A Case of Pleomorphic Xanthoastrocytoma with Intracranial Hemorrhage in a Child

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Intracranial hemorrhage associated with lower grade glioma is unusual. Furthermore, pleomorphic xanthoastrocytoma (PXA) with intracranial hemorrhage, especially in children, is extremely rare. We report here a rare case of child PXA with intracranial hemorrhage. An 11-year-old girl was admitted with headache and convulsions. A computed tomography scan demonstrated intracranial hemorrhage in the right temporal lobe. An angiogram revealed no vascular disease including arteriovenous malformation, angioma or aneurysm. Magnetic resonance (MR) imaging demonstrated no enhanced or cystic mass to suggest tumor presence. A follow-up study by MR imaging at 6 months after onset of the intracranial hemorrhage revealed a cystic mass lesion, with gadolinium-enhancement, in the right temporal lobe. This mass lesion was removed by surgery and diagnosed as PXA. Areas of tumor lesion could not be diagnosed immediately after the intracranial hemorrhage since bleeding lesion was prominent. Lower grade gliomas, including PXAs, should therefore be taken into consideration in the differential diagnosis of pediatric intracranial hemorrhage cases, separately from vascular disease and/or malignant brain tumor.

Keywords: pleomorphic xanthoastrocytoma, intracranial hemorrhage, pediatric brain tumor

Introduction

Pleomorphic xanthoastrocytoma (PXA) is rare, involving slowly growing neoplasms corresponding to World Health Organization (WHO) grade II. PXA accounts for less than 1% of all astrocytomas, and demonstrates a good clinical outcome compared to other gliomas. PXA typically arises from supra-tentorial locations in children or young adults.1 The most common clinical symptom of PXA is seizure, and intracranial hemorrhage associated with PXA is very rare. We report here an extremely rare case of child PXA with intracranial hemorrhage.

Case Report

An 11-year-old girl was admitted to another clinic with convulsions. She had a complaint of progressive headache 3 weeks before the convulsions. A computed tomography (CT) scan demonstrated intracranial hemorrhage in the right temporal lobe (Fig. 1A), and the patient was transferred to our hospital. Physical examinations displayed no abnormality, and there was no neurological deficit. Magnetic resonance (MR) imaging disclosed no enhanced or cystic mass to suggest tumor presence (Figs. 1B–1E). An angiogram revealed no vascular disease including arteriovenous malformation, angioma or aneurysm (Fig. 2A). She was observed conservatively and once discharged from our institution because repeated examinations by MR imaging and angiography had demonstrated no vascular disease and/or tumor mass (Figs. 2B–2D). MR imaging at 6 months after onset of the intracranial hemorrhage revealed a cystic mass lesion, with gadolinium-enhancement, in the right temporal lobe (Figs. 3A and 3B). She therefore underwent surgical resection and the tumor was completely removed (Figs. 3C and 3D). The intraoperative findings indicated that the tumor was reddish, soft, and vascular-rich. Pathological examinations of the tumor specimen demonstrated nuclear and cytoplasmic pleomorphism (Fig. 4A). Morphologically, the nuclei varied in their size, shape, and coarseness or dispersion of chromatin, but there was no mitosis or necrosis. Microvascular proliferation and bleeding scars were evident (Fig. 4B). The tumor revealed glial components including eosinophilic granular bodies, Rosenthal fibers and spindle-shaped tumor cells (Figs. 4A and 4B). Hemosiderin was present near the tumor vessels, and the tumor cells demonstrated cytoplasmic pleomorphism and xanthomatous changes (Figs. 4C and 4D). Glial fibrillary acid protein (GFAP) and S-100 protein were positive immunohistochemically (Fig. 4E). Vimentin was also positive. Synaptophysin was positive immunohistochemically in the focal area. On silver staining, reticulin fibers were evident surrounded by tumor cells (Fig. 4F). Immuno-activity for CD34 was observed in the tumor and endothelial cells. The point mutation of BRAF gene at codon 600 (BRAF V600E) was negative on the polymerase chain reaction. The MIB-1 labeling index was 2.0%. Epithelial membrane antigen was negative immunohistochemically. These pathological findings were consistent with PXA. The patient was discharged from our institution without severe
complications, except for slightly left-side hemi-motor palsy due to the tumor resection (Karnofsky Performance Status score: 80). Adjuvant therapy including chemotherapy or radiation was not required. There has been no sign of recurrence over a period of 24 months since the operation.

