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Pleomorphic xanthoastrocytoma in the posterior fossa: a case report with advanced neuroimaging findings

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ABSTRACT

Pleomorphic xanthoastrocytoma (PXA) is a rare glioma usually occurring in children and young adults. It is a benign World Health Organization (WHO) grade II tumor that accounts for < 1% of all astrocytomas. Its occurrence in the infratentorial compartment is rare, and the cerebellum is the most common of the unusual locations. Few case reports have described conventional imaging features of these tumors, but none has reported the advanced magnetic resonance (MR) neuroimaging features in dynamic susceptibility perfusion-weighted imaging (DSC-PWI), diffusion weighted-imaging (DWI) and MR spectroscopy. Therefore, the purpose of this study is to report a case of PXA in the cerebellum of a 28-year-old patient and discuss the MR advanced imaging characteristics compared to the more common PXA supratentorial type.

1. Case report

A 28-year-old woman presented with 4-day history sudden onset headaches, diplopia, nausea and vomiting. Past medical history included less severe headaches over the past two years. Initial neurologic examination demonstrated multidirectional nystagmus and discrete papilledema. Magnetic Resonance Imaging (MRI) (Figs. 1 and 2) revealed a left cerebellar periventricular heterogeneously enhancing mass on T1 post gadolinium weighted imaging (WI) with T2 and FLAIR hyperintensity without restricted diffusion. Gradient echo imaging (GRE) and CT revealed no evidence of calcifications. MR spectroscopy demonstrated increased choline and decreased *N*-acetylaspartate (NAA) peaks (Choline/NAA ratio = 1.9), increased choline/creatine ratio (2.5) and mean high relative ADC values of 1.6. Dynamic susceptibility contrast perfusion-weighted imaging (DSC-PWI) showed a mild increase in relative cerebral blood flow (rCBV) (maximum of 1.4) (Fig. 3), suggestive of a low-grade tumor. The mass was completely excised via midline suboccipital craniotomy. The tumor had no contact with adjacent cerebellar parenchyma and extended to the fourth ventricle. Post-operative course was uneventful, and patient was back at baseline 15 days post-surgery. The patient still had lesser intensity headaches, however these did not increase in intensity and she denied experiencing any diplopia, nausea or vomiting at 10 month follow up.

Histology demonstrated several compact irregular fragments with heterogenous tissue with an elastic surface and heterogeneous tissue, inferring clear cell neoplasia. Immunochemistry antibodies favored the diagnosis of a pleomorphic xanthoastrocytoma (PXA), WHO grade II.

2. Discussion

Pleomorphic xanthoastrocytoma (PXA) is a rare glioma usually occurring in children and young adults [1,2] accounting for < 1% of all astrocytomas [3,4], considered a benign grade II tumor arising from subpial astrocytes by the World Health Organization (WHO). The majority of PXAs are solid cystic, enhancing and located supratentorially most commonly in the temporal lobe [3,5], located superficially contacting the leptomeninges [6–8]. There are limited studies regarding supratentorial PXAs advanced MRI imaging features. Infratentorial PXAs are extremely rare and usually occur in the cerebellum [3,9] with only 24 cases currently reported in the literature [3] and only 14

Abbreviations: PXA, pleomorphic xanthoastrocytoma; DSC-PWI, dynamic susceptibility perfusion-weighted imaging; DWI, diffusion weighted-imaging; MRI, magnetic resonance imaging; CT, Computed tomography; WHO, World Health Organization; FLAIR, Fluid attenuation inversion recovery; NAA, *N*-acetylaspartate; ADC, apparent diffusion coefficient; GFAP, Glial fibrillary acidic protein; CBV, cerebral blood volume; IDH1, isocitrate dehydrogenase 1

