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Primary anaplastic pleomorphic xanthoastrocytoma in adults. Case report and review of literature



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ABSTRACT

BACKGROUND: Pleomorphic xanthoastrocytoma (PXA) classified as a low Grade (WHO II) astrocytic neoplasm. It is known for its relatively favorable prognosis. It most commonly occurs in young adults. Malignant progression in PXA has been frequently reported since its first description in 1979; however, the presentation of a primary anaplastic PXA tumor with an aggressive clinical course in adults is rare especially in the later age group.

CASE DESCRIPTION: We present a case of primary anaplastic PXA in a 53 year old male that manifested with an early recurrence pattern at 9 weeks. Treatment performed was surgical excision and external beam radiotherapy. The aforementioned tumor followed an aggressive clinical course. Tumor cells exhibited the characteristic expression of GFAP (Glial fibrillary acidic protein), higher proliferative index (8–10%) on Ki-67 staining along with the presence of increased mitoses (>5/10hpf). A review of previously reported primary anaplastic pleomorphic xanthoastrocytoma cases in adults with histological features was also done.

CONCLUSION: Our review of all reported cases of APXA in adults concludes that the clinical behavior of this tumor varies considerably from its benign variant. Early disease recurrence in anaplastic pleomorphic xanthoastrocytomas is associated with fatal outcomes. As per our review of literature it is seen that anaplastic variant of PXA shows histological characteristics as well as clinical course comparable with Grade III astrocytomas.

We recommend further evaluation of PXA with anaplastic features regarding their genetic characteristics to understand the origin as well as behavior of this tumor.

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1. Introduction

Pleomorphic xanthoastrocytoma (PXA) is an astrocytic neoplasm with a relatively favorable prognosis [8]. According to WHO classification for astrocytic neoplasms, it has been classified histologically as a grade II (benign) neoplasm [6]. The first case was reported in 1979 [11]. It is often superficially located in the cerebral cortex with leptomeningeal involvement. Morphologically it shows a pleomorphic histological appearance that includes lipidized, GFAP-expressing tumor cells with cytoplasmic xanthic change surrounded by a reticulin network [9]. It has been frequently seen that tumors initially diagnosed as PXA have later shown malig-

nant progression to high grade astrocytomas (grade III or IV). In these cases the initial histological findings corresponded to a grade II neoplasm; however over the recurrences it was found to be malignant [3]. To the best of our knowledge, only a few cases have been reported in the literature, which demonstrate a PXA tumor presenting with anaplastic features at initial presentation. These cases have been reported mostly in children and young adults ranging between 7–25 years [16]. Here we present a case of a primary anaplastic PXA tumor in the later age group with an unusual early recurrence pattern. We then review the literature of previously reported cases of primary anaplastic PXA tumors in adults.

2. Case description

55 years old male presented with a history of sudden onset headaches and two episodes of generalized tonic clonic seizures in 3 months. Neurological examination did not show any focal motor or sensory deficits. MRI brain showed a 2.2 × 1.3 × 1.1 cm nodular

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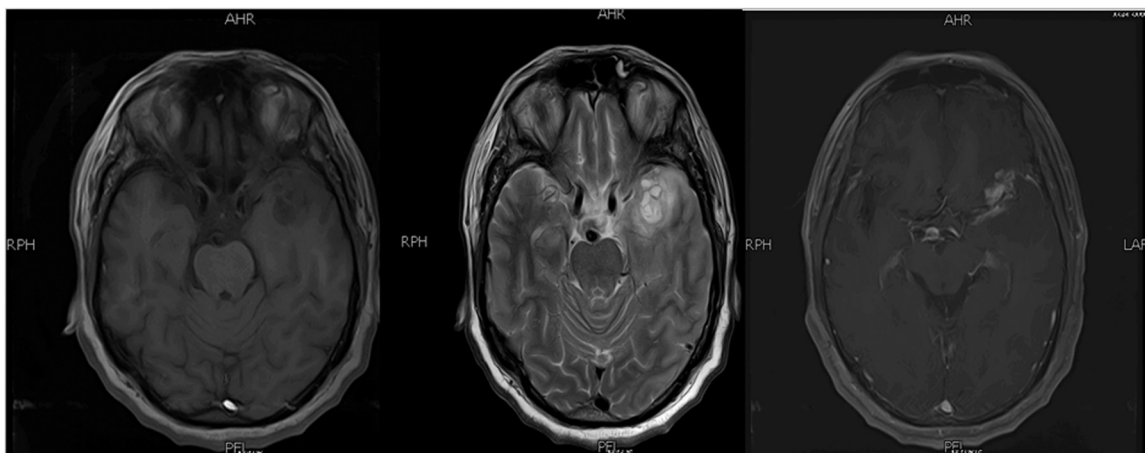


