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Review Article

Pleomorphic xanthoastrocytoma inside lateral ventricle: a rare case report and literature review

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Abstract: Pleomorphic xanthoastrocytoma (PXA) is a relatively rare, low grade astrocytic tumor that usually affects children as well as young adults. The reported cases were predominantly located superficially in the temporal lobe. To our knowledge, so far only two cases of PXA occurring in lateral ventricle were reported in English literature. Herein, we present the third case of PXA intra-lateral ventricle in a 28-year-old Chinese male. Histologically, the tumor was relatively well circumscribed and consisted of spindle-shaped, ovoid, and multinuclear giant cells admixed with scattered eosinophilic granular bodies, inflammatory cells, and xanthomatous cells. Immunohistochemically, the tumor cells were strongly positive for S-100, GFAP, oligo-2 and vimentin, focally positive for synaptophysin and CD34, and negative for cytokeratin, EMA, NeuN and IDH1. Ki-67 proliferation index was approximately 2%. A BRAF V600E mutation was then identified in the tumor. Based on morphologic features, the immunohistochemical staining and BRAF V600E mutation, the tumor was diagnosed as a PXA. Because of the presence of the bizarre multinuclear giant cells and xanthomatous cells and the unusual location, PXA was easily misdiagnosed as a high-grade tumor. It should be noted that PXA was also an important differential diagnosis for intraventricular tumors.

Keywords: Pleomorphic xanthoastrocytoma, astrocytic tumor, lateral ventricle, BRAF V600E mutation, epithelioid glioblastoma

Introduction

Pleomorphic xanthoastrocytoma (PXA) is an uncommon astrocytic tumor which accounts for approximately 1% of all astrocytic tumors [1]. Histologically, PXA is characterized by pleomorphic and lipidized cells, multinucleated giant cells and eosinophilic granular bodies in an inflammatory background. Because of the presence of worrisome cellular pleomorphism and multinucleated giant cells, the tumor may be confused with high grade astrocytic tumor such as glioblastoma, if one is not familiar with it or it is in an uncommon location. In fact, PXA frequently showed favorable prognosis, consequently, it was designated as a grade II tumor in World Health Organization (WHO) classification [2]. It is necessary for us to be familiar with its peculiar clinical and histologic characteristics, in order to avoid overdiagnosis. Typically, PXAs usually affected children as well as young adults, and were predominantly located superficially in the cerebral hemispheres [3]. Very rarely, PXA could arise in other locations including sella [4], spinal cord [5], retina [6] and ventricle [7-11]. To our knowledge, so far there was only two cases of PXA occurring in lateral ventricle was reported in the English literature [7, 9]. Herein, we reported the third case of PXA intra-lateral ventricle in a 28-year-old Chinese male. Our case was also the first case that completely inside the left lateral ventricle.

Case report

Clinical presentation

A 28-year-old man was admitted to our hospital for a regular examination, as he was caught in a minor traffic accident. Magnetic Resonance Imaging (MRI) revealed there was a solid and cystic mass measuring 2.7×2.5×2.4 cm with mixed equal T1 and T2 signal in the posterior horn of the left ventricle. FLAIR sequence showed high signal, and the parenchymal part of the lesion was enhanced obviously (**Figure 1**). Physical examination and routine laboratory