Discussion

Pleomorphic xanthoastrocytoma develops in children and young adults. The majority of symptoms include a fairly long history of seizures, and accordingly PXA tends to arise on the brain surface. The incidence of hemorrhage in gliomas is approximately 1.4–2.6%. In general, the frequency of hemorrhage increases with degree on the WHO classification, i.e. it is more common in high-grade gliomas such as glioblastomas and anaplastic astrocytomas. Thus, high-grade gliomas tend to display microvascular proliferation and necrosis. The cause of the hemorrhage occurring in lower grade gliomas is poorly understood. Vascular proliferation is an occasional
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Feature of such tumors. Retiform capillaries are sometimes observed in lower grade gliomas and have been found to be associated with hemorrhage.\(^3,4\) Intracranial hemorrhage associated with PXA is extremely rare. So far, only six cases have been reported in the English literature\(^5-10\) (Table 1). PXAs appear as hypervascular masses on angiogram, and histological hypervascularity has been reported in only one case.\(^9\) Our patient exhibited no tumor stain on angiogram, and microvascular proliferation with bleeding scars were evident in most of the tumor area without mitosis or necrosis on histological examination. These observations indicated that PXA with intracranial hemorrhage cases tend to display microvascular proliferation. In our patient, lymphocyte cells were present surrounded by tumor vessels. These findings suggested that vasculitis had led to intratumor hemorrhage and intracranial hemorrhage. PXAs with significant mitotic activity and/or with areas of necrosis have been designated as pleomorphic xanthoastrocytomas with anaplastic features. Such tumors exhibited an increased risk of early recurrence. In a previous report, approximately 15–20% of PXAs were inferred to have undergone malignant transformation.\(^11\) When a tumor became malignant, microvascular proliferation was more likely, and the volume of tumor vessels increased, leading to tumor bleeding.\(^8\)

**Table 1** Case of pleomorphic xanthoastrocytoma with intracranial hemorrhage

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age (year-old)</th>
<th>Sex</th>
<th>Location</th>
<th>Type of hemorrhage</th>
<th>Cyst</th>
<th>Pathological diagnosis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy et al. 1996(^{10})</td>
<td>46</td>
<td>F</td>
<td>Left temporal</td>
<td>ICH/SAH</td>
<td>–</td>
<td>PXA</td>
<td>Dead</td>
</tr>
<tr>
<td>Yoshida et al. 2005(^9)</td>
<td>61</td>
<td>F</td>
<td>Left temporal</td>
<td>ITH</td>
<td>+</td>
<td>PXA</td>
<td>Survived</td>
</tr>
<tr>
<td>Asano et al. 2006(^8)</td>
<td>59</td>
<td>F</td>
<td>Left temporal</td>
<td>ICH</td>
<td>–</td>
<td>Anaplastic PXA</td>
<td>Dead</td>
</tr>
<tr>
<td>Lee et al. 2007(^7)</td>
<td>64</td>
<td>M</td>
<td>Left frontal</td>
<td>ICH</td>
<td>+</td>
<td>PXA</td>
<td>Survived</td>
</tr>
<tr>
<td>Wind et al. 2009(^6)</td>
<td>5</td>
<td>F</td>
<td>Left temporal</td>
<td>ITH</td>
<td>–</td>
<td>PXA</td>
<td>Survived</td>
</tr>
<tr>
<td>Yoshikawa et al. 2010(^5)</td>
<td>60</td>
<td>F</td>
<td>Left temporal</td>
<td>ICH/SAH</td>
<td>–</td>
<td>PXA</td>
<td>Survived</td>
</tr>
<tr>
<td>Present case</td>
<td>11</td>
<td>F</td>
<td>Right temporal</td>
<td>ICH</td>
<td>+</td>
<td>PXA</td>
<td>Survived</td>
</tr>
</tbody>
</table>


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Fig. 4 Photomicrographs obtained by hematoxylin and eosin (H&E) staining (A–D) and immunohistochemical staining (E and F). (A) Pleomorphic neoplastic cells and spindle-shaped cells surrounded by tumor vessels (original magnification ×100, bar = 200 µm). (B) Microvascular proliferation and eosinophilic granular bodies (original magnification ×200, bar = 100 µm). (C) Lymphocyte cells surrounded by tumor vessels (original magnification ×400, bar = 50 µm). (D) Microvascular proliferation and xanthomatous neoplastic cells (original magnification ×400, bar = 50 µm). (E) Photomicrograph showing representative GFAP immunostaining (original magnification ×100, bar = 200 µm). (F) Photomicrograph showing representative silver staining (original magnification ×100, bar = 200 µm).
As described above, six cases of intracranial hemorrhage associated with PXA have been reported, and only one report described a pediatric case. The patient ages described in the other five reports ranged from 46 to 64 years old, and only one case demonstrated malignancy diagnosed as anaplastic PXA. Every past case underwent surgical treatment urgently and could be diagnosed early. In the present case, the intracranial hemorrhage did not require surgical treatment. Even though she underwent repeated investigations, we were therefore unable to reveal the cause of the intracranial hemorrhage upon first examination. In general, low grade brain tumor, including PXA, demonstrates a slow course. We failed to detect any tumor therefore by MR imaging until 6 months after the onset of the intracranial hemorrhage. In the period immediately after the intracranial hemorrhage, no tumor could be detected on imaging studies because the mass was masked by hemorrhage. We thus need to be aware that low grade brain tumor, including PXA, should not be excluded in the differential diagnosis of pediatric intracranial hemorrhage cases other than vascular disease and/or malignant brain tumor, and film follow-up is strictly necessary.

Conflicts of Interest Disclosure
The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

References

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