MR Imaging Features of Anaplastic Pleomorphic Xanthoastrocytoma Mimicking High-Grade Astrocytoma

D. She, J. Liu, Z. Xing, Y. Zhang, D. Cao and Z. Zhang

doi: [https://doi.org/10.3174/ajnr.A5701](https://doi.org/10.3174/ajnr.A5701)
http://www.ajnr.org/content/39/8/1446
ABSTRACT

BACKGROUND AND PURPOSE: Anaplastic pleomorphic xanthoastrocytoma, which has been recently defined as a distinct entity in the 2016 World Health Organization classification, may exhibit aggressive clinical behavior and relatively worse prognosis than pleomorphic xanthoastrocytoma. This study aimed to investigate whether there were any differences in MR imaging characteristics between these 2 tumors.

MATERIALS AND METHODS: This retrospective study included 9 patients with anaplastic pleomorphic xanthoastrocytoma and 10 patients with pleomorphic xanthoastrocytoma who underwent MR imaging before an operation. DWI was performed in 17 patients (8 with anaplastic pleomorphic xanthoastrocytoma, 9 with pleomorphic xanthoastrocytoma); and DSC-PWI, in 9 patients (5 with anaplastic pleomorphic xanthoastrocytoma, 4 with pleomorphic xanthoastrocytoma). Demographics, conventional imaging characteristics (location, size, cystic degeneration, enhancement, peritumoral edema, and leptomeningeal contact), minimum relative ADC ratio, and maximum relative CBV ratio were evaluated between the anaplastic pleomorphic xanthoastrocytoma and pleomorphic xanthoastrocytoma groups.

RESULTS: Anaplastic pleomorphic xanthoastrocytoma was more likely to demonstrate high-grade features than pleomorphic xanthoastrocytoma, including greater maximum tumor diameter (4.7 ± 0.6 cm versus 3.1 ± 1.1 cm, P = .001), more frequent heterogeneous contrast enhancement of solid portions (88.9% versus 20.0%, P = .01), more obvious peritumoral edema (2.3 ± 0.9 cm versus 1.0 ± 0.9 cm, P = .008), lower minimum relative ADC on DWI (1.0 ± 0.2 versus 1.5 ± 0.4, P = .008), and higher maximum relative CBV on DSC-PWI (2.6 ± 0.8 versus 1.6 ± 0.2, P = .036).

CONCLUSIONS: Anaplastic pleomorphic xanthoastrocytomas often have more aggressive MR imaging features mimicking high-grade astrocytomas than pleomorphic xanthoastrocytomas. DWI and DSC-PWI might be useful in the characterization and differentiation of anaplastic pleomorphic xanthoastrocytoma and pleomorphic xanthoastrocytoma.

ABBREVIATIONS: APXA = anaplastic pleomorphic xanthoastrocytoma; PXA = pleomorphic xanthoastrocytoma; rADC_{min} = minimum relative ADC; rCBV_{max} = maximum relative CBV; WHO = World Health Organization

Pleomorphic xanthoastrocytoma (PXA) is a rare circumscribed glioma composing <1% of all astrocytic tumors, usually occurring in children and young adults.1 It was first described in 1979 by Kepes et al2 and was recognized as a distinct brain tumor by the World Health Organization (WHO) in 1993.3 Although PXA was classified as a WHO grade II tumor, “PXA with anaplastic features” comprises 15%–50% of these lesions.4-7 The 2016 WHO classification system has divided PXA into 2 distinct entities based on histopathologic features: WHO grade II PXA and WHO grade III anaplastic PXA (APXA).8,9 The APXA is defined as the presence of ≥5 mitoses per 10 high-power fields. Only gross total resection may be performed for the patients with PXA, whereas attempted gross total resection and adjuvant therapies are required for the patients with APXA.5,10 Furthermore, APXA has been reported to have a worse prognosis than PXA, with 5-year overall survival of 57.1%.5,11 Therefore, preoperative differentiation between the 2 entities by MR imaging may aid in planning the treatment strategy and predicting prognosis.