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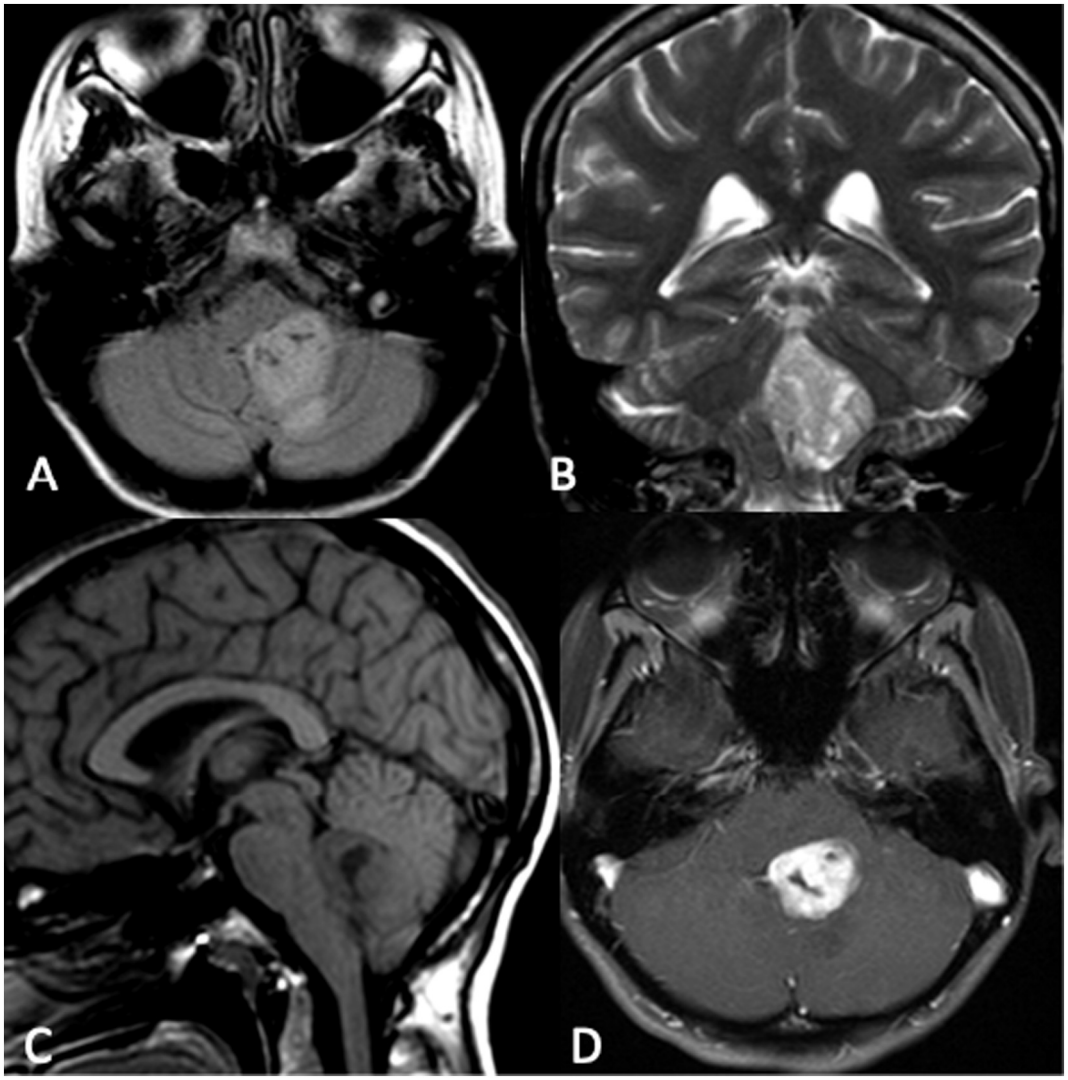

Fig. 1. 28-year-old female with a periventricular mass. FINDINGS: MRI (1.5 T) demonstrates a predominately T2/FLAIR hyperintense solid-cystic periventricular lesion, causing effacement of the IV ventricle (A, Axial FLAIR; B, T2WI), associated with minimal peripheral edema, central cystic/necrotic changes, mass affect upon the vermis and left middle cerebellar peduncle and avid contrast enhancement (C, non-contrasted Sagittal T1WI and D, Axial T1WI after gadolinium administration).

detailing conventional imaging characteristics [3,5,9–20] (Table 1). However, to the best of our knowledge, none has reported the advanced neuroimaging (DSC-PWI, DWI and spectroscopy) features in these tumors.

