Pleomorphic xanthoastrocytoma: magnetic resonance imaging findings in a series of cases with histopathological confirmation

Xantoastrocitoma pleomórfico: achados de ressonância magnética numa série de casos com confirmação histopatológica

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ABSTRACT

Pleomorphic xanthoastrocytoma (PXA) is a rare glioma. This paper aimed to analyze magnetic resonance imaging (MRI) characteristics in a series of patients diagnosed with PXA. We analyzed MRI findings in 9 patients with histopathologic diagnosis of PXA in our department over the last 12 years. The mean age of patients was 27.3 years. Cortical location was observed in all cases. The lesion imaging was solid-cystic in six cases. In eight cases, the solid component presented hypo or isointense on T1 and iso or hyperintense on T2. Contrast enhancement in the solid component was observed in eight cases. The observed imaging pattern of PXA was superficial location with leptomeningeal involvement, solid-cystic pattern and contrast enhancement in the solid component. We should consider that the association between PXA and other cortical tumors may occur, particularly, with gangliogliomas, which tend to be the main differential diagnosis in MRI.

Key words: magnetic resonance imaging, central nervous system, astrocytoma.

RESUMO

Xantoastrocitoma pleomórfico (PXA) é um glioma raro. Este estudo teve como objetivo analisar aspectos de imagem por ressonância magnética (RM) de uma série de pacientes com diagnóstico de PXA. Foram analisados exames de RM de 9 pacientes com diagnóstico histopatológico de PXA nos últimos 12 anos. A média de idade dos pacientes foi de 27,3 anos. Localização cortical foi observada em todos os casos. Padrão sólido-cístico foi observado em seis casos. Em oito casos, o componente sólido apresentou-se hipo ou isointenso em T1 e iso ou hiperintenso em T2. Foi observada captação de contraste na porção sólida em oito casos. O padrão de imagem observado do PXA foi de localização superficial com envolvimento leptomeníngeo, padrão sólido-cístico e captação de contraste pelo componente sólido. Devemos considerar que a associação entre PXA e outros tumores corticais pode ocorrer, particularmente, com ganglioglioma, que tende a ser o principal diagnóstico diferencial em RM.

Palavras-Chave: imagem por ressonância magnética, sistema nervoso central, astrocitoma.

Pleomorphic xanthoastrocytoma (PXA), classically described as a superficial supratentorial glioma that affects young patients, is associated with extensive meningeal involvement[1]. Moreover, it occurs in patients with a long history of epilepsy. Despite their histologic appearance of cellular pleomorphism and the presence of giant cells, literature reviews indicate a good prognosis for this tumor[2-7]. It is a grade II tumor, according to the World Health Organization (WHO) classification of tumors of the central nervous system (CNS)[8]. However, PXA is associated with high rates of recurrence, anaplastic transformation[9-11] and death[12] when comparing with other astrocytic tumors of good prognosis. This study aimed to analyze magnetic resonance imaging (MRI) characteristics in a series of patients diagnosed with pleomorphic xanthoastrocytoma in a university hospital.

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METHODS

Between January 1999 and December 2010, we obtained MRI findings of all patients with histopathologic diagnosis of PXA in our department. The sample comprised 9 patients (6 males and 3 females) and the age varied between 7 and 63 years (mean age=27.33). MRIs were performed using a 2T scanner (Elscint Prestige®, Haifa, Israel), with T1 and T2 acquisitions in three orthogonal planes, including T1-weighted SE gadolinium-enhanced images. MRI acquisition parameters were: sagittal T1 spin echo, 6 mm thick, 180° flip angle; repetition time (TR)=430 milliseconds, echo time (TE)=12 milliseconds, matrix 200×350, field of view (FOV)=25×25 cm; T2-weighted and proton density "fast spin echo" (FSE), 3 mm thick, 160° flip angle; TR=4.800 milliseconds, TE=108/18 milliseconds, matrix 256×256, FOV=22×22 cm; Axial T1-weighted spin echo (SE): TR=540 milliseconds, TE=28 milliseconds; axial T2-weighted fluid-attenuated inversion recovery (FLAIR) images TR=8.500 milliseconds and 2.000 or 100 milliseconds, and 2.200 milliseconds, TE=72 or 90 milliseconds, matrix of 256×296 and FOV of 22×22 cm. T1-weighted SE gadolinium-enhanced images were obtained in three orthogonal planes.