Fig. 1. (A) MRI Brain T1 weighted showing hypointense nodular thickening in the left temporal lobe and para sylvian fissure. (B) T2 weighted image showing hyperintense lesion in the left temporal lobe. (C) T1 contrast image showing patchy enhancement in the left temporal lobe.

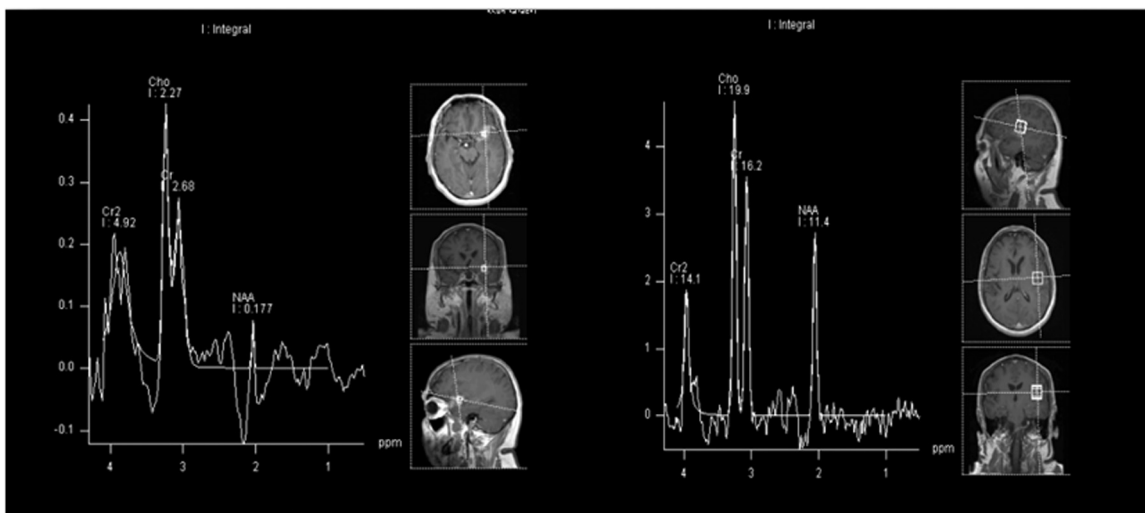


Fig. 2. MR spectroscopy showing high Choline/Creatine and high Choline/NAA ratios in the enhancing areas and persistent lactate peak in all enhancing areas favoring neoplastic lesion.