APXA is associated with histopathologic features of malignancy, such as increased mitotic activity, necrosis, or endothelial

http://dx.doi.org/10.3174/ajnr.A5701

1446 She Aug 2018 www.ajnr.org
neous enhancement with severe peritumoral edema. More-imaging features of APXA, which demonstrated intense heteroge-

neity in MR images and imaging protocols. Conventional MR im-

aging was available in 4 patients with PXA and 5 patients with

APXA. DSC-PWI was performed with a T2*-weighted gradient

called echo-planar imaging sequence during the intravenous

power injection of 0.1 mmol/kg of gadopentetate dimeglumine

or gadobenate dimeglumine at a flow rate of 5 mL/s. The pa-

tameters of DSC-PWI were as follows: TR/TE = 1000–1250/54

ms; FOV = 22 × 22 cm; section thickness/gap = 5 mm/1 mm.

The CBV maps were generated with a single-compartment

model and an automated arterial input function, as described

in our previous study.27

MR Imaging Analysis

All images were reviewed in consensus by 2 radiologists (readers 1

and 2 with 20 and 8 years of experience in neuroimaging, respec-

tively) to make a factual comparison and minimize the confound-

ing effects. The readers were blinded to tumor histology and re-

corded the following tumor characteristics: 1) tumor location

(frontal, occipital, temporal, or parietal; superficial or deep); 2) tumor size (largest diameter, in centimeters); 3) the presence

cystic degeneration; 4) enhancement characteristics of the solid

component (heterogeneous or homogeneous); 5) the presence

and degree of peritumoral edema (largest diameter, in centime-
ters); 6) leptomeningeal contact; and 7) the presence of restricted
diffusion, defined as high signal on DWI and corresponding low

signal on ADC maps compared with contralateral normal brain

parenchyma. Tumor size was defined as the largest diameter mea-
sured on contrast-enhanced T1WI. The peritumoral edema was
defined as the nonenhanced, T2-hyperintense regions surround-
ing the enhancing tumors on contrast-enhanced T1WI. The tu-
mor location was defined as the main lobe involvement when >1
lobe was involved.

When DWI or DSC-PWI examinations were available, an-
other experienced radiologist (reader 3 with 4 years of experience

in neuroimaging) blinded to tumor histopathology evaluated the

ADC maps and CBV maps separately. The ADC values of tumor

were calculated by placing an ROI inside the solid components

of the tumor on the ADC maps. Three nonoverlapping ROIs (20–30

mm²) were manually placed inside the solid components of the

tumor on the ADC maps where the tumor showed relatively low

signal. The minimum ADC values were taken into account. In 2

tumors with smaller solid components or obvious hemorrhage,

only 1 ROI could be placed on the enhancing portions of the

tumor. The ROI placement was made from the contrast-en-
hancing solid components of the tumor, avoiding cystic, hem-

orrhagic, or apparent vascular structures that might influence

the ADC values. To minimize variances of ADC values in an

individual patient, we placed a single ROI inside the contralat-

eral normal-appearing brain parenchyma on ADC maps. CBV

measurements were performed with the same ROI as used for

ADC measurements, and the maximum CBV values were con-

sidered. Tumor/parenchyma minimum relative ADC ratios

(rADCmin) and maximum relative CBV ratios (rCBVmax) were

calculated.

Statistical Analysis

The normality of all continuous parameters was initially assessed

using the Kolmogorov-Smirnov test. The Fisher exact test was

used to assess the differences in the categoric variables (age, sex, location, cystic degeneration, enhancement characteristics, leptomeningeal contact, and the presence of restricted diffusion) between the PXA and APXA groups. The Mann-Whitney U test was used to assess the differences in continuous variables (edema and size) between the PXA and APXA groups because of a lack of normality of the data. The Student t test was used to assess the differences for rCBV_{max} and rADC_{min} parameters between the 2 groups. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS 22.0 Version for Windows; IBM, Armonk, New York). P values < .05 indicated statistical significance.