All patients underwent surgical biopsy or tumor excision, according to clinical indication. The surgical specimens were processed for routine histopathology, and the classification of tumor type was performed following the World Health Organization (WHO) guidelines.

MRI files were evaluated by one neuroradiologist (FR). We analyzed the following variables: tumor location, signal on T1 and T2-weighted images, contrast enhancement, edema and association with other tumors in histological examination. The project was submitted to the Ethics Committee of our service, which approved the research protocol (process nº 0722.0.146.000-10, approved Protocol nº 928/2010). Statistical analysis was performed with assessment of the statistics department of our service.

RESULTS

Tables 1 and 2 summarize patient's data. Patients ages ranged between 7 and 63 years (mean age=27.33 years; median=28.0; standard deviation=19.072). All patients were

Table 1. Clinical data.

Patient	Gender	Age	Symptom and clinical examination	Time of symptom	Recurrence (time) – follow-up
1	M	7	Generalized tonic-clonic seizures	3 years	-
2	F	28	Seizures	13 years	No – 3 yrs
3	F	31	Partial epilepsy, altered alertness and blurred vision	8 years	No – 2 yrs
4	F	29	Seizures	2 weeks	Yes (10 yrs) – 15 yrs
5	M	15	Seizures	9 years	No – 6 yrs
6	M	7	Simple partial epilepsy and left parietal headache	-	-
7	M	63	Confusion, behavior changes, apathy and depression	1 month	No – Death (1 mo)
8	M	16	Generalized tonic-clonic seizures	1 year	No – 10 yrs
9	M	50	Confusion and syncope	3 months	No – 9 yrs

M: masculine; F: feminine; yrs: years; mo: month.

Table 2. Imaging data.

Patient	Location	Side	Imaging pattern*	Leptomeningeal contact	Edema	T1WI	T2WI	Contrast enhancement	Histopathology
1	Paracentral lobule	Left	Solid	No	No	Hypointense	Hyperintense	Yes (homogeneous)	Isolated PXA
2	Parietal lobe	Right	Solid-cystic I	Yes	No	Iso/ Hypointense	Hyperintense	Yes (heterogeneous)	PXA + ganglioglioma
3	Middle temporal gyrus	Right	Solid-cystic I	Yes	No	Hypointense	Hyper/ Isointense	Yes (minimal)	PXA + ganglioglioma
4	Superior parietal lobule	Left	Solid	Yes	Marked	Isointense	Isointense	Yes (homogeneous)	PXA + ganglioglioma + ependymoma
5	Temporal pole	Right	Cystic	No	No	Hypointense	Hyperintense	No	PXA + cortical dysplasia
6	Parieto-occipital region	Left	Solid-cystic II	Yes	No	Iso/ Hypointense	Iso/ Hyperintense	Yes (heterogeneous)	Isolated PXA
7	Frontal region	Right	Solid-cystic III	Yes	Mild	Iso/ Hypointense	Hyper/ Isointense	Yes (heterogeneous)	Isolated PXA
8	Precentral and postcentral gyri	Left	Solid-cystic I	Yes	Mild	Hypointense	Hyperintense	Yes (heterogeneous)	Isolated PXA
9	Frontal pole	Left	Solid-cystic I	Yes	Mild	Hypointense	Hyperintense	Yes (minimal)	Isolated PXA

PXA: pleomorphic xanthoastrocytoma.

