Int J Clin Exp Pathol 2016;9(6):6391-6396
www.ijcep.com /ISSN:1936-2625/IJCEP0024239

Original Article

Infratentorial pleomorphic xanthoastrocytoma: report of two cases and review of literature

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Received January 17, 2016; Accepted March 26, 2016; Epub June 1, 2016; Published June 15, 2016

Abstract: Pleomorphic xanthoastrocytoma (PXA) typically has benign histology, but may show different prognosis and clinical characteristics in atypical locations. A case each of cerebellar PXA and IV ventricle PXA is reported along with a review of the rare presentations and atypical features of this tumor. A review of the available literature dating back to 1999 revealed 25 cases of PXA in the posterior fossa, of which 17 were in adults, with an average age of 31 years, while supratentorial forms had a younger age profile (26.2 years). PXA in the posterior fossa had a higher rate of recurrence, mortality and malignant progression. In contrast, patients with PXA-ganglioglioma and PXA-pilocytic astrocytoma had good prognosis. The clinicopathological features of infratentorial PXA differ from PXA located in the cerebral hemispheres. Recognizing these atypical manifestations in the different subgroups of PXA is critical for accurate diagnosis and treatment.

Keywords: Pleomorphic xanthoastrocytoma, infratentorial, prognosis, treatment

Introduction

Pleomorphic xanthoastrocytoma (PXA) is a rare, primary, low-grade, astrocytic tumor, which was first described in 1979 by Kepes [1]. PXA accounts for 1% of all astrocytomas, and commonly occurs in the temporal lobe of children and young adults. It has a characteristic histopathological appearance with pleomorphic cells that exhibit cytoplasmic xanthic changes and express glial fibrillary acidic protein (GFAP). PXAs are typically supratentorial, but infratentorial lesions have also been described. After a thorough literature review, we found only 26 cases in the posterior fossa. Although PXA is usually a benign lesion with a favorable prognosis after gross total resection (GTR), infratentorial PXAs tend to recur or progress to malignancy.

Case reports

Between January 1999 and May 2013, 11 patients were pathologically diagnosed as PXA at our institution, two of which were in the infratentorial compartment. This report describes these two cases, highlighting their clinical features, pathological findings and the therapeutic approaches adopted.

Case 1

A 21-year-old man presented with 20-day history of gait instability, falling, nausea and vomiting. CT scan and MRI revealed a right cerebellar mass along with a cyst lesion; with irregular enhancement after contrast injection (**Figure 1**). The lesion was middle hypointense in T1, and hyperintense in T2-weighted images. The patient underwent a midline suboccipital craniectomy with microscopy. The tumor was completely removed with no complications post-surgery. Immunohistochemical analysis showed CD56 (+), GFAP and CD68 (±) (**Figure 2**). Pathology diagnosis indicated PXA with anaplasia. The patient developed neurological signs of brainstem 22 months after completion of radiation therapy. MRI showed tumor recurrence and the patient died after two months.

Case 2

A 56-year-old man presented with one-month history of blurred vision, diplopia, headache,