Similar to the supratentorial compartment, the posterior fossa PXA may show heterogeneous contrast enhancement of solid portions, cystic degeneration, and peritumoral edema. However, leptomeningeal enhancement, a characteristic feature of supratentorial PXAs, was not systematically demonstrated in the cases published in the literature to date. The most popular locations for infratentorial PXAs were the periventricular and midline/vermis regions (see Table 1).

There is scarce literature regarding advanced imaging characterization of the more common supratentorial PXAs [4]; nevertheless, to the best of our knowledge, there has been no report on the advanced imaging features of the infratentorial types. Few studies focusing on advanced imaging of PXAs showed that these tumors follow MRI features similar to other astrocytomas. Whereas Grade II PXAs tend to be smaller and less heterogeneous in signal, associated with little or no peripherical vasogenic edema, have higher rADC and lower rCBV values on DSC-PWI, higher grade (i.e., anaplastic PXA) has more heterogeneous contrast enhancement, obvious peritumoral edema, lower rADC values on DWI, and higher rCBV values on DSC-PWI [4,21].

In the current case, the infratentorial PXA demonstrated mild increase in relative rCBV on DSC-PWI and higher rADC on DWI, suggestive of a low-grade tumor. On the contrary, anaplastic PXAs may show higher rCBV and lower rADC measures, as shown by a series of 19 patients with supratentorial and anaplastic PXAs [4].

Accordingly, advanced imaging with DSC-PWI, spectroscopy and ADC features may help differentiate these tumors from other more common infratentorial enhancing lesions, such as metastatic tumors and lymphoma, which would have higher relative rCBV and lower ADC values, respectively. Imaging differentiation from posterior fossa pilocytic astrocytoma remains difficult, as it may share overall similar characteristics in morphologic and advanced imaging. However, pilocytic astrocytomas may have higher lactate peaks [22], which was not observed in this single case. Also, higher mean ADC values have been associated with pilocytic astrocytomas compared to PXA in the supratentorial compartment, with a 93.8% sensitivity and 100% specificity for a value > 1.19 [23]. Additionally, ADC values may also help differentiation between PXA and the highly hypercellular cerebellar hemispheric adult medulloblastomas, since the latter show obvious restricted diffusion on DWI. High-grade astrocytomas and anaplastic astrocytomas have more aggressive characteristics, including greater maximum tumor diameter, more frequent heterogeneous contrast