symptomatic at diagnosis, and the time of symptom presentation was higher than three years in four of them. Seven patients presented history of epilepsy and the other two, mental confusion. Cortical location was observed in all nine cases. More than one lobe was affected in three patients. The parietal lobe was the most affected (five cases), followed by frontal (four) and temporal lobes (two). The lesion imaging was solid-cystic in six cases. Three imaging patterns were differentiated: first, a cystic mass containing a mural nodule (four cases); second, a predominantly solid mass that showed cystic changes (one); and third, a mixed pattern (one). On T1-weighted images, the solid component presented hypo– or isointense in all nine cases. While on T2-weighted images, the solid component presented isointense in four cases and hyperintense in seven. Leptomeningeal involvement was observed in seven cases, and contrast enhancement in the solid component was observed in eight cases. Peritumoral edema was observed in four cases and its magnitude was marked (one) or mild (three). In three cases, PXA was associated with other cortical tumors in histopathology. Ganglioglioma was associated with PXA in two cases and with ependymoma and ganglioglioma in another one. Furthermore, cortical dysplasia was associated with PXA in one case. Seven out of nine patients were followed up, one of whom had tumor recurrence (in the 10th postoperative year) and one died one month after surgery. The other five patients are still alive, well and clinically free from recurrence at different follow-up periods, ranging from two to ten years.

Statistical analysis showed that the presence of edema was associated with a symptom duration of less than one year prior to diagnosis ($p<0.03$) by Fisher's exact test. Older age was associated with atypical clinical presentation ($p<0.05$) by Mann-Whitney test. No association was found between imaging patterns and clinical data or histological examination.

DISCUSSION

In 1979, Kepes et al.[1] described for the first time a series of 12 young patients presenting with a distinctive form of astrocytoma. In all cases, the tumor was supratentorial and superficial, with extensive leptomeningeal involvement and, despite pleomorphism and bizarre giant cells in the microscopic picture, the prognosis was relatively favorable. Since this study, over 200 cases of PXA have been reported, most as single cases or small series[13].

Typical clinical presentation includes a long history of epilepsy, especially in young patients, most commonly in the second decade of life[9]. Although 7 patients have presented seizures in our study and 6 of them were younger than 30 years, we had two patients with mental confusion as initial symptom, who were the oldest patients of our series (50 and 63 years). In our sample, the atypical clinical presentation was significantly associated with older age ($p<0.05$) by Mann-Whitney test. According to our knowledge, there are few reports of elderly patients with PXA in the literature; however, Ng et al.[14] suggest that elderly patients with PXA may have a poor prognosis, considering age as an independent risk factor. In our sample, the oldest patient had a bad prognosis and died one month after surgery (Fig 1).

The most common single location is the temporal lobe, followed by parietal and occipital lobes. Moreover, out of the tumors that involve more than one lobe, the contiguous temporal lobe is the most affected[9]. In our study, temporal, parietal and frontal lobes were equally affected (two cases each lobe), and, of the three tumors that involve more than one lobe, the parietal lobe was the most affected (three cases), followed by frontal lobe (two cases).

Despite its classic cortical location, PXA is rarely seen in the thalamus, cerebellum, spinal cord or within the eye[15-19]. Two cases of intraventricular PXA were recently described[20,21].

On MRI, the solid component of PXA is predominantly isointense on T1-weighted images and mildly hyperintense on T2-weighted images, enhancing intensely after intravenous contrast administration. Surrounding edema usually is minimal[13]. In our study, the solid component was hypo — or hyperintense in eight cases on T1-weighted images and iso — or hyperintense on T2-weighted images in eight cases. Contrast enhancement was minimal (two), homogeneous (three) or heterogeneous (three). Peritumoral edema