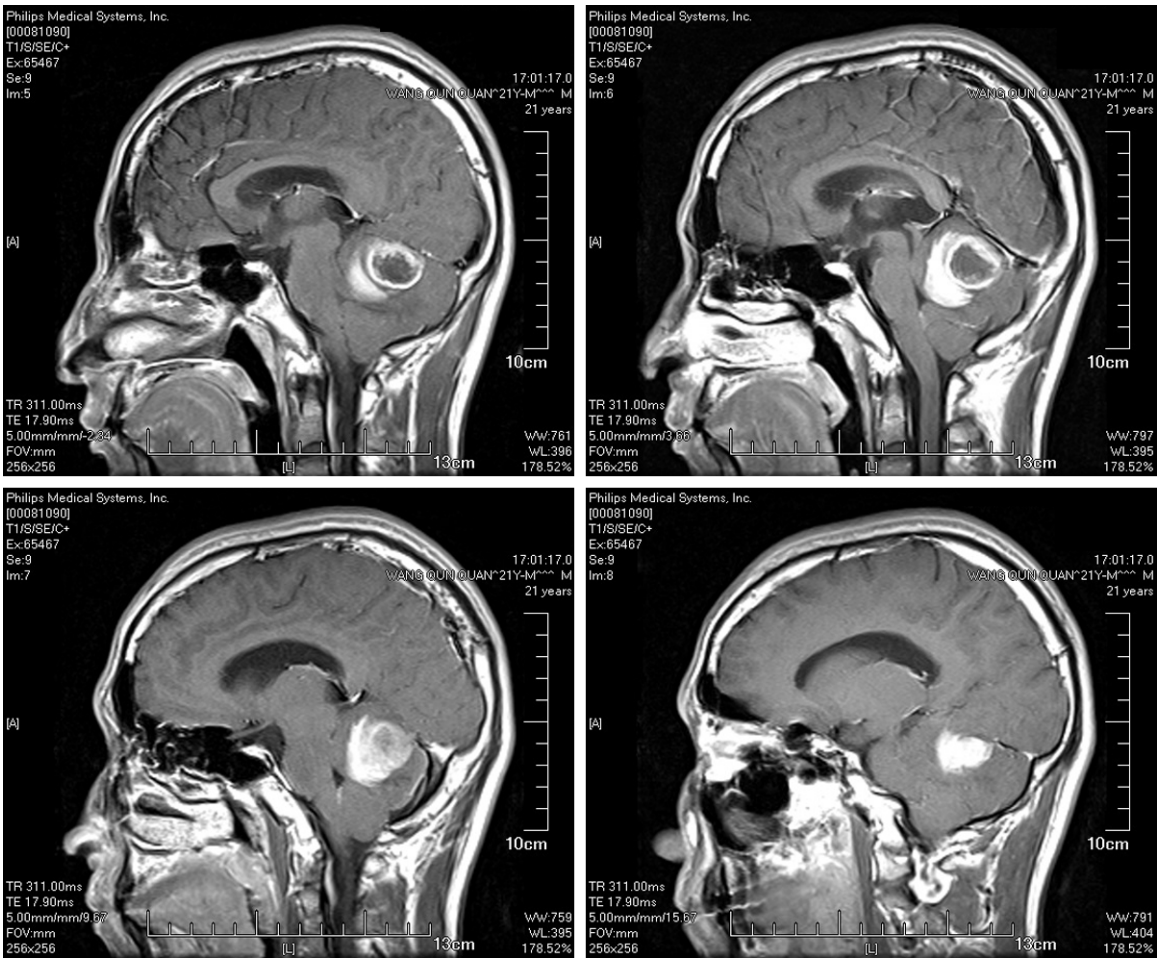

Figure 1. T1-weighted sagittal MRI scan with contrast (case 1) showing a right cerebellar irregular mass along with a cyst lesion.

giddiness, and fall while walking. MRI showed a small solid lesion in IV ventricle mass, with irregular enhancement after contrast injection (**Figure 3**). The patient underwent a midline suboccipital craniectomy but the tumor could not be completely removed due to its deep infiltration. Histological examination revealed a lesion with multinucleated giant cells and perivascular lymphocytes. Immunohistochemical analysis showed vimentin and GFAP (+), CD68 (±), and CD34, CD21 and EMA (-). Pathology diagnosis indicated PXA. The patient rejected radiotherapy, had tumor recurrence after five months and died after one month.

Discussion

Pleomorphic xanthoastrocytoma (PXA) is a rare, usually low-grade, astrocytic tumor, frequently with a good prognosis. PXA typically occurs in superficial cerebral hemispheres (predominantly in the temporal lobe) of young patients, and is amenable to surgical resection. However, several case reports indicate that PXAs differ in location and prognosis.

Clinical analysis

In atypical tumor sites, such as cerebellum, periventricular, thalamus and corpus callosum, PXAs show different clinical characteristics and prognoses from typical supratentorial cortex PXAs. About 80% of atypical PXAs recurred, and 60% of atypical PXA patients died within 16 months [2].

Infratentorial PXA, including cerebellar PXA and IV ventricular PXA are rare, with fewer than 25 cases reported till date. Two-third of cerebellar PXAs occurred in adults; the average age at the time of diagnosis was 31 years, and the prognosis was rarely poor. In contrast, supratento-

