Anaplastic Pleomorphic Xanthoastrocytoma With a Component of Anaplastic Astrocytoma Presenting as Skull Base Tumor Followed by Downward Extracranial Extension

—Case Report—

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Abstract

A 16-year-old female, with unremarkable medical and family history, presented with a huge dural-based mass in the right frontotemporal fossa, manifesting as headache. The patient underwent subtotal tumor resection. Intraoperative findings revealed focal erosion in the temporal fossa dura mater and skull adjacent to the lesion. Most of the tumor was located extraaxially, but a part of the tumor had invaded the temporal lobe, and had tightly adhered to the middle cerebral artery and its perforating vessels. Histological examination revealed cellular pleomorphism with mitotic activity, focal necrosis, but lacking endothelial proliferation, consistent with anaplastic pleomorphic xanthoastrocytoma (PXA) with component of anaplastic astrocytoma. Postoperatively, the patient underwent local irradiation and temozolomide administration, but the tumor relapsed 13 months later. Second tumor resection was performed followed by gamma knife radiosurgery, but the residual tumor progressively grew, extending into the contralateral hemisphere, and formed an enormous mass in the left frontal lobe at 17 months. Magnetic resonance imaging performed at 18 months revealed extracranial infiltration of the frontal tumor, through the cribriform plate, with enormous extension into the paranasal sinuses, nasal cavity, and orbit during the next month. The patient died at 20 months after the initial surgery. PXA with anaplastic appearance may have a component of anaplastic astrocytoma with more aggressive behavior.

Key words: anaplastic pleomorphic xanthoastrocytoma, anaplastic astrocytoma, bone erosion, extracranial tumor extension

Introduction

Pleomorphic xanthoastrocytoma (PXA) is an uncommon type of primary brain tumor initially documented in 1973 and currently classified as glial tumor of World Health Organization (WHO) grade II. PXA predominantly occurs in patients in the first decade of life as a superficially located, well-circumscribed, cystic or solid enhanced mass, and tends to affect the adjacent meninges with cerebrospinal fluid (CSF) seeding. Inner table remodeling of the skull was identified on neuroimaging in 12.5% of patients with PXAs, and meningeal invasion was identified microscopically in 92% of patients. PXA may rarely mimic pituitary adenoma and meningioma.

Infrequently PXAs transform into an anaplastic histological type. Anaplastic PXA is a WHO grade III tumor characterized by monotonous proliferation of pleomorphic cells accompanied by mitotic activity, focal necrosis, and microvascular proliferation, with inconsistent correlation between the histological profiles and biological behavior. Here we describe a case of anaplastic PXA that was assumed to have a component of WHO grade III anaplastic astrocytoma presenting as extraxial tumor in the right temporal lobe, and followed by relapse as an intraxial mass in the left frontal lobe which showed rapid extracranial extension into the paranasal sinuses, nasal cavity, and orbit.

Case Report

A healthy 16-year-old female suffered sustained headache for 1 year followed by gradual exaggeration in the last 2 months. Her past medical history was unremarkable and family history was not suggestive of brain tumor, cancer, or neurofibromatosis. Physical examination revealed no
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focal neurological deficit. Computed tomography of the head showed a huge hyperdense mass in the right frontotemporal fossae with focal bony erosion in the temporal fossa floor (Fig. 1). No calcification was found in the tumor. Magnetic resonance (MR) imaging confirmed a well-demarcated, broad-based, apparently extraaxial solid mass $6 \times 5 \times 6$ cm in diameter; which appeared as isointense on T1- and hyperintense on T2-weighted imaging, with homogeneously intense enhancement (Fig. 2). Cerebral angiography was not performed.

The patient underwent tumor resection via a frontotemporal craniotomy. Intraoperative observation found an area of dural erosion in the affected temporal fossa, $5 \times 5$ mm in diameter, and focal erosion in the adjacent inner plate, not associated with surgical manipulation. Most of the tumor mass was located extra-axially, but a part of the lesion was poorly circumscribed and blended with the temporal lobe. The tumor was tightly adhered to the horizontal portion of the middle cerebral artery and its perforating branches, so only subtotal resection was car-

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Fig. 5 Axial (A) and coronal (B) T1-weighted magnetic resonance images with contrast agent performed 18 months after the initial surgery revealing emergence of a heterogeneously enhanced mass in the left frontal lobe (arrow), extending into the ethmoidal sinus, left orbit, and nasal cavity (arrowheads), accompanied by marked displacement of the midline structure of the brain.

Fig. 6 Coronal computed tomography scan of the head taken 19 months following the initial surgery demonstrating significant enlargement of the extracranial part of the tumor with prominent bone destruction and occlusion of the left maxillary sinus (arrowhead).

ried out. Histological examination revealed cellular pleomorphism with mitotic activity and focal necrosis, but no endothelial proliferation (Fig. 3). Immunohistochemical staining was positive for glial fibrillary acidic protein (GFAP), S-100 protein, epithelial membrane antigen, synaptophysin, and INI-1. The MIB-1 labeling index was 6% (Fig. 4). The histological findings were consistent with anaplastic PXA with a component of WHO grade III anaplastic astrocytoma.