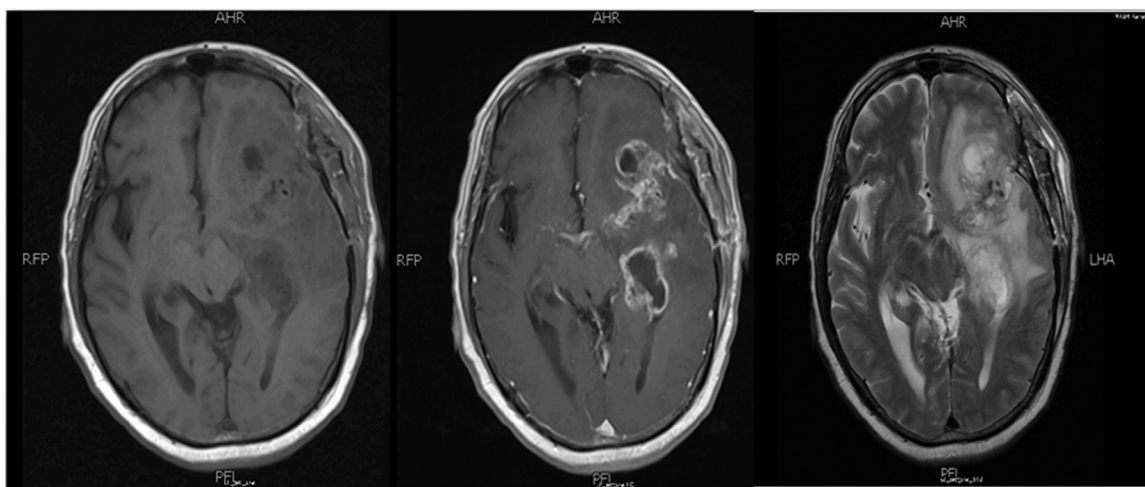


Fig. 3. MRI Brain showing significant overall increase in the size of tumor involving the left frontal, temporal and parietal lobes with perilesional edema and post surgical changes in T1, T1 post contrast and T2 weighted images respectively.

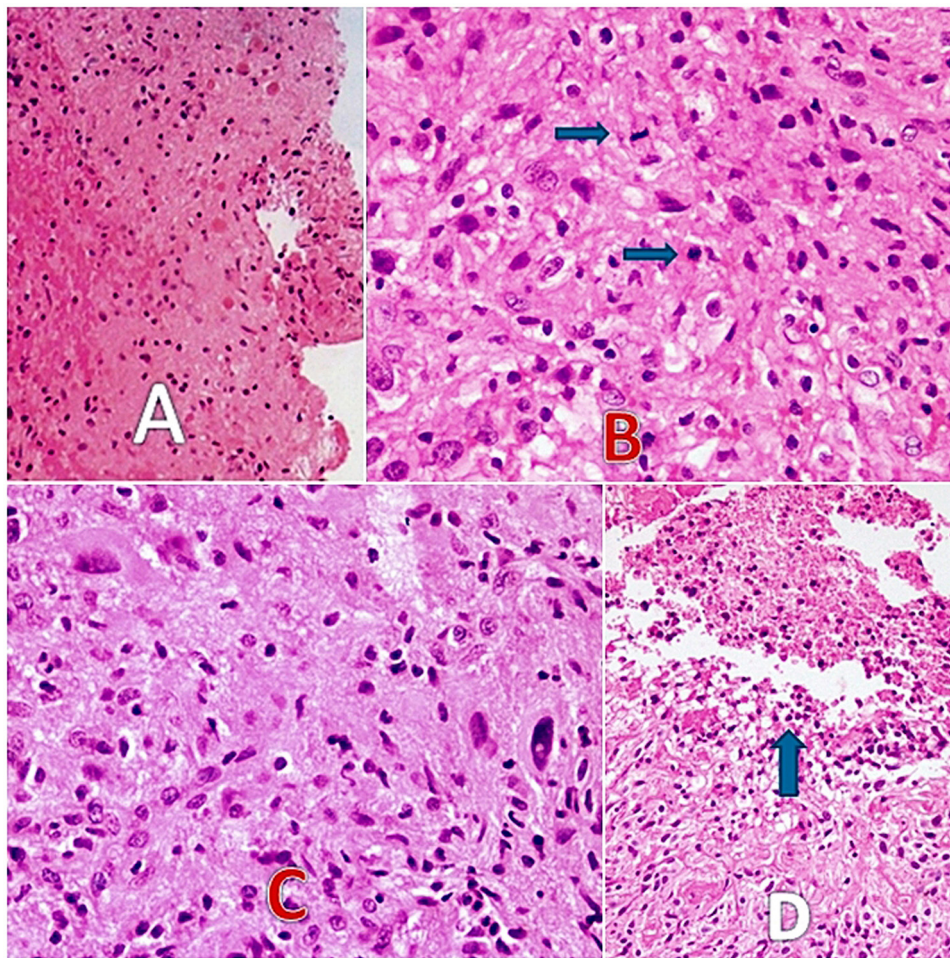


Fig. 4. A. PXA tumor exhibiting numerous eosinophilic hyaline globule. B. Tumor showing sheets of astrocytic cells having pleomorphic nuclei with some cells having xanthomatous cytoplasm. Presence of frequent mitoses (arrows showing two mitotic figure) 40 \times . C. Tumor showing sheets of spindly to large polygonal astrocytic cells having pleomorphic nuclei with nuclear inclusions 40 \times . D. PXA exhibiting necrosis.

