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Case Report

Anaplastic pleomorphic xanthoastrocytoma in a 12-year-old with early leptomeningeal dissemination: a rare pediatric case report from Central India

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ABSTRACT

Pleomorphic xanthoastrocytoma (PXA) is a rare glioma subtype, making up less than 1% of astrocytoma, mainly affecting young adults. It typically appears in solid, cystic, or mixed forms in the supratentorial region, especially the temporal lobe, with a peak onset around age 20. Reported cases describe cerebrospinal fluid dissemination, often occurring months after diagnosis. We report a case of 12-year-old boy presenting with headache and vomiting for over a month, with no significant medical or family history. Magnetic resonance imaging brain showed lesion in the right fronto-parietal region. He underwent surgery to excise the lesion, which was diagnosed as a PXA, classified as World Health Organization (WHO) grade 3. Immunohistochemical analysis indicated positivity for ATRX, H3K27me3, and p53 protein suggesting high-grade glial tumor. After surgery, he had recurrence of headache within a month. Follow-up magnetic resonance imaging revealed residual tumor, leading to second surgery for tumor re-exploration. He received adjuvant radiation therapy and chemotherapy with Temozolomide. Despite treatment, he re-developed symptoms, and further imaging showed metastasis in the left medial temporal lobe and lumbar spine. Unfortunately, he did not respond to chemotherapy and passed away within a month. This case highlights the complex behavior of PXA, which complicates disease management. It denotes surgical excision alone is inadequate and should be complemented by spine staging scans and radiation therapy. Poor prognosis indicators include necrosis, high mitotic activity and incomplete resection underscoring the need for comprehensive treatment approach.

Keywords: Anaplastic pleomorphic xanthoastrocytoma, Pediatric glioma, Leptomeningeal dissemination, WHO CNS grade 3, Drop metastasis

INTRODUCTION

Pleomorphic xanthoastrocytoma (PXA) is an uncommon astrocytic tumor, accounting for less than 1% of all astrocytomas, and predominantly affects children and young adults. These tumors are typically supratentorial, with a predilection for the temporal lobe, and often present as superficial cortical lesions with solid, cystic, or mixed components. Seizures are the most frequent presenting symptom, reflecting their cortical location. Despite being traditionally considered a low-grade neoplasm with a relatively favorable prognosis, PXAs demonstrate a variable clinical course, with potential for recurrence, malignant transformation, and cerebrospinal fluid (CSF) dissemination, particularly in tumors exhibiting anaplastic features.

Kepes et al first described PXA in 1979 as a distinct clinicopathological entity characterized by marked cellular pleomorphism, lipid-laden astrocytes, and a rich reticulin network.[1] Subsequent studies have identified a subset of PXAs with aggressive histological features, now classified as anaplastic pleomorphic xanthoastrocytoma (APXA). These tumors are associated with higher mitotic activity,

increased proliferative indices, early recurrence, and poorer outcomes.

Herein, we report a rare pediatric case of anaplastic pleomorphic xanthoastrocytoma in a 12-year-old male, notable for rapid postoperative recurrence and early leptomeningeal dissemination, highlighting the aggressive biological behavior and therapeutic challenges associated with this entity.

CASE REPORT

A 12-year-old male child presented with complaints of progressively worsening holocranial headache and recurrent episodes of vomiting for over one month. There was no history of seizures, trauma, prior neurological illness, or significant family history.

Magnetic resonance imaging (MRI) of the brain revealed a large heterogeneously enhancing mass lesion measuring 5.8×8.1×7.1 cm involving the right fronto-parietal region, centrum semiovale, corona radiata, and gangliocapsular area, with associated mass effect and compression of the right lateral ventricle. Acute lacunar infarcts were noted in the splenium of the corpus callosum (Figures 1 and 2).

The patient underwent a right fronto-temporo-parietal craniotomy with gross tumor excision. Histopathological examination revealed features consistent with pleomorphic xanthoastrocytoma with anaplastic characteristics. Immunohistochemistry showed tumor cells positive for ATRX, H3K27me3, Olig-2, CD34, and p53, with a Ki-67 labeling index of 11.2% and MIB-1 index of 8–10%. Tumor cells were negative for IDH1 R132H mutation. Based on histomorphology and proliferative index, a diagnosis of anaplastic pleomorphic xanthoastrocytoma was rendered.

Within one-month post-surgery, the patient redeveloped symptoms of headache. Repeat contrast-enhanced MRI brain demonstrated a residual enhancing lesion measuring 3.9×2.8×4.6 cm in the right fronto-parietal region. The patient underwent re-exploration and excision of residual tumor, following which postoperative contrast-enhanced computed tomography (CT) scan confirmed the absence of residual disease (Figure 3).

