-grade astroblastoma. Radiation therapy was undertaken and in the interim repeat imaging demonstrated significant recurrence. Patient was taken for further resection and continued postoperatively with adjuvant radiotherapy. Patient carried a poor prognosis despite continued treatment and decided to transition to palliative treatment and subsequently expired 4 months after the final resection.

DISCUSSION

In the most recent updated WHO classification of CNS tumors, astroblastomas are classified in the category of “other neuroepithelial tumors,” formerly designated as neuroepithelial tumors of uncertain origin.^[9,13] The latter is attributed to the fact that the proposed cell of origin (tanycyte) shares features of both astrocytomas and ependymomas.^[18] Histologically, spindle-shaped cells with short, broad tapering processes are arranged in a perivascular pattern forming pseudorosettes, reminiscent of ependymomas.^[16] These tumors stain positive for vimentin and S-100, which is more characteristic of an astrocytic origin.^[3,17] Astroblastomas are also GFAP, epithelial membrane antigen (EMA), cytokeratin, and Olig2 positive, and are negative for IDH1/2 and TP53 mutations.^[8] Given these myriad histopathological features, astroblastomas are considered by some to be a unique tumor that shares more features with

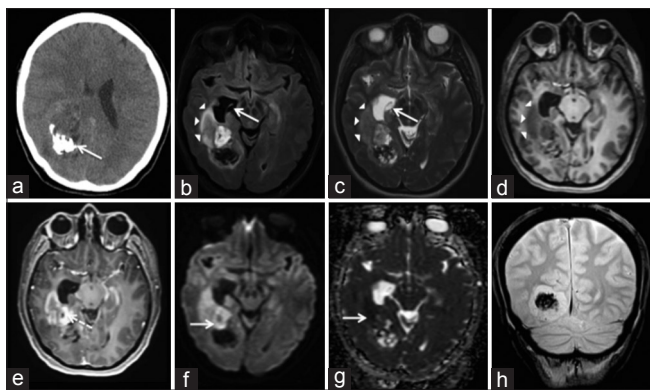


Figure 1: Astroblastoma – Axial NECT (a) shows a heterogeneous mass in the right temporal lobe with calcification (arrow). Axial FLAIR (b), T2W (c), and TIW pre-contrast (d) images show T1 & T2 prolongation in the right temporal lobe (arrowheads) and right temporal horn. There is dilation of the right temporal horn (arrow). The TIW post-contrast image (e) shows lesion enhancement and enhancement of cysts (dotted arrow). There is diffusion restriction (arrow) on DWI (f) and ADC (g). The coronal gradient T2* image (h) shows a region of susceptibility artifact compatible with calcification.

ependymomas versus astrocytomas. Because of the lack of clinicopathologic correlation and the updated WHO classification of a grade 4 neoplasm, it is imperative that more rigorous follow-up be considered. With respect to the tumor grade and, thus, therapeutic options, differentiation of low and high-grade tumors is based on features such as the mitotic rate and degree of cellular atypia and necrosis. In addition, the existence of two distinct cellular zones has been described.^[8] The first zone comprises layer(s) of cells around blood vessels with extensive sclerosis (astroblastoma pseudorosettes). These cells are GFAP and S-100 positive and demonstrate a low Ki-67 index. The second zone is highly cellular with distinctly fewer rosettes and contains non-cohesive cells depicting a more rhabdoid appearance. This region is also S-100 positive but negative for GFAP and has a higher Ki-67 labeling index. The latter zone confers a higher grade to the diagnosis and as such would warrant consideration of adjuvant radiotherapy in addition to resection.

Demographics can be helpful in differentiating astroblastoma from other tumors. A bimodal distribution is commonly observed, with the majority of reported cases occurring in patients between 10 to 30 years of age.^[4] This is in contrast to glioblastoma multiforme (GBM), meningioma, and oligodendroglioma, which affect older adults, while ependymoma and atypical teratoid rhabdoid tumor (ATRT) are often found in younger children. There is also a female predominance among patients diagnosed with astroblastoma.^[3,6,20]

Imaging findings can offer additional clues to support the diagnosis and prognosis. Astroblastomas often demonstrate T1 and T2-prolongation relative

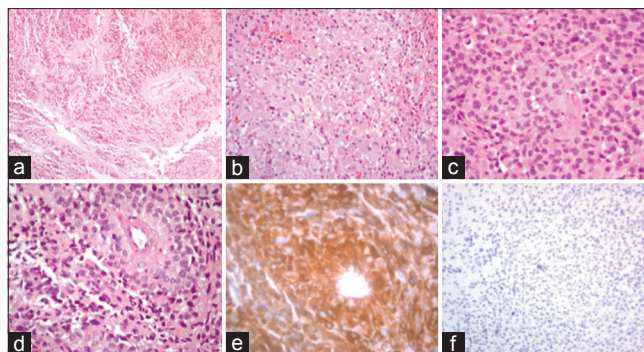


Figure 2: Astroblastoma Immunohistochemistry – x100, x200, and x400 hematoxylin and eosin (H&E) staining depicting epithelioid cells of the astroblastoma (a-c). x400 H&E staining demonstrating astroblastoma cells with short cytoplasmic processes arranged in perivascular pseudorosettes (d). x400 GFAP+ staining (e). x200 PHH3 positive staining at (f)