thickening and enhancement along left medial temporal lobe and sylvian fissure. It appeared as a multicystic lesion with peripheral enhancement and marked perilesional oedema (Fig. 1). MR Spectroscopy showed high choline/creatine and high choline/NAA ratios in the enhancing areas (Fig. 2). Patient underwent a left sided pterional craniotomy for excision of the lesion. Gross total resection of the tumor was performed. Immediate post operative MRI scan was not done due to financial constraints. Biopsy report suggested a neoplastic lesion composed of plump spindle-shaped pleomorphic cells having elongated nuclei with eosinophilic cytoplasm and other cells having bizarre pleomorphic nuclei with abundant cytoplasm. GFAP (glial fibrillary acidic protein) immune staining showed diffuse expression in tumor cells. Ki-67 staining showed a proliferative index of upto 8–10% in some areas along with the presence of increased mitoses (>5/10hpf). H & E staining also showed a few xanthomatous cells along with areas of focal necrosis. CD34 immune staining was negative excluding epithelioid cell glioblastoma (Figs. 4 and 5). Overall findings were suggestive of an anaplastic pleomorphic xanthoastrocytoma. Case was discussed in the tumor board meeting and external beam radiotherapy was advised. On follow up visit patient exhibited mild to moderate cognitive impairment, sensory dysphasia and disorientation. MRI scan was repeated 9 weeks after surgery. Repeat scan showed a significant overall increase in tumor size with both multifocal cystic and solid components involving left frontal, temporal and parietal lobes

measuring approximately $9.6 \times 5.1 \times 5$ cm clearly elicited disease progression (Fig. 3). The prognosis of the patient was discussed with family regarding further management plan and it was decided to continue radiotherapy and no surgical intervention was planned. Patient died at 16 weeks from the time of initial diagnosis.

3. Discussion

PXA with anaplastic features is a rare tumor hence no definitive treatment guidelines have been established so far. The recent consolidated review of literature by Tmara et al. [24] in 2012 has reported 20 cases of primary anaplastic PXA in adults (18 above) so far. We report a total of 24 cases of primary APXA in adults from 1979 to 2016. We describe this case of primary anaplastic PXA in an adult male with special regard to a rapid disease progression only after a 9 weeks interval. To the best of our knowledge only one case of primary anaplastic PXA has been reported to have an earlier recurrence at 1 month (Kim et al., 2009) [12]. The average recurrence interval as per our literature review was approximately 14 months from the time of initial diagnosis. The APXA lesion was found to be mostly located in temporal and parietal lobes in most of the cases. It showed similar pattern involving the medial temporal lobe and para sylvian fissure in the aforementioned case description. Previous studies have shown presence of neuroglial tumor markers like GFAP expression with reticulin