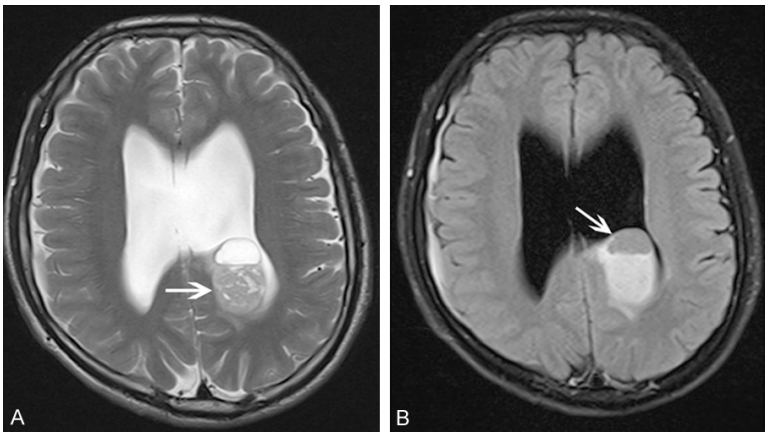

Figure 1. MRI presentation of the tumor. A, B. MRI revealed a solid and cystic mass in the posterior horn of the left ventricle.

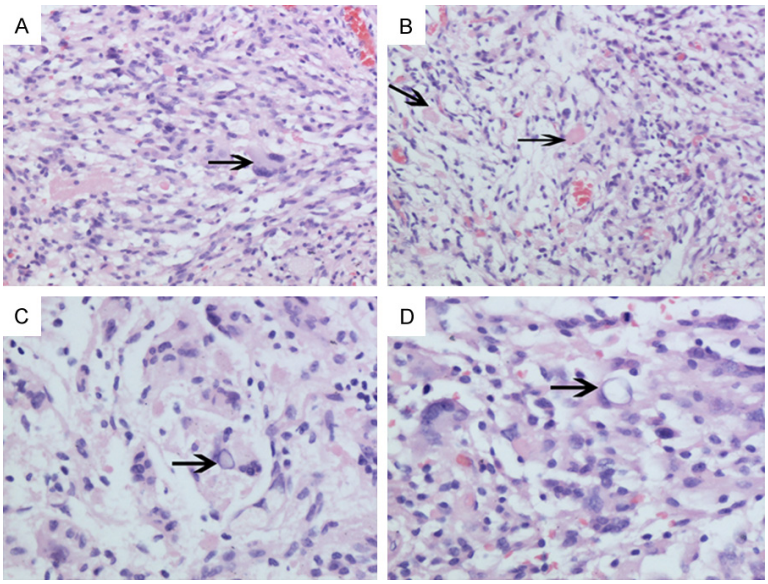

Figure 2. Morphologic change of the tumor. A. The tumor was composed of irregular spindle-shaped, ovoid cells with scattered multinuclear giant cells (Arrow). B. Eosinophilic granular bodies (Arrow) were occasionally identified in an inflammatory background. C. Occasionally, a nuclear inclusion (Arrow) was present in tumor nuclei. D. A xanthomatous cell with cytoplasmic vacuole could also be observed in the tumor (Arrow).

studies were all within normal values. The patient then underwent tumor resection in our hospital. The postoperative course was uneventful.

Materials and methods

The resected specimens were fixed with 10% neutral-buffered formalin and embedded in paraffin blocks. Tissue blocks were cut into 4-μm slides, deparaffinized in xylene, rehydrated with graded alcohols, stained with hematoxylin and eosin or immunostained with the following ready antibodies (MaiXin, China): cytokeratin (CK, AE1/AE3), Epithelial Membrane Antigen (EMA, E29), glial fibrillary acidic protein (GFAP, GA-5), S-100 protein (4C4.9), synaptophysin (SP-11), mutant IDH1 (R132H), Nuclear Protein (NeuN, A60), CD34 (QBEnd/10), Ki67 (MIB-1), oligodendrocyte lineage transcription factor 2 (oligo-2), p53 (DO-7) and Vimentin (MX034), Sections were stained with a streptavidin-peroxidase system (KIT-9720, Ultrasensitive TM S-P, MaiXin, China). The chromogen of immunostaining used was diaminobenzidine tetrahydrochloride substrate (DAB kit, MaiXin, China), then the slide was slightly counterstained with hematoxylin, dehydrated and mounted. Special stain for reticulin was performed using standard methods. A CFDA-approved human BRAF V600E ARMSPCR kit (Amoy Diagnostics Co. Ltd., Xiamen, China) was used on DNA extracted from formalin-fixed paraffin-embedded tissues by PCR.