Adjuvant treatment was initiated with intensity-modulated radiotherapy (IMRT) to a dose of 59.4 Gy in 33 fractions, delivered concurrently with temozolomide (75 mg/m² daily). This was followed by maintenance temozolomide, during which the patient was kept on close monthly follow-up.

After seven months of maintenance chemotherapy, the patient presented with new onset headache and back pain. MRI of the brain and lumbosacral spine revealed multiple enhancing metastatic deposits involving the left medial temporal lobe, falx cerebri, fourth ventricle, and dural-based nodular lesions at L2 and L4 levels measuring 4.7×3.7 mm and 4×3.2 mm consistent with leptomeningeal drop metastases (Figure 4). Despite initiation of second-line chemotherapy, the disease progressed rapidly, and the patient succumbed to the illness within two months.

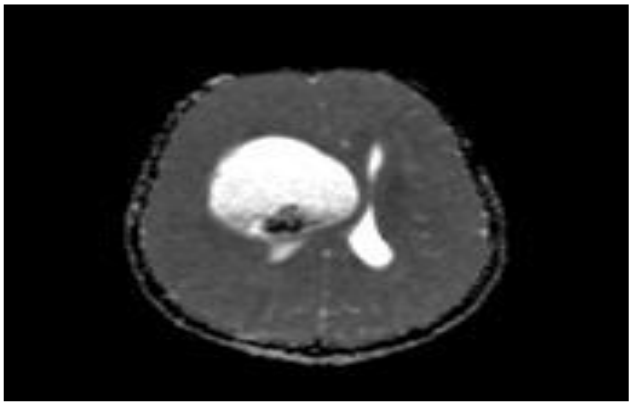

Figure 1: T2-weighted MRI brain (P+C), axial view showing a cystic lesion in the frontoparietal lobe causing significant compression of the right lateral ventricle.

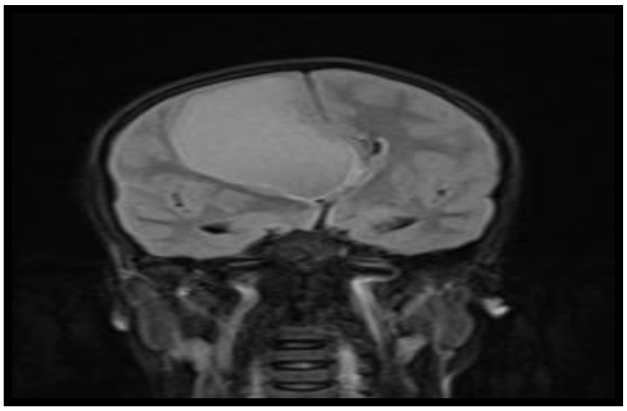

Figure 2: T1-weighted MRI brain (P+C), coronal view showing a cystic lesion in the frontoparietal lobe causing significant compression of the right lateral ventricle.

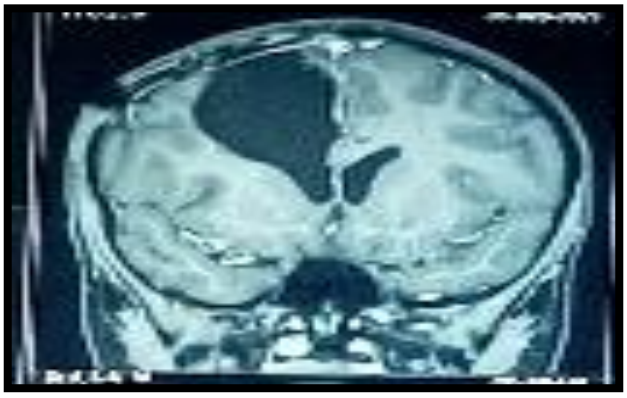

Figure 3: Coronal T1-weighted contrast-enhanced MRI showing postoperative cavity with CSF signal intensity in the right frontal lobe.

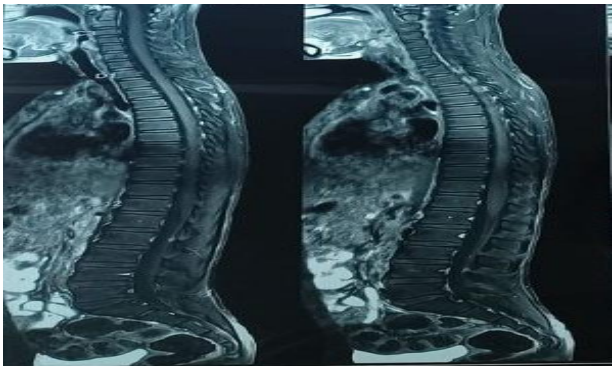

Figure 4: T2-weighted contrast-enhanced MRI of the whole spine showing isointense nodular deposits at L2 and L4 levels.