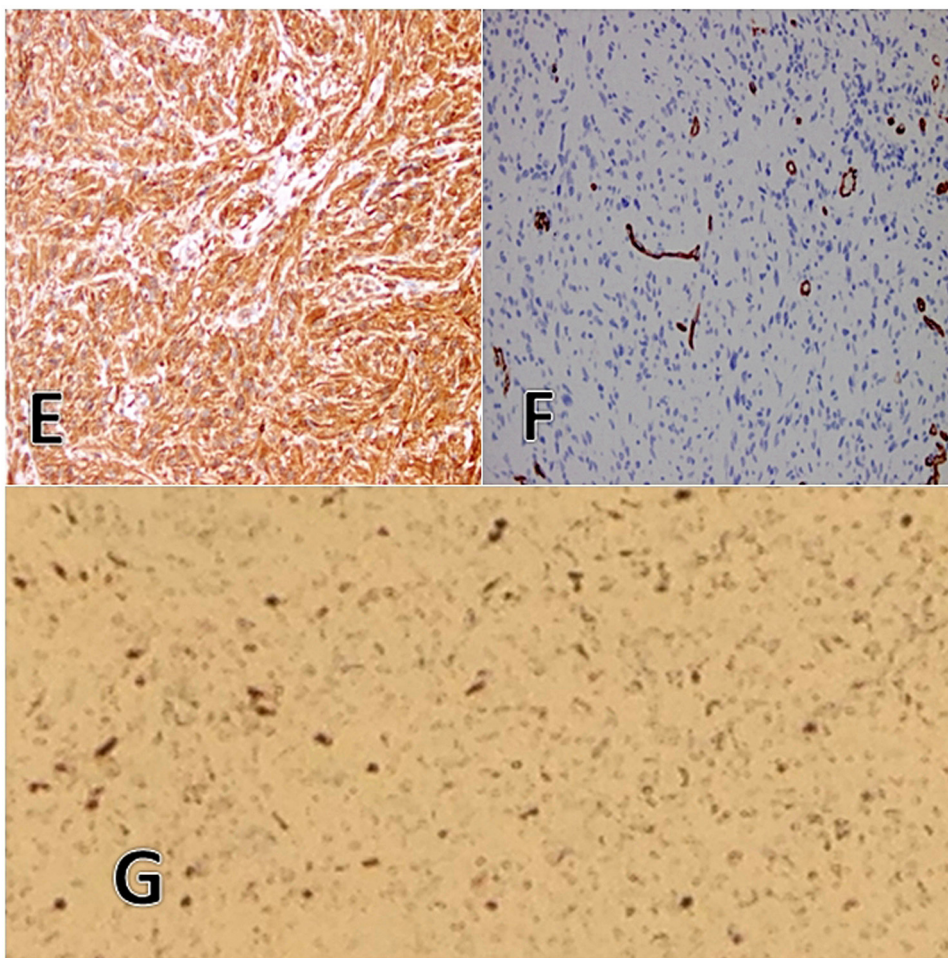


Fig. 5. E. Immunohistochemistry showing diffuse GFAP staining. F. Negative CD34 staining. G. ki 67 staining showing diffuse proliferative index of 8–10% and presence of increased mitosis (>5–10/hpf).

deposition as it was seen in this case [23]. Our inference about behavior of PXA as an anaplastic tumor stems from the fact that tumor showed proliferative index of 8–10% in some areas, which along with the presence of increased mitoses (>5/10hpf) corresponded to WHO grade III classification of diffuse astrocytomas [15]. Previously reported cases of APXA also have shown similar histological characteristics (Table 2). It was seen that presence of pleomorphism was a consistent feature in majority of the cases. The APXA tissue sections show bizarre giant cells that are multinucleated or have multilobulated nuclei, with intracytoplasmic lipid-containing vacuoles (xanthic), and are generally organized in alveolar structures, with an abundant surrounding reticulin network and perivascular lymphoid infiltrates. In contrast to benign PXA, the anaplastic variants have consistently shown high mitotic activity along with areas of focal necrosis in most of the cases. Long term control of anaplastic PXA with recurrences has been attributed to postsurgical stereotactic radiation therapy (Koga, Tomoyuki, et al) [13]. However due to its unavailability in our facility we planned to provide external beam radiation therapy for long term palliative control of tumor. According to the current review of literature the most commonly used treatment option was surgical excision and post surgical radiotherapy. Complete surgical excision is still an effective treatment in benign PXA with excellent 5 year and 10 year survival rates; however, we found that gross total resection in APXA is still associated with frequent recurrences. Previously there was no sufficient literature supporting the role of chemotherapy in the

treatment of pleomorphic xanthoastrocytomas in adults, recent studies have shown the role of BRAF V600E inhibitors in treatment of PXA tumors pertaining to the high frequency of these mutations in PXA tumors [22]. Due to the lack of BRAFV600E testing in our facility, no chemotherapy was planned for this patient. The average survival in months among the reported APXA cases was approximately 24 months from the time of initial diagnosis according to our case review (Table 1). This indicates a relatively poor prognosis in patients with anaplastic PXA tumor at the initial presentation when compared with the benign PXA tumors in adults [19].

4. Conclusion

Our review of all reported cases of APXA in adults concludes that the clinical behavior of this tumor varies considerably from its benign variant. As per this review of literature it is seen that anaplastic variant of PXA shows histological characteristics as well as clinical course comparable with Grade III astrocytomas. Early disease recurrence in anaplastic pleomorphic xanthoastrocytomas is associated with fatal outcomes.

We recommend further evaluation of PXA with anaplastic features regarding their genetic characteristics to understand the origin as well as behavior of this tumor.

Table 1
Review of previously reported primary anaplastic Pleomorphic xanthoastrocytoma cases in adults.