Results

Histologic features

Histologically, the tumor showed a relatively clear border with the normal cerebral tissue. The tumor was predominately consisted of irregular spindle-shaped, ovoid cells with scattered multinuclear giant cells. The tumor cells seemed to demonstrate moderate cellular pleomorphism, whereas, the mitosis of the tumor cells was absent. Occasionally, the nuclear inclusion was present in the nuclei of the tumor cell. Moreover, the scattered lymphocytes, eosinophilic granular bodies and xanthomatous cells could also be observed among the tumor cells (**Figure 2**).

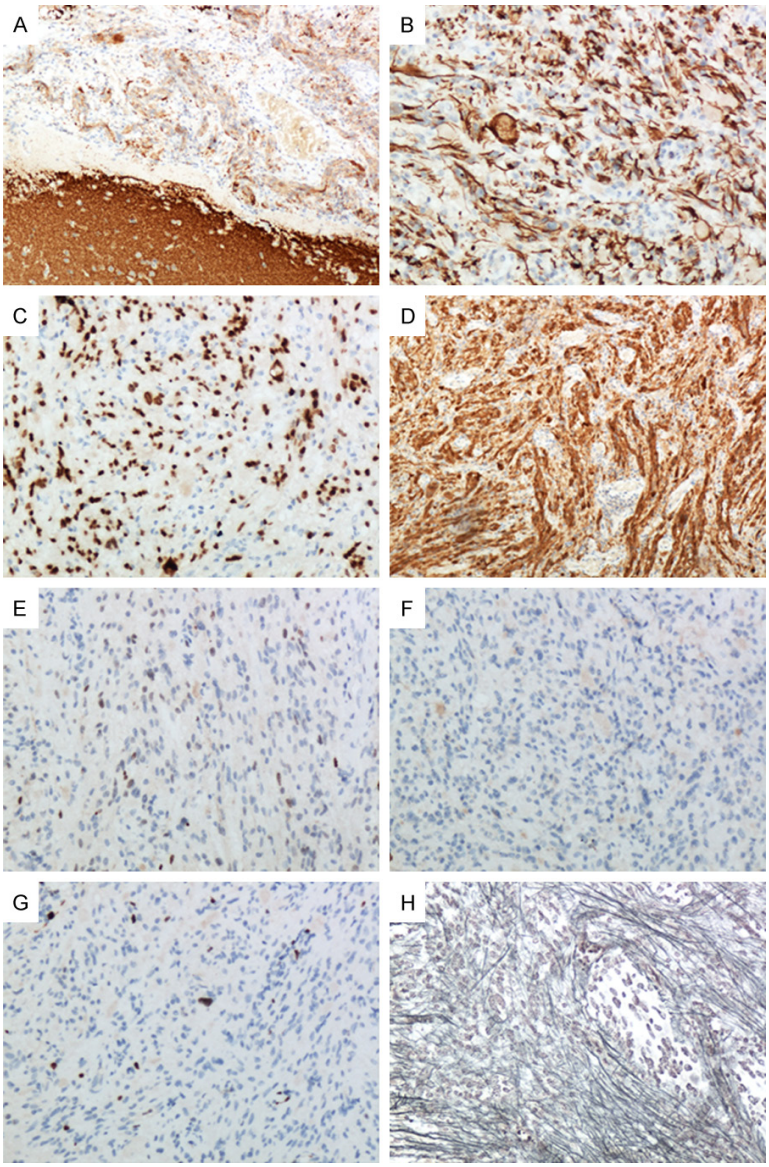

Figure 3. Immunohistochemical and special staining of the tumor. A. The neoplastic cells were focally and weakly positive for synaptophysin, in contrast to the strong staining of synaptophysin in normal brain tissue, highlighting the relative clear border of the tumor. B. Diffuse and strong staining for GFAP could be observed in the tumor. C. Most of the neoplastic cells were positive for oligo-2. D. The diffuse and strong staining for S-100 could also be observed in the tumor. E. The staining pattern of p53 suggested the absence of P53 mutation in the tumor. F. The tumor cells were entirely negative for NeuN. G. The Ki-67 proliferative index was approximately 2%. H. Reticulin staining highlighted the presence of reticulin fibers surrounding the individual tumor cells.