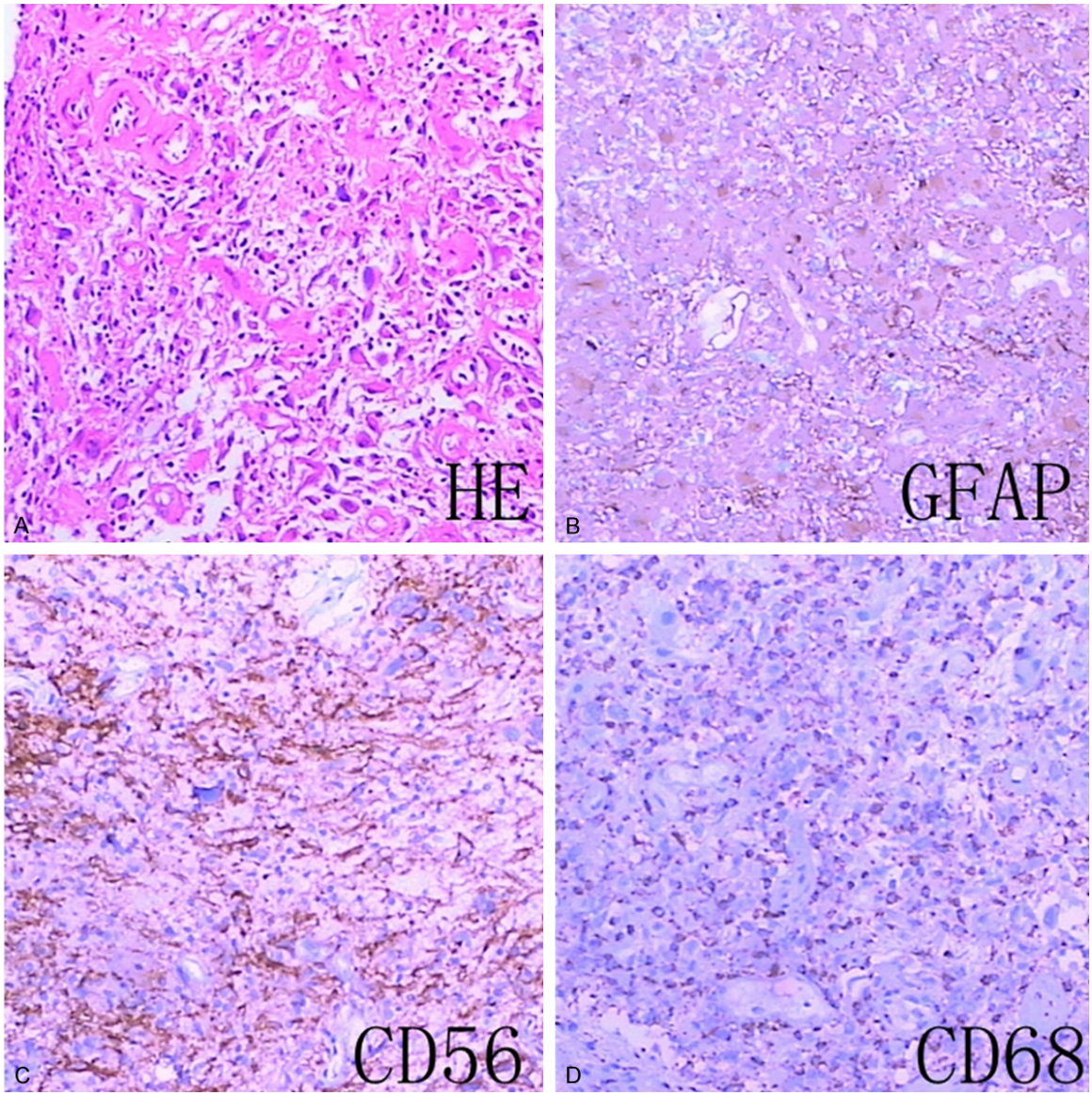

Figure 2. Histopathological changes of infratentorial PXA. A. Case 1 is characterized by cellular and nuclear pleomorphisms, prominent nuclear atypia, cytoplasmic lipid droplets (H&E, X400). B. The neoplastic glial cells are immunoreactive for glial fibrillary acidic protein (X400). C. The neoplastic glial cells are immunoreactive for CD56 (X400). D. The neoplastic glial cells are weak immunoreactive for CD68 (X400).

rial forms were observed in patients with a younger average age (26.2 years) [3]. In some instances, it can also be associated with other diseases of the central nervous system, such as neurofibromatosis type 1 [4, 5]. Composite PXAs and gangliogliomas are frequently reported in the cerebellum [6].

Radiological features

T1-weighted image demonstrates a lesion of low to isointensity. Solid masses are heterogeneously enhanced with Gd-DTPA, and cyst-associated tumors are occasionally observed in infratentorial regions. A higher incidence of solid enhancing tumor is found in the posterior fossa [7]. Imaging studies are not useful for diagnosis before pathological examination because there are no radiological features pathognomonic of PXA [5].