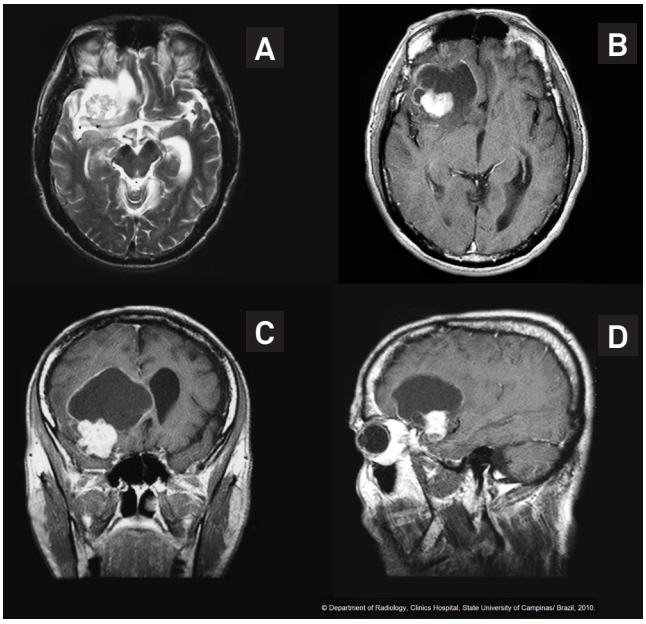

Fig 1. Male, 63 years old. (A) Contrast-enhanced axial T2-weighted magnetic resonance (MR) image shows a frontal expansive solid-cystic lesion, with lobulated delineation. Cystic component shows hyperintensity. Contrast-enhanced axial T1-weighted MR image (B), coronal (C) and sagittal (D) shows enhancement in the solid component and at the periphery of the cystic component.

was observed in four cases, being predominantly mild. Thus, these imaging findings corroborate a typical imaging pattern as described in the literature.

In the four cases in which edema was present in our sample, the duration of symptoms to diagnosis was less than or equal to one year, being significantly different from the other five cases, with greater time of evolution ($p<0.03$) by Fisher's exact test. This finding may suggest that the presence of edema on PXA tumors may be associated with early tumor growth. Logically, the sample size does not allow generalizations, so further studies are essential.

In a histopathological study, PXA was associated with other tumors in three cases, two with ganglioglioma and another with ependymoma and ganglioglioma (Fig 2). Moreover, another case of PXA showed association with cortical dysplasia (Fig 3). Furuta et al.[22] proposed that PXA and ganglioglioma grow from a migration failure, resulting in an ectopic position of neuronal and glial cells. That would explain the fact that PXA coexists in some cases with ganglioglioma or other cortical tumors. Furthermore, Lach et al.[23] presented three cases of cortical dysplasia associated with PXA that suggest a possible preneoplastic role of cortical dysplasia in the subsequent development of PXA.

In conclusion, although this sample comprises only nine patients, most reports of PXA have included only a single case or small series. MRI findings in this series corroborated a typical description of PXA. The observed imaging pattern of PXA was superficial location with leptomeningeal involvement, solid-cystic pattern and contrast enhancement in the solid component. On T1-weighted images, the solid component presented hypo — or isointense and, on T2-weighted images, it was iso — or hyperintense. In our sample, when edema was present, the duration of symptoms to diagnosis was less than or equal to one year. We should consider that the association of PXA with cortical dysplasia or other cortical tumors may occur, particularly with gangliogliomas, which tend to be the main differential diagnosis for MRI.

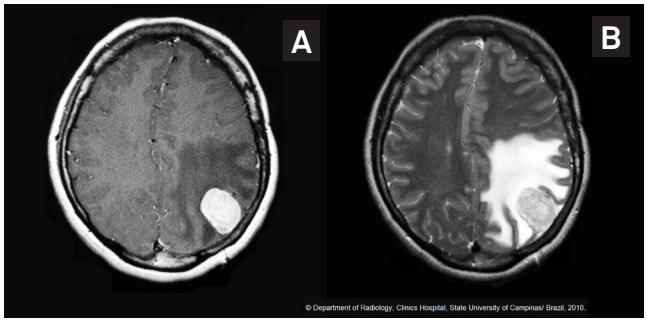

Fig 2. Female, 29 years old. (A) Contrast-enhanced axial T1-weighted magnetic resonance (MR) image shows expansive cortical lesion in the left parietal lobe, with intense enhancement. (B) Axial T2-weighted MR image shows lesion predominantly isointense and moderate edema. Anatomopathology: Mixed tumor, with PXA, ganglioglioma and ependymoma components.