Immunohistochemical staining

Immunohistochemically, the tumor cells were strongly positive for S-100, GFAP, oligo-2 and vimentin, focally positive for synaptophysin and CD34, negative for cytokeratin, EMA, NeuN and IDH1. The staining p53 showed a pattern of wild type. Reticulin staining highlighted the presence of reticulin fibers surrounding the individual tumor cells. Ki-67 proliferation index was approximately 2% (**Figure 3**).

BRAF V600E mutation

We then examined BRAF V600E mutation in the tumor, and a BRAF V600E mutation was confirmed.

According to the morphologic and immunohistochemical findings and BRAF V600E mutation, the tumor was diagnosed as a PXA.

Follow-up

The patient did not undergo adjuvant therapy after operation. There was no evidence of relapse after 8 months of follow-up.

Discussion

In astrocytic tumors, PXA is relatively rare, which most commonly involved the superficial cerebral hemispheres of children or young adults. Rarely, PXA could involve the sites including sella [4], spinal cord [5], retina [6] and ventricle [7-11]. To our knowledge, so far there were only two cases of PXA occurring in lateral ventricle reported in English literature [7, 9]. In 2010, Fu et al reported the first case of PXA occupying the right lateral ventricle and the third ventricle [7]. Subsequently, Yang et al also reported a case of PXA in the right lateral ventricle with extensive subarachnoid dissemination [9].

We reviewed all the literature in PubMed about PXA in uncommon locations. As listed in **Table 1**, so far there are 8 cases of PXA that reportedly occurred inside a ventricle or involved a

Table 1. Pleomorphic xanthoastrocytomas (PXA) involving the ventricle

Case	Age/ Sex	Location	Pathology	Specialstains/Immunohisto-chemistry/molecular finding	Treatment	Follow-up
Klein et al	18/F	Hypothalamus, the third ventricle	Astrocytoma Grade II	-	Subtotal resection, radiotherapy	Died, 12 years after resection
Abe et al	41/F	Hypothalamus, protruding into the third ventricle	PXA	Positive for GFAP, S-100 and vimentin, Ki-67 index less than 0.5%	Partial resection without additional therapy	No signs of tumor regrowth, 6 years
Fu et al	52/M	Right lateral ventricular wall and the third ventricle	PXA with anaplastic features	Positive for GFAP, S-100 and vimentin; partly positive for NF protein, CD34 and synaptophysin, Ki-67 index 7-11%	Subtotal resection, postoperative radiotherapy and chemotherapy	Alive, 6 months after surgery
Gonçalves et al	15/M	Left temporo- occipital paratrigonal region, growth into the ventricular system	PXA	-	-	Recurred after 5 years; free of disease, 10 years
Rodríguez-Mena R et al	54/M	Parietooccipital tumour extending through the ipsilateral ventricle	PXA	Positive for synaptophysin, GFAP S-100 protein, vimentin and CD56.	Resection	Relapse and anaplastic changes, 9 months
Yang et al	42/F	Right lateral ventricle, extensive subarachnoid dissemination, bilateral trigeminal and oculomotor nerves metastasis	PXA	Positive for GFAP, synaptophysin, S-100 protein and vimentin	Operation	Died 3 days after operation
Menendez R et al	24/M	The third ventricle	PXA	Positive for GFAP, NF protein; Ki-67 index was low	Surgery	No evidence of tumor, relapse, 48 months
The present case	28/M	Left lateral ventricle	PXA	Strongly positive for S-100, GFAP, oligo-2 and Vimentin, focally positive for synaptophysin and CD34, Ki-67 index 2%; BRAFV600E mutation	Total resection	No evidence of tumor relapse, 8 months