RESULTS

Demographic Data and Conventional MR Imaging

The demographic data and MR imaging features are summarized in Table 1. All 19 tumors were in the supratentorial region. Eight APXAs (8/9, 88.9%) and 9 PXAs (9/10, 90%) were superficial (on the surface of the brain parenchyma). There was no significance in the tumor location between PXA and APXA groups.

On the preoperative imaging, the lesion was significantly larger in patients with APXA than in those with PXA (4.7 ± 0.6 cm versus 3.1 ± 1.1 cm, P = .001). Peritumoral edema was observed in 7 PXA cases and 9 APXA cases, respectively. Eight patients with APXA (8/9, 88.9%) and 4 with PXA (4/10, 40.0%) had obvious peritumoral edema (defined as ≥1 mm in diameter). The maximum diameter of peritumoral edema in the APXA group was significantly larger than that in the PXA group (P = .008). The presence of heterogeneous enhancement of solid portions was observed less frequently in patients with PXA than in those with APXA (2/10 versus 8/9, P = .01). Leptomeningeal contact was seen in 7 APXA cases and 9 PXA cases.

Advanced MR Imaging Findings

Table 2 summarizes the findings of 17 cases with DWI and 9 cases with DSC-PWI. Compared with contralateral normal brain parenchyma, relatively high signal intensity on DWI was more likely to be present in cases with APXA (5/8, 62.5%) than in those with PXA (1/9, 11.1%) (P = .027). Moreover, the rADC_{min} values of APXA were significantly lower than those of PXA (1.0 ± 0.2 versus 1.5 ± 0.4; P = .008). On CBV maps, the rCBV_{max} values of APXA were significantly higher than those of PXA (2.6 ± 0.8 versus 1.6 ± 0.2; P = .036). Representative cases are shown in Figs 1–3.

Table 3 summarizes the MR imaging findings of APXA previously reported in the literature.20-26,28-35
Our results show that APXA had MR imaging features similar to those of other high-grade astrocytomas, namely more heterogeneous contrast enhancement, obvious peritumoral edema, lower rADC_{min} ratio on DWI, and higher rCBV_{max} ratio on DSC-PWI. According to the 2016 WHO classification of the central nervous system, PXA is classified as a grade II astrocytoma histologically. Previous studies have found that PXAs may undergo spontaneous malignant transformation into high-grade gliomas across time without any treatment. In a study of the histologic evolution of the PXA, an abrupt transition from a typical PXA without mitoses to a clearly high-grade tumor was found in a repeat biopsy during long follow-up, which was considered a secondary malignant change on a pre-existing PXA. Thus, APXA (grade III astrocytoma) is more likely to be derived from a previous PXA with the development of anaplastic histologic features. In the present study, APXA accounted for 47.4% of the cases, which is much higher than the number previously reported by Giannini et al. However, the results reported by Hirose et al were that about 50% of PXAs showed anaplastic features, findings comparable with those in our study.

PXA most frequently occurred in children and young adults in our study, consistent with previous studies. In contrast, 6 of 9 patients with APXA were middle-aged adults (40–65 years of age) with a mean age of 47.7 years at their first presentation, which was discordant with previous studies. It has been reported that high-grade astrocytomas, including anaplastic astrocytoma and glioblastoma, were more common in older adults with a median age of 56–64 years. However, most of the patients with APXA in our series were middle-aged adults and tended to be younger than those with other high-grade astrocytomas.

PXA is an overwhelming, superficial supratentorial tumor with a predilection for the temporal lobe. Previous studies reported that PXA occurred rarely in the cerebellum, hypothalamus, quadrigeminal plate, or pineal gland. Similar to PXA, almost all APXA tumors in our series showed a superficial location in the cerebral hemispheres with involvement of the superficial cortex and leptomeninges. Both PXA and APXA are believed to develop from subpial astrocytes, which partly explains why these 2 tumors preferably arise from superficial cortical sites. Our findings demonstrate that a superficial location with leptomeningeal contact was a frequent feature of APXA and PXA. In addition, our results show that the common tumor location of PXA was the temporal lobe (50.0%), which is in keeping with findings in previous studies.