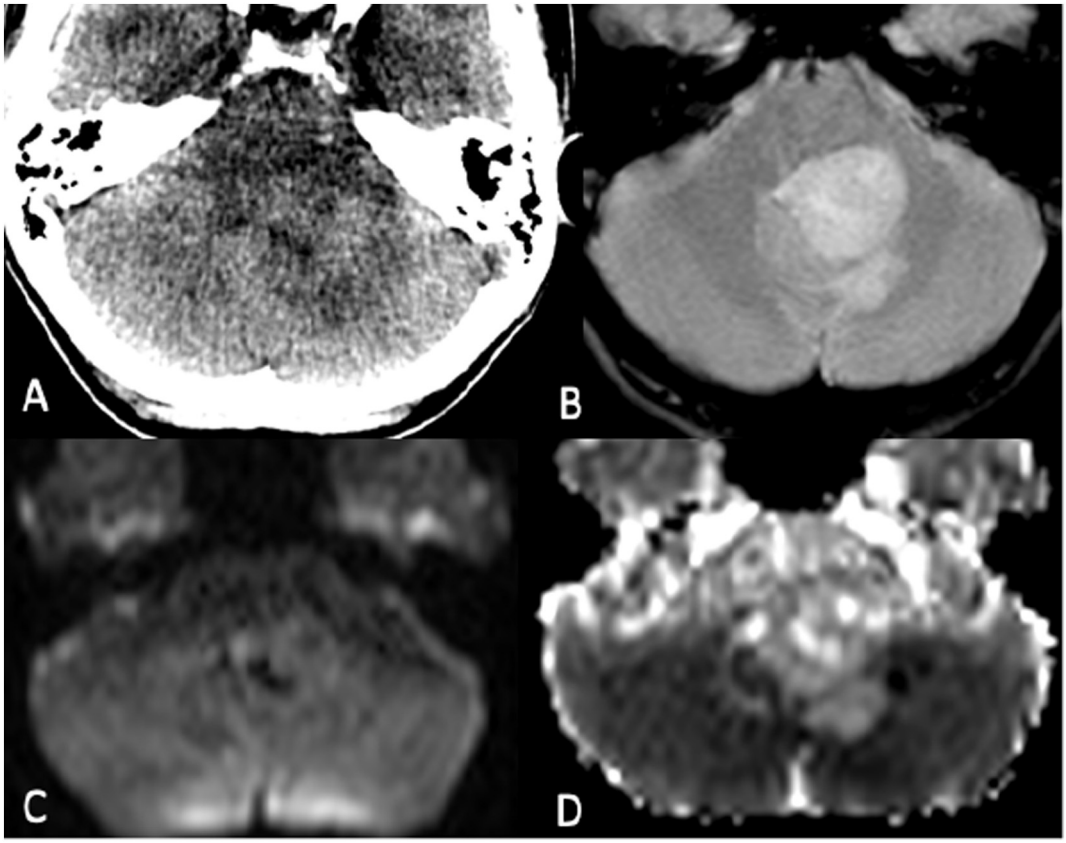

Fig. 2. 28-year-old female with a periventricular mass. FINDINGS: Axial non contrasted CT shows no evidence of calcification (A). MRI (1.5 T) shows no signs of hemorrhage on axial *gradient echo* (GRE) sequence and no restricted diffusion (C, diffusion-weighted image – DWI, D, apparent diffusion coefficient - ADC).

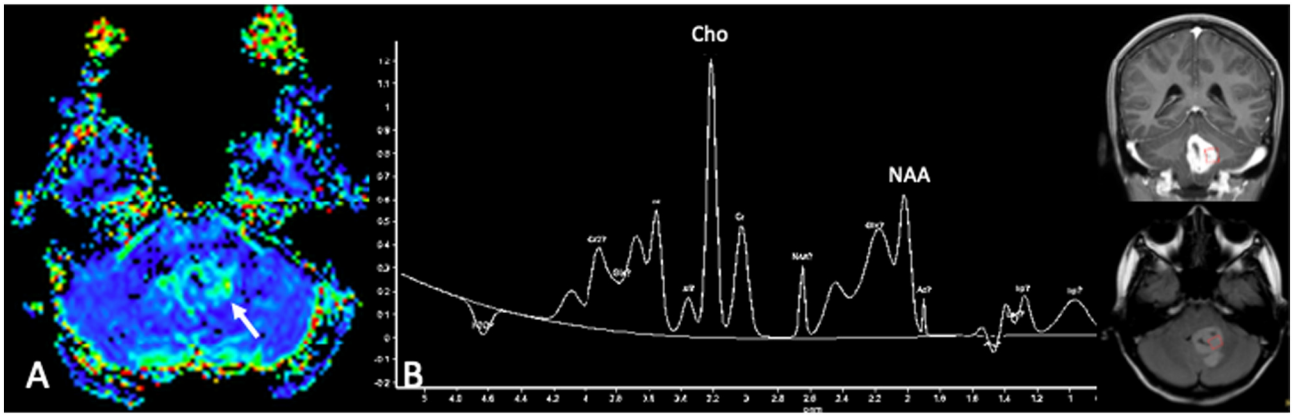

Fig. 3. 28-year-old female with infratentorial PXA. Advanced imaging characteristics. FINDINGS: MRI (1.5 T) showing A, mild increase in relative cerebral blood volume (rCBV) (arrow) on DSC-PWI and B, increased choline/NAA radio (1.9) on MR spectroscopy.

enhancement of solid portions, more peritumoral edema, lower minimum rADC on DWI and higher rCBV on DSC-PWI [4].