Author (Date)	Age/sex	Site	Treatment	Recurrence Interval (months)	Net survival (months)
Goldring et al. [7]	24/female	Temporal lobe	Surgery + chemotherapy	12 months	12 months
Iwaki et al. [9]	30/male	Parieto-occipital sulcus	Surgery + radiotherapy	6 months	10 months
Perry et al. [21]	18/male	Temporal lobe	Surgery + radiotherapy + chemotherapy	Multiple recurrences	48 months
Tonn et al. [23]	18/male	Temporal + occipital lobe	Surgery + radiotherapy + chemotherapy	8 months	30 months
Chakrabarty et al. [3]	49/male 40/male	Temporal + occipital lobe	Surgery + radiotherapy	Not reported	Not reported
Buccerio et al. [2]	65/male	Thalamic	Surgery + Radiotherapy	22 months	22 months
Zhuang et al. [25]	53/female	Frontal lobe	Surgery + radiotherapy + chemotherapy	Not reported	24 months
Gelpi et al. [5]	43/female	Occipital lobe	Surgery + Radiotherapy	36 months	Alive
Asano et al. [1]	59/female	Temporal lobe	Surgery	Not reported	36 months
Marton et al. [16]	40/female	Temporal lobe	Surgery	30 months	30 months
Hirose et al. [8]	52/male 39/female 25/male	Frontal lobe Frontal + Temporal lobe Cerebellum	Surgery Surgery + radiotherapy + chemotherapy Surgery	Not reported Not reported Not reported	Alive Not reported Not reported
Kim et al. [12]	45/male	Temporal lobe	Surgery	1 month	17 months
Koga et al. [13]	47/female	Frontal lobe	Surgery + Radiotherapy	Not reported	Not reported
Frank et al. [4]	28/male	Temporal lobe	Surgery + radiotherapy + chemotherapy	14 months	Not reported
Lacoste-Collin et al. [14]	45/female	Peri ventricular	Biopsy only	Not reported	Not reported
Nern, Christian et al. [18]	57/male	Temporal lobe	Surgery + radiotherapy + chemotherapy	10 months	12 months
Kosuke, et al. [10]	61/female	Pineal Gland	Surgery + radiotherapy + chemotherapy	Not reported	Alive
Montano el al. [17]	22/male	Parietal lobe + Temporal lobe	Surgery + radiotherapy + chemotherapy	Not reported	Alive
Usama et al. (Present study)	53/male	Temporal lobe + sylvian	Surgery + Radiotherapy	2 months	4 months

Table 2
Comparison of histological features of previously reported Anaplastic PXA tumors with the present study. (Mitosis; 0–2 cells/hpf = +; 3–5 cells/hpf = ++; 5–10 cells/hpf = +++).

Author	Pleomorphism	Eosinophilic hyaline globules	Nuclear inclusions	Xanthomatous cells	Mitosis	Spindle cells	Necrosis	GFAP
Iwaki et al. [9]	+		+	+	+++	+		
Perry et al. [21]	+				+++		+	
Tonn et al. [23]	+	+			+	+	+	
Buccerio et al. [2]	+	+	+		+	+		+
Asano et al. [1]	+		+	+	+++	+		+
Marton et al. [16]	+		+	+	+++			+
Hirose et al. [8]	+	+	+	+	+++	+	+	+++
Kim et al. [12]	+			+	++		+	
Koga et al. [13]	+	+		+	+			+
Frank et al. [4]	+	+		+	+			+
Lacoste-Collin et al. [14]	+	+	+		+++			+
Nern, Christian et al. [18]	+			+	++		+	+
Kosuke, et al. [10]	+	+			+			+
Usama et al. (Present study)	+	+	+	+	+++	+	+	+

Conflicts of interest

None.

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None.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent will be made available for review by the Editor-in-Chief of this journal on request.

Author contribution

1. Saad Akhtar Khan – data analysis, interpretation, manuscript drafting.

2. Usama Khalid Choudry – study concept, study design, data collection, manuscript writing.
3. Amjad Qureshi – study concept, data analysis, proof reading.
4. Ehsan Bari – critical review of literature, data interpretation.

Guarantor

Dr. Ehsan Bari, section head, Department of Neurosurgery, Aga Khan Hospital.

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2. Dr. Anita George, Resident; Department of histopathology, Aga Khan University Hospital, Karachi, Pakistan.

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