Conventional MR imaging can provide useful information regarding tumor size, contrast enhancement, peritumoral edema, necrosis, hemorrhage, and cystic degeneration, which are all helpful in characterizing tumor aggressiveness and evaluating tumor grading. In our study, we found that APXA had significantly
greater tumor size than PXA, which may be due to the relatively high proliferative potential of APXA. Previous case reports demonstrated that APXA showed intense heterogeneous enhancement and obvious peritumoral edema on conventional MR imaging. In our study, we also found that all except 1 APXA showed heterogeneous contrast enhancement with marked peritumoral edema. In contrast, only 2 PXA cases showed heterogeneous enhancement, and 3 cases had marked peritumoral edema. The enhancement pattern of APXA could be explained by the presence of necrosis, hemorrhage, and vascular proliferation within the tumor, which was observed in most APXAs by Rutkowski et al. Additionally, our cohort showed results similar to those in a previous study for the frequency of the peritumoral edema. In the study of Lim et al, all PXAs with anaplastic features (4 cases) had severe perilesional edema, while only 1 of 18 PXAs presented with severe peritumoral edema, 6 cases had none, 8 cases had mild edema, and 3 cases had moderate edema. Our study demonstrated that the area of peritumoral edema in APXA was larger than that in PXA. Peritumoral edema was defined as nonenhancing, T2-hyperintense regions surrounding the enhancing tumors, which represented a heterogeneous mixture of infiltrative neoplastic cells and vasogenic edema in other high-grade astrocytomas. Despite appearing as a circumscribed tumor, most PXAs demonstrated infiltration into the surrounding brain. However, the pathology of peritumoral "edema" in APXA remains uncertain. Further pathologic investigations are required to explore whether the peritumoral edema surrounding the APXA tumor represents vasogenic edema or tumor infiltration.

DWI has been described as a useful tool for glioma grading using ADC values, which negatively correlate with cellularity and the Ki-67 labeling index in tumors. Only a few prior studies in the literature evaluated PXA and APXA using DWI. In a small group study of 11 children with PXA, Moore et al demonstrated that the mean ADC ratio of 6 PXAs, including 1 APXA, was 1.13, without statistical analysis. In the present study, we found that the signal intensity in the solid components of the APXA tended to be hyperintense relative to normal-appearing brain parenchyma on DWI. In addition, the signal intensity of APXA was significantly higher than that of PXA on DWI. The rADC ratio of PXA and APXA in our study was 1.29 ± 0.44, which was consistent with that in a recent study. To the best of our knowledge, the differences in ADC ratios between APXA and PXA have not been reported. Our study demonstrates that the rate of water diffusion of APXA, as reflected by the ADC ratio, was significantly lower than that of PXA. Compared with PXA, the association of lower ADC ratios in APXAs might be due to markedly high cellularity and a high nuclear/cytoplasmic ratio, which were also observed in other high grade astrocytomas. Therefore, our findings reveal that ADC could be a useful imaging parameter for assessing the differences between APXA and PXA based on distinct cell density and the nuclear/cytoplasmic ratio.

DSC-PWI has become an important tool in the preoperative characterization and grading of brain gliomas using rCBV values. Although many studies have reported that rCBV parameters were useful in astrocytoma grading, most of these studies failed to group APXA as a high-grade glioma or even to consider it as a separate cohort. To our knowledge, there are no studies assessing the differences in CBV values between APXA and PXA. Limited evidence suggested that the tumor vascularity of PXA was distinct from that in APXA. In a histopathologic study of PXA, 4 of 6 APXAs showed microvascular proliferation, while no PXA exhibited this phenomenon. We found that the rCBV values of APXA and PXA were 2.6 ± 0.8 and 1.6 ± 0.2, respectively. The rCBV values of contrast-enhancing portions of APXA seemed to be higher than those of PXA. These preliminary findings may be explained by more microvascular proliferation in anaplastic lesions, resulting in an increase in the CBV value. However, the small number of patients did not allow making generalizations such as discrimination of APXA from PXA with DSC-PWI. Future investigations with emphasis on DSC-PWI of APXA and PXA may be of benefit.