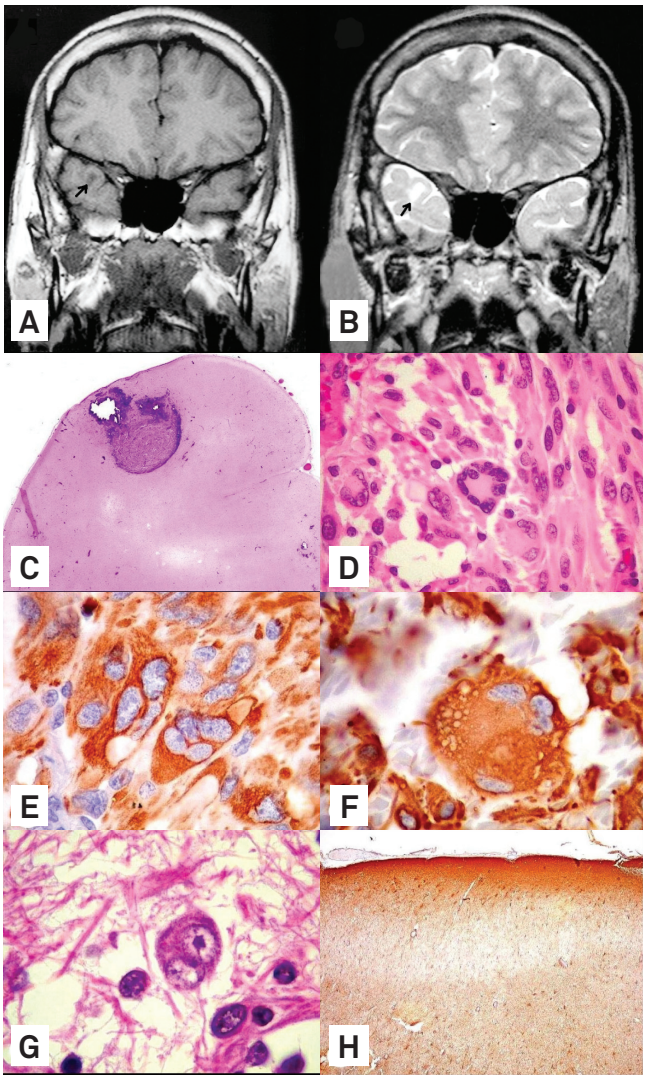

Fig 3. Male, 15 years old. (A) Coronal T1-weighted magnetic resonance (MR) image shows a hypointense subcortical lesion and (B) Coronal T2-weighed MR image shows a hyperintense lesion. (C) Area of cortical dysplasia in right temporal lobe with incidental finding of a small pleomorphic xanthoastrocytoma, appearing as a well delimited, basophilic intracortical nodule. HE, X 10. (D) Pleomorphic xanthoastrocytoma is characterized by atypical rounded or fusiform tumor cells, some of which were multinucleated (center). HE, X 100. (E) Pleomorphic tumor cells with cytoplasmic positivity for GFAP, confirming their astrocytic lineage. Immunohistochemistry for GFAP, X 200. (F) Occasional cells displayed cytoplasmic xanthomatous change. Immunohistochemistry for vimentin, X 200. (G) Dysplastic area of cerebral cortex near the xanthoastrocytoma showing a binucleated neuron. HE, X 400. (H) Same area, gliosis of molecular layer of cerebral cortex (top). Immunohistochemistry for GFAP, X 40.

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