to white matter, with well-demarcated boundaries and heterogeneous contrast enhancement.^[3,17] The enhancement characteristics can help set it apart from meningiomas, which tend to exhibit a homogeneous enhancement. Their characteristic supratentorial location also helps set them apart from ependymomas, which usually involve the posterior fossa. Calcifications are a consistent imaging finding, and would be unusual for GBMs and ATRTs. Although once thought to be predominantly punctate, our case demonstrates globular calcifications, which may be a favorable prognostic feature.^[11,17] Astroblastomas tend to be peripherally oriented and may involve or arise primarily from the ventricular system.^[3] In these instances, additional imaging of the neural axis should be considered to exclude drop metastases.^[10] Although rim enhancement seen around its cystic components may resemble that of a necrotic GBM, astroblastomas usually have minimal peritumoral white matter T2-prolongation. However, in a recent article by Janz and Buhl, the extent of peritumoral edema was considered an unfavorable radiological feature that suggested early recurrence or progression in astroblastoma, even when initial pathology is consistent with low grade. The authors demonstrated a recurrence rate of 23.5% in high grade vs. 60% in low-grade, although the recurrences in low grade astroblastomas were highly correlated with preoperative peritumoral edema on MRI.^[11]

As a consequence of their extreme rarity, comprising a few hundred reported cases, astroblastomas present a challenge in terms of diagnosis and selection of appropriate treatment.^[1,11,20] There currently exists no Class I–III clinical evidence to guide treatment and the optimal mode of therapy remains disputed. In the largest series to date ($n = 239$), Ahmed suggested that surgery is superior to radiation alone and the combination of both did not improve survival.^[1] Other authors support GTR as the optimal way of treating a

low-grade astroblastoma.^[2,18] In a review of 85 patients by Sughrue *et al.*, those undergoing GTR experienced improved survival compared to those undergoing subtotal resection, with 85% survival at 5 years in the gross total resection group vs. 55% in the subtotal resection group.^[20] Alternatively, Shen *et al.* suggests approaching treatment along the National Comprehensive Cancer Network guidelines for low-grade infiltrative supratentorial astrocytoma/oligodendroglioma with gross total resection being the goal, followed by radiation or chemotherapy for high-risk patients.^[19] Utilization of adjuvant therapy for high-grade lesions is supported by other authors.^[18] Mangano, for instance, analyzed outcomes and treatment strategies in low and high grade astroblastomas; among the patients with high-grade tumors, those who received surgery and radiotherapy had the highest survival rate.^[14]

Certain indices suggestive of high grade/malignant lesions include the extent of peritumoral T2 signal on MRI, cytological atypia, high Ki-67 labeling index, tumor necrosis, increased cellularity, and vascular proliferation.^[8,12] The absence of these features in the present case helped guide our initial decision for gross total resection in the setting of a low-grade tumor. However, such prognostic criteria are not always reliable. Janz and Buhl present a case in which there was early recurrence of a low-grade variant that warranted postoperative radiotherapy with no further recurrence.^[11] Lau *et al.* and Yao *et al.* describe low-grade astroblastomas treated with GTR that recurred at 12 and 20 months, respectively, warranting another operation followed by adjuvant radiotherapy.^[12,21] Similarly, our patient had little peritumoral edema on imaging and a staining profile consistent with a low-grade tumor. Nevertheless, on follow-up she demonstrated signs of recurrence, including diffuse leptomeningeal spread on imaging, for which adjuvant radiotherapy was pursued. Our case ultimately demonstrated features suggestive of a higher-grade neoplasm that warranted more aggressive therapy. As discussed above, treatment for astroblastoma is variable without any standardization. With our patient ultimately succumbing to her disease following a delay in therapy, implementation of adjuvant radiotherapy during treatment of this neoplasm is emphasized.

CONCLUSIONS

When encountering a well-demarcated supratentorial mass with heterogeneous enhancement and macrocalcifications in a child or young adult, astroblastoma should be considered in the differential diagnosis. Based on the micro/macrosopic features, clinicians should address this tumor more along the lines of ependymoma with respect to treatment, with gross total resection being the primary goal. In the same manner, despite the lack of standardized treatment

protocols, the literature indicates that gross total resection provides the best outcome for low grade lesions, which can be followed closely with imaging, while adjuvant radiotherapy should be offered for high risk patients presenting with significant peritumoral preoperative edema on T2 sequences and high grade histopathological features. However, close follow-up is recommended because tumors with low-grade features have been shown to recur and warrant additional treatment.

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Conflicts of interest

There are no conflicts of interest.

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