DISCUSSION

PXA is a rare primary glial tumor that is predominantly benign in nature. WHO CNS 2021 classification recognizes anaplastic pleomorphic xanthoastrocytoma as WHO grade 3 tumor with defined molecular features. PXA primarily affects children and young adults and most commonly arises in the supratentorial compartment, particularly within the temporal lobe. Seizures are the most frequent presenting symptom due to cortical involvement.[2] Histopathologically, PXA is characterized by marked cellular pleomorphism, the presence of lipid-laden xanthomatous cells, perivascular lymphocytic infiltration, and an abundant reticulin network. Features such as increased mitotic activity and necrosis are associated with more aggressive tumor behavior and poorer outcomes.

The clinical manifestations of PXA can be broadly divided into localizing and non-localizing symptoms. Localizing symptoms reflect the involvement of specific neuroanatomical regions, with seizures being the most common initial presentation. Non-localizing symptoms result from raised intracranial pressure and include headache, nausea, vomiting, diplopia, and somnolence. Although uncommon, dissemination through the CSF has been reported, particularly in cases of progressive or recurrent disease.[3] A subset of PXAs exhibit anaplastic features. The term "PXA with anaplastic features" was first introduced in 1999. Giannini et al proposed diagnostic criteria for anaplastic PXA, defining it as a tumor demonstrating a mitotic count of five or more mitoses per 10 high-power fields, with or without necrosis.[4] Hirose et al further emphasized the role of necrosis, microvascular proliferation, marked cellular anaplasia, and a high Ki-67 labeling index in identifying anaplastic variants.[5] In the present case, the Ki-67 labelling index was 11.2%, fulfilling the criteria for anaplastic PXA.

In the 2016 WHO classification, APXA was formally recognized as a distinct entity and assigned WHO grade III status, defined by a mitotic activity exceeding 5 mitoses per 10 high-power fields. APXA remains an exceptionally rare tumor. Choudry et al reviewed adult cases of primary APXA reported between 1979 and 2016 and observed a mean interval of 14 months between diagnosis and tumor recurrence.[6] Histologically, anaplastic PXAs often show lymphocytic infiltration, pseudopapillary architecture, and extensive necrosis. Importantly, the presence of anaplastic features may indicate a propensity for malignant progression, including transformation to glioblastoma.[7-9] Consequently, PXAs presenting with anaplastic features are generally associated with an unfavorable prognosis at diagnosis.[10]

Radiologically, conventional PXAs typically appear as well-circumscribed lesions with cystic and solid components, displaying iso- to hypointensity on T1-weighted images, hyperintensity on T2-weighted images, and heterogeneous contrast enhancement. In contrast, anaplastic PXAs may demonstrate atypical imaging characteristics and show early dissemination either at presentation or following treatment.[11] Previously reported cases have been summarized in Tables 1 and 2. To date, 17 cases of PXA presenting with anaplastic features at initial diagnosis have been described in the literature.[12]

Table 1: Previously reported cases.

Authors, year	Patients' details	Location	Surgery	RT	CT	Recurrence	Outcome/total survival
Jones et al 1983[18]	14/F	P	GTR	45 Gy	-	15 months	Died/2 years
Goldring et al 1985[19]	24/F	T	STR	-	12 months	-	Died/1 year
Grant et al 1986[20]	17/F	P	GTR	-	-	-	Died/1 month
Iwaki et al 1987[21]	30/M	PO	GTR×2	60 Gy after 2nd with spinal RT	-	6 months	Alive/10 months
Gaskill et al 1988[22]	10/F	TP	-	-	-	-	-
Bavinder et al 1997[23]	9/M	T	GTR	RT after 1st recurrence	-	6, 10, 15 months	Died/16 months
Perry et al 1997[4]	18/M; 82/M	T; F	STR×4; GTR	Cranial RT after 1st	CT after 1st	3 recurrences in 4 years	Died/4 years; lost to follow up

Continued.

