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Case Report

# A Rare Case of a High-Grade Astroblastoma with 5-Year Follow-up

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**Abstract**

Astroblastoma is a very rare glial tumor derived from astroblasts. It has been controversial in terms of its features and diagnosis. The objective of this report is to present the findings of the high-grade astroblastoma with a good prognosis in a 21-year-old female who presented to us with diplopia and headache. While imaging led to the foremost differentials of pleomorphic xanthoastrocytoma and Ganglioglioma which are low-grade neoplasms, the final diagnosis was established on microscopy and immunohistochemistry after excision. Treatment protocol included surgery with postoperative radiotherapy and chemotherapy. Due to controversial and limited literature, this tumor poses difficulties in diagnosis and management. This is a rare, successfully managed case of astroblastoma with a positive outcome 5 years after the diagnosis was established. In this case report, we review the steps of diagnosis, the differentials, the pathological and histological features, and the management of this rare entity.

**Keywords:** *Astroblastoma, brain neoplasm, neuroepithelial, prognosis, treatment outcome*

## Introduction

Astroblastoma is a rare neuroepithelial tumor associated with ambiguity in diagnosis and treatment, with very few cases reported in the Indian demographic.[1] The tumor is usually seen in the cerebrum and can be classified into two grades based on histological and pathological features. While the low-grade tumors have a good prognosis, the high-grade tumors usually have a poor prognosis with majority of the cases not surviving beyond a year.[2] This is a case of a high-grade astroblastoma in a 21-year-old female with a good prognosis and full functionality after 5 years. This case has been presented due to its rarity, difficult, and ambiguous diagnosis as well as unique long-term survival of the patient.

## Case Report

A 21-year-old female from Chengalpattu district, Tamil Nadu, presented with complaints of headache for 2 weeks and diplopia for 1 week. Computed tomography scan showed an intracranial lesion. Magnetic resonance imaging (MRI) brain and magnetic resonance venography were performed and revealed a large cortical-based intra-axial lesion of size 5.7 cm × 5.3 cm × 4.4 cm in the left frontal lobe, causing a significant midline shift to the left [Figure 1]. The lesion was predominantly cystic, with suppression on fluid-attenuated inversion recovery (FLAIR) with a peripherally based heterogeneous mural nodule showing intense contrast enhancement. Few areas of blooming, suggestive of calcification, were noted with adjacent dural thickening with no perilesional edema. Spectroscopy showed a reversal in choline -creatine* ratio, with a reduction in N-Acetyl Asparatate (NAA) and an increase in lipid and lactate, which is suggestive of a glioma. Due to the presence of a cystic lesion with a mural nodule, there was a high suspicion of pleomorphic xanthoastrocytoma and ganglionoma, both of which are less aggressive tumors warranting a conservative approach. After much discussion, the decision to go with gross total resection was taken, as a precaution. The gross specimen was 4 cm × 3 cm × 1 cm with multiple cystic spaces and soft tissue fragments. On microscopy, a tumor of oval cells with moderate eosinophilic cytoplasm, arranged in sheets along with papillae and tubules, was viewed [Figure 2]. Most of the nuclei were round, with coarse chromatin, and only some had eosinophilic inclusions [Figure 3]. Perivascular



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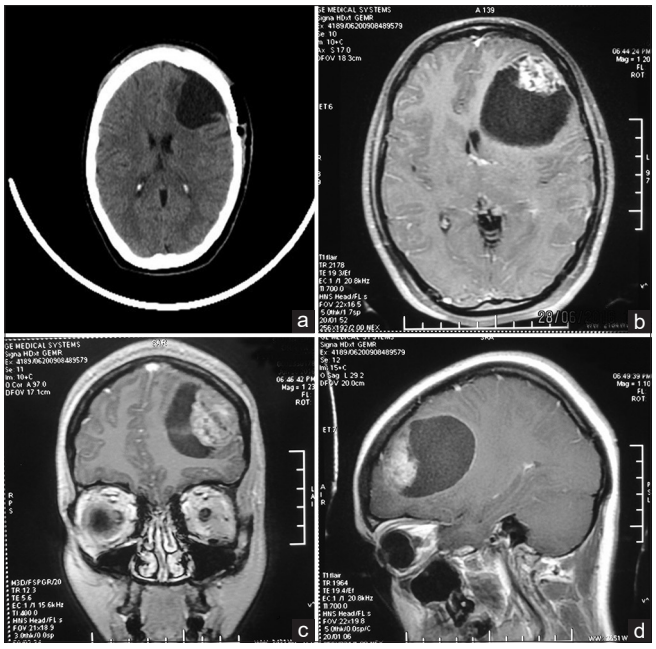