In addition to the intrinsic limitations of a retrospective study, our study had several other limitations. First, the number of patients with advanced MR imaging remained limited; therefore, the conclusions should be interpreted with caution, especially for DSC-PWI. Future studies of larger cohorts with advanced MR imaging at advanced centers will be particularly useful.

Table 3: Summary of MR imaging findings of APXA previously reported in the literature

<table>
<thead>
<tr>
<th>No.</th>
<th>Author [Year]</th>
<th>Age (yr)/Sex</th>
<th>Location</th>
<th>Size (cm)</th>
<th>Imaging Pattern</th>
<th>Enhancement</th>
<th>Peritumoral Edema</th>
<th>Well-Circumscribed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tekkok and Sav (2004)</td>
<td>13/M</td>
<td>Frontal</td>
<td>–</td>
<td>Solid-cystic</td>
<td>Heterogeneous/intense</td>
<td>Severe</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>Koga et al (2009)</td>
<td>47/F</td>
<td>Frontal</td>
<td>6</td>
<td>Solid</td>
<td>Homogeneous/intense</td>
<td>Severe</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>Fu et al (2010)</td>
<td>52/M</td>
<td>Ventricule</td>
<td>–</td>
<td>Cystic-solid</td>
<td>Heterogeneous/intense</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>Vu et al (2012)</td>
<td>50/M</td>
<td>Temporal</td>
<td>2.7</td>
<td>Solid-cystic</td>
<td>Heterogeneous/intense</td>
<td>Severe</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>Lim et al (2013)</td>
<td>37/F</td>
<td>Corpus callosum</td>
<td>4</td>
<td>Cystic</td>
<td>–</td>
<td>Severe</td>
<td>+</td>
</tr>
<tr>
<td>12</td>
<td>Montano et al (2013)</td>
<td>22/M</td>
<td>Multicentric</td>
<td>–</td>
<td>Solid</td>
<td>Without enhancement</td>
<td>Mild</td>
<td>–</td>
</tr>
<tr>
<td>13</td>
<td>Benjamin et al (2015)</td>
<td>65/M</td>
<td>Temporal</td>
<td>3.7</td>
<td>Cystic-solitic</td>
<td>Heterogeneous/intense</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>14</td>
<td>Patibandla et al (2016)</td>
<td>35/M</td>
<td>Frontal</td>
<td>–</td>
<td>Solid</td>
<td>Heterogeneous/intense</td>
<td>Severe</td>
<td>–</td>
</tr>
<tr>
<td>15</td>
<td>Chaodry et al (2016)</td>
<td>55/M</td>
<td>Temporal</td>
<td>2.2</td>
<td>Solid</td>
<td>Heterogeneous/intense</td>
<td>Mild</td>
<td>–</td>
</tr>
<tr>
<td>16</td>
<td>Thara et al (2017)</td>
<td>42/M</td>
<td>Temporal</td>
<td>8</td>
<td>Solid</td>
<td>Mild</td>
<td>Mild</td>
<td>+</td>
</tr>
</tbody>
</table>

Note: + indicates yes; –, no.
imaging are necessary to generalize these findings. Second, the patients with APXA seemed to be older than those with PXA, but the difference was not significant, possibly due to the small size of this study. Hence, the difference in age may affect the values of CBV and ADC. However, these parameters of the tumors were normalized by contralateral normal-appearing brain parenchyma to reduce intersubject variance including age and sex. Third, we only focused on imaging appearances and parameters, but there is a lack of a direct pathologic correlation. Therefore, we cannot state with certainty whether the imaging parameters represent true pathophysiologic information of the tumor. Thus, further prospective study with strict pathologic validation is recommended.

CONCLUSIONS
APXA can present with more aggressive conventional and advanced MR imaging features, mimicking high-grade astrocytoma at initial diagnosis, than PXA. Greater maximum tumor diameter, heterogeneous contrast enhancement, obvious peritumoral edema, and lower rADC\textsubscript{min} and higher rCBV\textsubscript{max} are more common features in APXA compared with PXA. DWI and DSC-PWI might be useful in the characterization and differentiation of APXA and PXA.

REFERENCES