The postoperative course was complicated by CSF leakage with expansive subcutaneous fluid accumulation due to incomplete dural closure at the site of bony erosion in the temporal base, which necessitated additional repair surgery and consequent ventriculoperitoneal shunting. Postoperatively, the patient underwent local irradiation 56 Gy by intensity-modulated radiation therapy and synchronous temozolomide administration (75 mg/day × 42 days). The tumor was controlled until 13 months after the initial surgery, when remarkable growth of the residual tumor occurred manifesting as intractable seizure attacks. The patient underwent additional subtotal tumor resection and consecutive gamma knife radiosurgery for the residual tumor. Histological examination of the resected specimens showed identical appearance with the initial tumor resection, including MIB-1 index of 6%. The residual tumor had partially invaded the right frontal lobe, rapidly extended into the left frontal lobe through the frontal white matter fibers, and formed an enormous, heterogeneously enhanced intraaxial mass, at 17 months after the initial surgery. The patient became semicomatose, but her family refused further surgery. MR imaging performed at 18 months revealed downward extracranial extension of the left frontal tumor, through the eroded cribiform plate, which rapidly enlarged to obstruct the paranasal sinuses and nasal cavity with an extension into the orbit, within a month (Figs. 5 and 6). Intracranial dissemination was not found and spinal MR imaging did not identify any CSF seeding. The patient died of tumor progression at 20 months after the initial surgery, 3 months from the second relapse. Autopsy was not performed.

Discussion

Osteolytic change of the skull associated with PXA is exceptionally rare, with only 2 documented cases. In the previous case, neuroimaging showed the PXA as a small intraaxial cystic mass, located superficially in the parietal lobe with marginal enhancement, and mimicking an epidermoid tumor.18 In contrast, in our case the tumor was a huge solid mass located in the frontotemporal fossae with intense enhancement, resembling a meningioma at first presentation. Bony erosion is a rare manifestation usually associated with superficially located, slow growing brain tumors such as astroblastoma, oligodendroglioma, astrocytoma, anaplastic astrocytoma, and convexity meningioma.

The present PXA showed aggressive extracranial tumor infiltration through the cranial base with focal erosion in the dura mater and adjacent skull, much more extensively at the relapse than at the initial presentation. The tumor initially originated superficially in the right temporal lobe and relapsed as an intraaxial huge mass in the left frontal lobe. The frontal lesion showed aggressive extracranial extension accompanied by destructive changes in the medial anterior fossa, ethmoidal sinus, nasal cavity, and the medial wall of the orbit. Anatomically, both the dura and arachnoid extend downward into the olfactory foramen at the medial anterior cranial base, forming a subarachnoid space around the exiting olfactory nerve, with no bony element at the bottom of the foramen.17 The present patient showed no clinical or neuroimaging signs of brain herniation. In addition, the ventriculoperitoneal shunt placed in the patient had been functioning and was thought to compensate for any increase in the intracranial pressure.
Therefore, we thought that the extracranial growth had occurred by tumor infiltration following malignant transformation, rather than downward displacement of the tumor caused by increased intracranial pressure.

The present case showed aggressive clinical behavior refractory to multimodal management including repeated surgical resections and chemoradiation therapy. The inconsistencies between the descriptions of the histological appearance and the final outcomes of anaplastic PXAs may result from the limitations of the diagnosis based only on the morphological characteristics that cannot differentiate “conventional” anaplastic PXA from more malignant, “aggressive” types with biological behavior compatible with WHO grade IV tumors. In the present case, histological examination demonstrated pleomorphic tumor cells haphazardly arranged in desmoplastic stroma with infrequent intracytoplasmic vacuoles, lacking microvascular proliferation, and accompanied by hyperchromasia, mitotic activity, and focal necrosis, with MIB-1 labeling index of 6%. Immunohistochemical evaluation of the tumor cells confirmed the presence of GFAP and S-100 protein. In addition, synaptophysin, a neuronal marker, was also present. Epithelial membrane antigen showed a growth pattern of the tumor involving the meninges. Those patterns were consistent with anaplastic PXA, anaplastic astrocytoma, and glioblastoma multiforme. Therefore, we finally concluded that anaplastic PXA with a component of anaplastic astrocytoma was the most likely diagnosis, which may partly explain the more aggressive behavior of the present tumor compared to the previously reported cases of primary anaplastic PXA. Anaplastic astrocytoma in the setting of anaplastic PXA has never been described. Recent investigations have suggested that INI-1 immunohistochemistry is valuable for identifying bidirectional, neuronal and glial, differentiations, commonly associated with a myc gene amplification, for which atypical teratoid/rhabdoid tumor commonly demonstrates negative staining. In the present case, INI-1 staining was useful for evaluating the uncommon histological appearance. Anaplastic PXA was thought to be distinguishable from glioblastoma multiforme in terms of the histological findings, but this may not be sufficient to explain the full spectrum of discrepancy between the histological appearance and diverse clinical appearances of anaplastic PXA.

In the present case, the histological appearance of the tumor was identical at the initial and second resection with MIB-1 index of 6%, but the tumor progressed rapidly after the second operation. We assume that the present PXA might have undergone malignant transformation after the second operation into glioblastoma multiforme, although histological verification was not achieved. Interestingly, despite the high index of affinity to the meninges of the present PXA, CSF dissemination was not identified over the whole clinical course. A previous case of atypical teratoid/rhabdoid tumor arose in the setting of PXA, which may suggest that genetic analysis is indispensable to understand the etiology of PXA. To predict the exact biological nature of PXA in relation to the grading system, and to select the optimum treatment strategy, more comprehensive understanding with genetic exploration is required.

We should be cautious in treating PXA with anaplastic characteristics because aggressive biological behavior associated with a component of high-grade astrocytoma may follow.

References
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