**Figure 1: Cranial computed tomography and magnetic resonance imaging revealed a large cortical-based lesion of approximate size 5.7 cm × 5.3 cm × 4.4 cm in the left frontal lobe, causing a significant midline shift to the left. The lesion is predominantly cystic, with suppression on fluid-attenuated inversion recovery with a peripherally based heterogeneous mural nodule showing contrast enhancement. (a) Computed tomography scan showing tumor, (b) magnetic resonance imaging axial, (c) magnetic resonance imaging coronal, (d) magnetic resonance imaging sagittal**

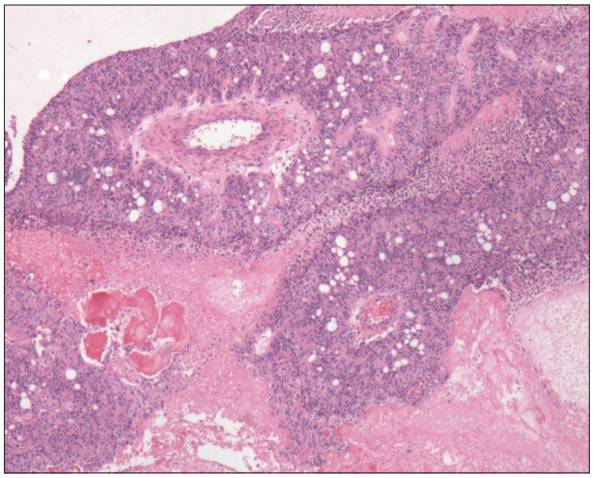

**Figure 3: Microscopic appearance: Tumor composed of perivascular rosettes and surrounding tumor necrosis (H and E, ×200)**

pseudorosettes were also seen [Figure 3]. Mitotic figures and necrosis were visible. Immunohistochemistry was performed, and the tumor cells were positive for glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA), and synaptophysin, suggesting a glial origin. Positivity for S100 and chromogranin was also noted. In addition, IDH1 and IDH2 were negative. Ki67 labeling index was high (approximately 50%), indicating active proliferation of tumor cells [Figure 4]. Due to the vascularity, necrosis, and high tumor turnover indicated by ki67, this tumor was classified as a high-grade

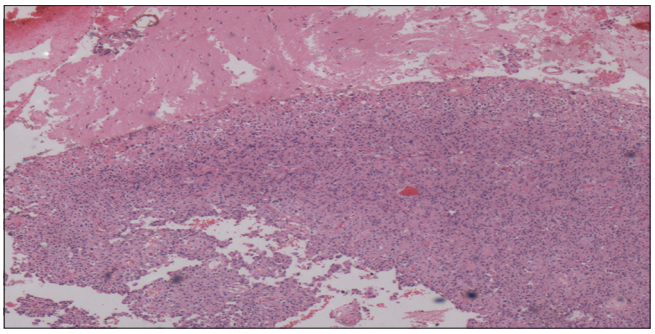

**Figure 2: Microscopic appearance: Compact tumor in sheet along and tubules abutting adjacent normal brain parenchyma (H and E, ×100)**

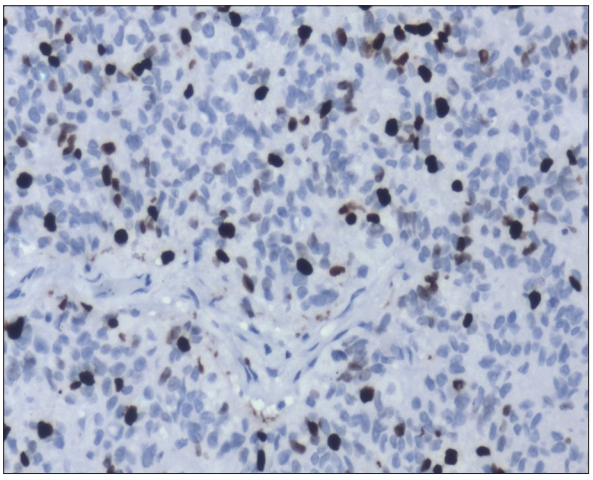

**Figure 4: Immunohistochemistry: High Ki67 labeling index indicating increased proliferation of tumor cells (immunohistochemistry; ×400)**

tumor. Postoperative radiation therapy was performed. The patient was given three cycles of postoperative adjuvant radiotherapy and temozolomide-based (TMZ) chemotherapy at another center. Five years later, the patient is on postoperative medication including antiepileptics, reports no complications, and is going for regular work. Informed consent was obtained from the patient for case report.