Authors, year	Patients' details	Location	Surgery	RT	CT	Recurrence	Outcome/total survival
Tonn et al 1997[24]	18/M	TO	GTR×2	60 Gy after 1st	After 1st	8 months	Alive/2.5 years
Chakroborthy et al 1999[25]	49/M; 40/M	TP; T	STR; GTR	Yes; yes	-; -	-; -	Alive/3 months
Lubansu et al 2004[10]	7/F	T	GTR	-	Yes	4 weeks	Alive/26 months
Tekkok et al 2004[26]	13/M	F	STR	-	-	-	Died/4 months
Chang et al 2006[27]	4/F	Cerebe-llum		Yes	Yes	-	Alive/12 years
Okazaki et al 2009[2]	5/M	F T spine diffuse nodules	Biopsy	-	Yes 12 cycles	-	Alive/3 years
Koga et al 2009[8]	47/F	F	GTR	SRS for all relapses	For 2nd relapse	20, 40, 47, 60 months	Died/66 months
Tsutsumi et al 20108[29]	16/F	FT	STR	56 Gy IMRT	Yes Temozola mide	17 months	Died/20 months

Table 2: Summary from the previously reported cases.

Parameter	Value
Total cases	17
Gender – male: female	9:8
Mean age at presentation	23.5 (4–82 years)
Site	
Frontal	3
Temporal	5
Parietal	2
Frontotemporal	2
Temporoparietal	2
Temporoparietal	1
Cerebellum	1
Spine	1
Histological confirmation	All cases
Necrosis	12
Surgery	17
Biopsy	1
Partial resection	7
Gross total resection	9
Radiation	10
Linear accelerator	8
IMRT	1
SRS	1
Chemotherapy	8
Died	8
Mean survival	26.1 (1–66 months)
Conventional radiotherapy	8
IMRT	1
SRS	1
Chemotherapy	8
Leptomeningeal dissemination	2
Mean time for 1st recurrence	11 (1–20 months)

In the present case, the tumor demonstrated classical radiological features, including a cystic component; however, evidence of tumor dissemination was observed both at diagnosis and following treatment. Despite

aggressive multimodality management, early recurrence occurred. Notably, this case illustrates an unusually rapid progression from initial diagnosis to leptomeningeal drop metastasis. Although early postoperative recurrences of PXA within one to two months have been previously reported, these were typically confined to the primary surgical site rather than associated with leptomeningeal dissemination.[13]

Maximal safe surgical resection remains the cornerstone of treatment for anaplastic PXA. However, the role of adjuvant radiotherapy and chemotherapy remains unclear due to the rarity of this entity and the absence of prospective clinical trials. In view of the diffuse growth pattern and residual disease, concurrent chemoradiotherapy with temozolomide was administered in this case. Nevertheless, the tumor recurred and disseminated despite continued temozolomide therapy.

The therapeutic efficacy of temozolomide is known to correlate with the methylation status of the MGMT promoter.[14] Marucci et al evaluated MGMT promoter methylation in nine PXA patients and two APXA patients and found promoter methylation in only two conventional PXA cases, while both anaplastic cases were unmethylated.[15] Similarly, Martínez et al investigated DNA methylation patterns in conventional and anaplastic PXAs and identified overlapping promoter hypermethylation in genes such as HOXA5, CD81, ASCL2, HCK, and TES. However, larger cohort studies are required to validate these findings and to identify reliable molecular biomarkers that could guide targeted therapy in anaplastic PXA.[16] BRAF V600E mutation has been identified in a significant proportion of PXA cases and may offer therapeutic implications with targeted inhibitors.[17] However, molecular profiling was not available in the present case.

Overall, PXA carries a favorable prognosis following gross total resection, with reported 5-year and 10-year survival rates of up to 81% and 70%, respectively. Poor prognostic factors include leptomeningeal dissemination, anaplastic histology, subtotal resection, and advanced age. Given the aggressive clinical course observed in the present case, we recommend routine craniospinal imaging at diagnosis or early during follow-up in patients with APXA. Early detection of dissemination may facilitate timely therapeutic intervention and potentially improve disease control using currently available adjuvant treatment strategies.

CONCLUSION

We present a case of anaplastic PXA, which poses significant management challenges. Anaplastic PXA is a rare and aggressive tumor with unpredictable clinical behavior. Despite gross total resection and adjuvant chemoradiotherapy, early recurrence and leptomeningeal dissemination may occur, particularly in pediatric patients with high proliferative indices. This case highlights the importance of recognizing anaplastic features, performing early spinal staging, and maintaining vigilant follow-up. Larger multicentric studies are required to establish optimal treatment strategies and identify reliable prognostic biomarkers for this rare entity.

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