Pathology

A diagnosis of PXA can only be confirmed by histological examination. Typical PXA is characterized by cellular and nuclear pleomorphisms,

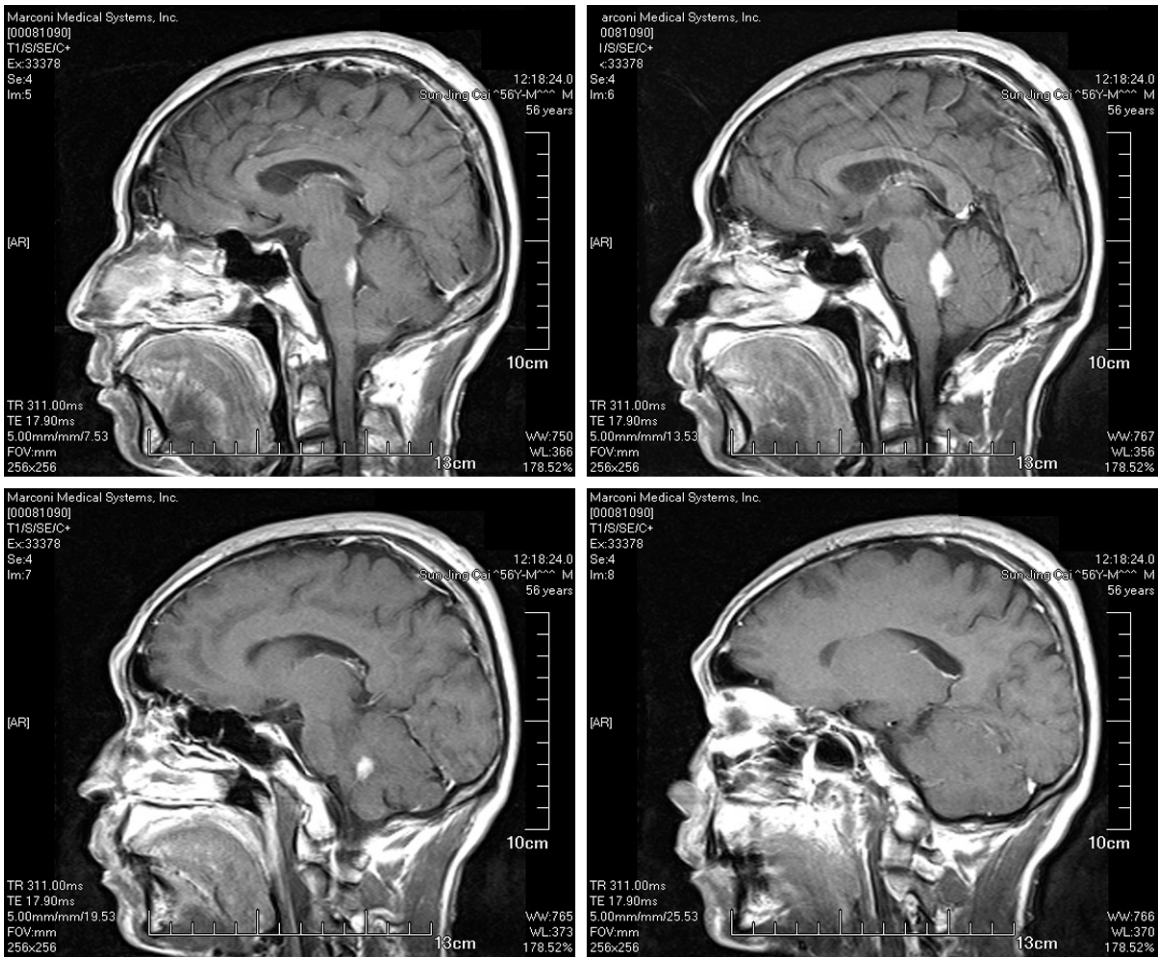

Figure 3. T1-weighted sagittal MRI scan with contrast (case 2) showing a small solid lesion in IV ventricle.

prominent nuclear atypia, cytoplasmic lipid droplets, spindle-shaped cells with elongated nuclei, abundant eosinophilic cytoplasm, eosinophilic granular bodies and multinucleated giant cells with abundant reticulin fibers. PXA can be easily distinguished from the surrounding tissue, although it may sometimes exhibit direct parenchymal infiltration. A tumor cell with cytoplasmic GFAP is very helpful in differential diagnosis [5, 8-10] of mesenchymal tumors. However, PXAs differ in expression of glial phenotypes [11, 12] and neuronal [11], epithelial or other markers, such as vimentin, CD34 and CD68. Ki67 is very high in anaplastic PXA. A review of 25 cases of infratentorial PXAs showed five subtypes. Composite PXAs and gangliogliomas are common, and accounted for six cases. Additionally, three cases of PXA-pilocytic astrocytoma, two cases of PXA-oligodendroglioma, three cases of anaplastic PXA (WHO III), and 11 cases of typical pure PXA (< 50%) were found.