## Discussion

Astroblastoma is an extremely rare glial tumor accounting for only 0.45%–2.8% of all brain gliomas.[1,3] It is most commonly seen in the cerebral hemispheres, but rarely, it can be localized to the cerebellum or brainstem.[3] Supratentorial tumors are generally associated with a worse prognosis than infratentorial tumors.[4] It was first described by Bailey and Cushing in 1926, then revised by Bailey and Bucy in 1930.[5] Since then, there have been less than a few hundred confirmed cases of this tumor in the world.[5,6]

It is now believed to originate from astroblasts, an intermediate cell between glioblasts and astrocytes. There was initially some controversy in its origin due to Russell and Rubenstein's theory of its origin from the dedifferentiation from mature cells.[7-9] It is now classified

under "other gliomas" in the "2016 WHO Classification of tumors in the Central Nervous system."[9] Most of the cases fall within a bimodal distribution, with two peaks between the ages of 5–11 and 21–30; our patient falls within the second peak.[10] The tumor also shows a female predominance.[10] It usually shows up on an MRI as a solid–cystic lesion, as seen in our case.

There has been much controversy as to whether astroblastomas should be assigned a separate entity; however, recent studies reveal that there are some pathological features that distinguish it from other tumors.[11] The features include a characteristic 'bubbly' appearance which is due to its vasculature. Other features are the presence of perivascular pseudorosettes, spaces between the rosettes and hyalinization of vessels.[10,11] Some tumors show calcifications, but it is an uncommon finding. Many cases also show eosinophilic inclusions, such as eosinophilic granular bodies, hence boding similarity to oligodendrogliomas and astrocytomas.

Immunohistochemistry is highly variable, showing positivity for GFAP and EMA in most cases and vimentin and S100 in some, all of which were positive in our case.[10,12] Recently it was discovered that most astroblastomas do not express IDH1 or IDH2 which is seen in many low grade gliomas. Many astroblastomas show Olig2 expression.[12] Studies also show that the lack of IDH1 in astroblastoma bodes similarities to ependymomas, which suggests a possible origin from ependymoglial cells.[13] Recently, the expression of BRAF V600 was found in 1/3 of the cases tested, opening up the possibility of targeted molecular therapies.[12] The expression of neuron-specific enolase, EMA, cytokeratin, and CAM 5.2 expression is highly inconsistent.[12] Recent developments show other molecular targets, which has not yet been studied extensively like MGMT promoter methylation, which could also be used to derive targeted therapies in the future.[12] A case series reported a *MN1* (meningioma 1 gene) rearrangement detected by Florescent *in situ* hybridization in five out of eight cases tested, which can be a potential confirmatory immunohistochemistry marker.[14]

Astroblastoma can be divided into low-grade and high-grade subtypes, both of which have their distinction in features and prognosis.[15] The low-grade variety has a well-ordered growth pattern with no necrosis and the high grade shows a degree of anaplastic growth, pseudopalisading necrosis, and high cellular atypia. The low-grade tumors have a good prognosis, while the high-grade tumors have a comparatively poorer outcome with a lower survival rate according to one of the first case series by Bonnin and Rubinstein in 1989, where five out of eight patients in the low-grade category survived for 3–20 years and all the patients in the high-grade category died within 2 years.[11] There have been some studies that report a long-term survival for a high-grade astroblastoma,[16] but most report a lower survival rate and increased rate of recurrence.[10,11,17] According to Barakat *et al*., the overall survival rate of astroblastomas is reported to be 2.4 years, with a recurrence rate of 34%.[18]

The treatment protocol is ambiguous due to the paucity of cases, but surgery is the mainstay of treatment. It is very difficult to make a diagnosis with radiology as it presents a relatively benign tumor and bodes many similarities to other CNS tumors. Therefore, clinicians must exert a high level of suspicion while determining the treatment protocol as a subtotal resection may lead to a different outcome. High-grade tumors also require adjuvant radiotherapy as seen in our case. This has also been met with some controversy since the largest review of astroblastomas states that the radiotherapy has no therapeutic benefit.[4,19] There are contradicting views about the role of chemotherapy in the management of astroblastoma. Some studies state that there is no clear benefit of adjuvant chemotherapy in both low- and high-grade tumors,[18] while others show some improvement.[17] Many studies have used a combination of etoposide, cisplatin, and cyclophosphamide therapy with no significant results. In recent years, TMZ-based chemotherapy has shown promise, but there is no conclusive evidence about its efficacy.[20] In our case, the combination of surgery with adjuvant radiotherapy and chemotherapy showed good results with full recovery of the patient, unlike other similar cases.[13,18,19]

## Conclusions

Astroblastoma is a rare and challenging tumor to diagnose and manage and requires a multidisciplinary team of surgeons and pathologists to make the diagnosis. The team must exert a high level of suspicion when planning treatment as it initially presents as a low-grade lesion. In addition, most cases of high-grade astroblastoma have a very poor prognosis. Hence, gross total resection with adjuvant radiotherapy is currently the best protocol for this tumor.

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### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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