The main histopathological features are pleomorphic neoplastic cells, sometimes multinucleated, and there may be nuclear inclusions, in addition to frequent cytoplasmic xanthomatous changes (Fig. 4). Neoplastic cells may also present as spindle cells arranged in bundles and fascicles. Other features include perivascular lymphocytic cuff in Virchow-Robin spaces, eosinophilic granular bodies, rich reticulin fibrosis weave, hemorrhage, and protein granular degeneration [24]. There is also immunoexpression of GFAP and S100 [25], Reticulin, beta class III tubulin, and variable expression of neuronal markers, including synaphysphine.

Surgical gross total resection of the tumor is the preferred treatment [26]. The prognosis of PXA is in general good with overall survival of 74%–81% at 5 years and 67%–70% at 10 years follow-up [2,3,27]. In a recent study including 37 patients with histologically proven PXA, patients with tumors located in supratentorial compartment had statistically significant better outcomes in progression free survival as compared to infratentorial tumors [27]. About 15%–30% of PXA undergo recurrence or malignant transformation with anaplastic features such as necrosis and high mitoses, leading to a poorer prognosis [3,26]. Further details on clinical, surgical and histological aspects involving these tumors have been extensively discussed in the literature (for example references 2, 3, 26–30) [2,3,26–30] and are out of the scope of this paper.

This case stresses that infratentorial PXAs may follow the advanced

Table 1
Cases with imaging findings of infratentorial PXA reported in the literature

No	Author (year)	Age (yr)/sex	Histology	Location	Imaging pattern	Enhancement
1	Wasdahl et al., 1994 [10]	48/F	PXA	Posterior cerebellar/Periventricular	Solid-cystic	Intense/heterogeneous
2	Perry et al., 1997 [11]	24/F	PXA-GG	Mid-line cerebellar vermis	Solid-cystic, calcifications	Intense/heterogeneous
		14/F*	PXA-GG	Right cerebellar peduncle	Cystic, hemorrhagic	Minimal ring enhancement
3	Lim et al., 1999 [12]	3 m/F	PXA	Posterior cerebellar/Periventricular	Solid	Intense/heterogeneous
4	Saikali et al., 2005 [13]	30/F	PXA	Right cerebellar hemisphere	Solid-cystic	Intense/heterogeneous
5	Chang et al., 2006 [14]	4/F	PXA	Mid-line cerebellar vermis	Solid-cystic	Intense/heterogeneous
6	Kurschel et al. 2006 [15]	6/F	PXA	Inferior left cerebellum/CPA	Solid-cystic, calcifications	Intense/heterogeneous
7	Hamlat et al., 2007 [9]	58/F	PXA	Left cerebellar hemisphere/Vermis/Periventricular	Solid	Intense/heterogeneous
8	Chapman et al., 2009 [5]	15/M	PXA	Periventricular	Solid-cystic	Intense/heterogeneous
9	Mano et al., 2009 [16]	36/M	PXA	Mid-line cerebellar vermis	Solid-cystic	Intense/heterogeneous
10	Yeaney et al., 2009 [17]	16/M	PXA	Right cerebellar hemisphere/Vermis/Periventricular	Solid-cystic	Intense/heterogeneous
11	Gardiman et al., 2012 [18]	14/F	PXA	Left cerebellar hemisphere/Vermis/Periventricular	Solid-cystic	Intense/heterogeneous
12	Jeong et al., 2014 [19]	13/F	PXA-AT/RT	Left cerebellar hemisphere/Vermis	Solid-cystic	Intense/heterogeneous
13	Takei et al., 2015 [20]	33/F	PXA	Left cerebellar hemisphere	Solid/gyriform pattern	Intense/heterogeneous
14	Gupta et al., 2018 [3]	16/M	PXA	Left middle cerebellar peduncle/Periventricular	Solid-cystic	–