Treatment

Total resection remains the gold standard of treatment but is hard to achieve in infratentorial PXA since the lesion is close to brainstem and important tissues. The efficacies of radiotherapy and chemotherapy in the management of PXA are controversial.

Prognosis

Age at diagnosis, histological grade and extent of resection are independent factors for prognosis [13]. We report two cases of infratentorial PXA from a total of 11 cases of PXAs treated at our institute from January 1999 to May 2013. During the follow-up, one patient died 6 months postoperatively and another died 24 months

Table 1. The cases reported in the literature

Reference	Age (y)/Sex	Histology	Treatment	Recurrence	Follow-up
Chang et al. [11]	4/F	PXA-GG	S + RX + Ch	No	Well/144 mo
Chapman et al. [14]	15/M	PXA	S	No	Well/12 mo
Evans et al. [15]	60/M	PXA-GG	S + Rx	No	Well/16 mo
Gardiman [16]	14/F	PXA	S	NA	NA
Gil Gouvea et al. [8]	40/M	PXA-pilo	S/S	27 mo	Well/27 mo
Glasser et al. [17]	36/F	PXA	S + Rx/S	C/16 y-F	NA
Hamlat et al. [7]	58/F	PXA-oligo	S/S + Rx + Ch	8 mo	Died at 17.5 mo
Hirose et al. [18]	24/F	PXA	S	No	Well/3 mo
Hirose et al.	51/M	PXA-ana	S + Rx + Ch	Yes	AWD/8 y 2 mo
Hirose et al.	25/M	PXA-ana	S	NA	NA
Kumar et al. [12]	15/M	PXA	S	NA	NA
Kurschel et al. [19]	6/F	PXA	S	No	Well/36 mo
Lim et al. [20]	3/F	PXA	S	No	Well/13/16 mo
Lindboe et al. [21]	27/M	PXA-GG	S/S	12 y	Well/11 mo
Naidich et al. [4]	51/F	PXA-pilo	B/S + Rx/S	No	NA
Perry et al. [6]	14/F	PXA-GG	S + Rx + Ch/S	12 mo	Well/18 mo
Perry et al.	24/F	PXA-GG	S	No	Well/7 mo
Powell et al. [22]	14/F	PXA-GG	S	NA	NA
Rosemberg et al. [10]	68/M	PXA	S	No	Well/5 mo
Saikali et al. [5]	36/F	PXA-oligo	S/S + Rx + Ch	Yes	Died at 36 mo
Lim [2]	35/F	PXA	S/S/S + Rx	27 mo	Well/33 mo
Wasdahl et al. [23]	48/F	PXA-pilo	S	No	Well/18 mo
Yeaney [24]	16/M	PXA	S	No	NA
Present case 1	20/M	PXA-ana	S	22 mo	Died at 24 mo
Present case 2	56/M	PXA	S	5 mo	Died at 6 mo

PXA-ganglioglioma: PXA-GG; PXA-pilocytic astrocytoma: PXA-pilo; PXA-oligodendroglioma: PXA-oligo; PXA with anaplasia features: PXA-ana; S: surgery, Rx: radiotherapy, Ch: chemotherapy, NA: not available, Well/3 mo: well at 3 months after the last surgery, AWD: alive with disease.

postoperatively. Overall 5-year survival of superficial cerebral hemispheres PAXs is 76% [13]. Infratentorial PXAs show different prognosis than superficial PXAs. Being adjacent to the brain stem and IV ventricle, GTR is difficult to perform in infratentorial PXAs, and they easily disseminate. According to literature (**Table 1**) nearly 50% of cases with follow-up data had relapsed. Four (21%) out of 19 cases had died with a median follow-up of 27 months. Infratentorial PXAs occasionally have other composite tumors with anaplastic features, which can be divided into five subtypes. Patients with PXA-ganglioglioma and PXA-pilocytic astrocytoma subtypes had good prognosis, with no death observed. A total of four cases died, including two cases of PXA-oligodendroglioma subtype (2/2), one case of anaplastic PXA subtype (1/3) and one cases of PXA (1/11).

Conclusion

The present two cases and others reported in the literature reveal that the clinicopathological features of infratentorial PXAs differ from PXAs located in the cerebral hemispheres. It is crucial to realize the unusual clinicopathological features of infratentorial PXAs, since they will facilitate the accuracy of diagnosis and treatment.

Disclosure of conflict of interest

None.

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