ventricle. Among them, 3 females and 5 males were included, and age ranged from 18 to 52 years (mean, 34 years), generally consistent with the cases in other locations [3]. 3 cases involved the third ventricles, 4 cases involved the lateral ventricles, and one case involved the third ventricle and the lateral ventricle concurrently. Half of them were periventricular and protruding into the ventricle, rather than inside the ventricle. Our case was the third case of PXA intra-lateral ventricle and the first case that completely inside the left lateral ventricle without other location involvement.

In contrast to other low-grade astrocytic tumors, such as diffuse astrocytic tumor, PXA is morphologically characterized by a mixture of pleomorphic cells, multinucleated giant cells and xanthomatous cells. The presence of bizarre pleomorphic cells and multinucleated giant cells may cause a diagnostic confusion with glioblastoma, especially if PXA showed anaplastic features. Moreover, PXA may share common characteristics such as well-circumscribed solid and/or cystic mass and leptomeningeal involvement or dissemination with glioblastoma in macroscopy and MRI [12]. Our case was also a well-circumscribed solid and cystic mass, consistent with cases reported by Fu et al and Yang et al [7, 9]. In contrast, the case reported by Fu et al was located inside the third ventricle and the lateral ventricle concurrently [7], and the case reported by Yang et al had subarachnoid dissemination [9].

Immunohistochemically, PXA showed consistent reactivity for S-100, GFAP and oligo-2, suggesting its nature of astrocytes [7-11]. However, PXA occasionally showed neuronal differentiation and expressed neuronal markers including synaptophysin and neurofilament [5]. The uniform staining results were also observed in the cases involving ventricles including our case. Ki-67 index was generally low, whereas, anaplastic PXA had a significantly higher Ki-67 index. Another useful diagnostic tool is reticulin fiber staining, as reticulin network was always present among the individual cells [5]. Recently, molecular detection was widely used in diagnosis of tumors of the central nervous system. From the data in a large series of PXA, approximately 60% of PXAs had BRAFV600E mutation [13, 14]. Our case also showed BRAFV600E mutation. Unfortunately, other 7 cases did not supply the information on BRAFV600E mutation. Thus, we need gather more cases in the uncommon locations to further know the status of BRAF. It should be noted that BRAFV600E

mutation was also present in epithelioid glioblastoma, thus the BRAFV600E mutation was not useful for discriminating them [12, 16].

The differential diagnosis of PXA includes ganglioglioma, glioblastoma, and subependymal giant cell astrocytoma. The correct diagnosis could be made based on histologic features, adequate immunohistochemical staining, and molecular detection.

Generally, PXA tends to show a relatively good prognosis. Anaplastic PXA or PXA with leptomeningeal spread or other locations involvement may have a worse prognosis [17-19]. Furthermore, patients with gross total resection had a better prognosis compared with patients with PXA with subtotal resection [19]. More importantly, according to the studies by Tabouret et al and Cristiane et al respectively [15, 18], BRAF mutation tended to be associated with better prognosis. Of the 8 cases involving ventricles, 2 cases died and 4 cases recurred. In the present case, the tumor was totally resected, and there was no evidence of relapse after 8 months of follow-up. Our case also showed a BRAFV600E mutation, suggestive of good prognosis.

Conclusion

In conclusion, we present the third case of PXA intra-lateral ventricle in a 28-year-old Chinese male. Our case was also the first case that completely inside the left lateral ventricle without other location involvement. We then confirm a BRAFV600E mutation in this location. It should be noted that PXA may be an important differential diagnosis for a tumor located in the ventricle, in order to avoid misdiagnosis.

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Disclosure of conflict of interest

None.

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