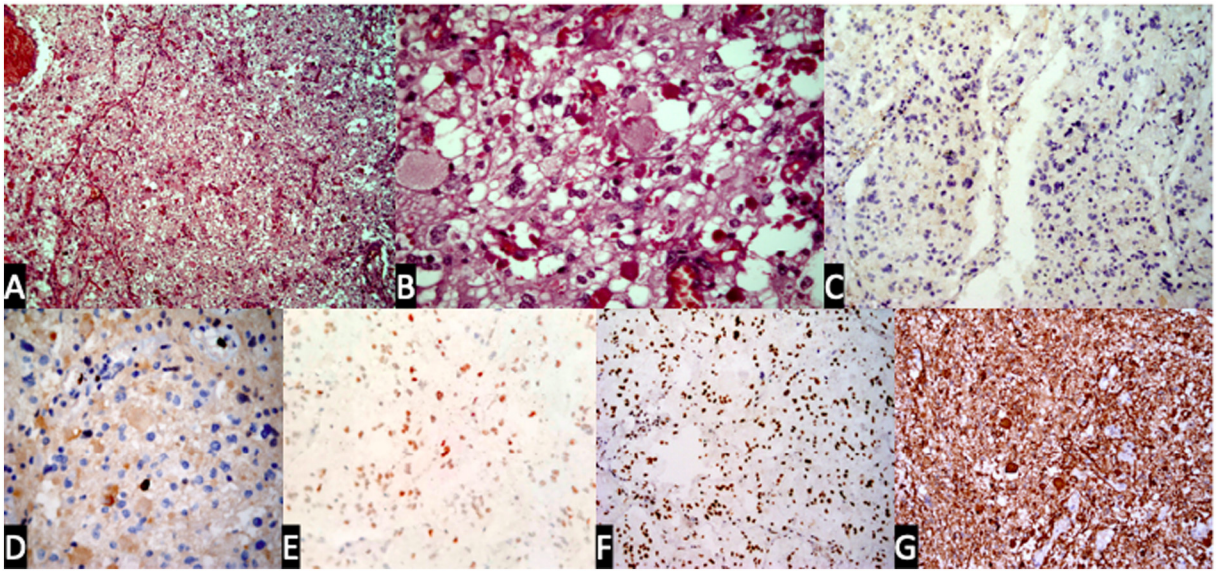

Fig. 4. 28-year-old female with infratentorial PXA. Histopathological findings: A, Astrocytic glial neoplasia showing pleomorphic cells, with frequent xanthomatous alterations and prominent vascularization (HE stained histological sections, 20× magnification). B, In greater magnification, details of the pleomorphism of sometimes multinucleated neoplastic cells and the cytoplasmic xanthomization with frequent hemorrhage and intercellular edema. Absence of necrosis, glomeruloid vascular proliferation and elevated mitotic activity (HE stained histological sections, 40× magnification). C, Absence of immunoexpression in neoplastic cells for IDH1-R132H (Immunohistochemical reaction for IDH1-R132H). D, Low proliferative index detected by ki-67 (Immunohistochemical reaction for KI-67). E, Presence of p53 gene mutations (Immunohistochemical reaction for p53). F, Maintained ATRX gene positivity, ruling out co-mutations in this pathway (Immunohistochemical reaction for ATRX).

imaging characteristics of those located in the supratentorial compartment. DSC-PWI and spectroscopy also follow the rules for astrocytic glial tumors for high/low-grade discrimination. Although rare, an infratentorial periventricular solid-cystic lesion with no restricted diffusion in a young patient in the second or third decades of life should raise suspicion for these glial tumors.

Authors' contributions

Conception and design: Luna, LP. Acquisition of data: all authors. Analysis and interpretation of data: Luna, LP, Gerson, G., Ramos Jr., F., Drafting the article: Luna, LP. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Administrative/technical/material support: Luna, LP, Ponte, IM.

Consent

Authors obtained written informed consent from the patient for submission of this manuscript for publication.

Declaration of competing interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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