

ANGIOMATOUS PLEOMORPHIC XANTHOASTROCYTOMA AS A COMPONENT OF GANGLIOGLIOMA

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Pleomorphic xanthoastrocytomas (PXA) were first described by Kepes et al. in 1979.¹ They are superficially located supratentorial gliomas with a predilection for the temporal lobes and a relatively favorable prognosis.² Gangliogliomas and gangliocytomas, which are tumors composed of mature ganglion cells and a variable number of glial cells, share numerous clinical characteristics with PXAs, including the predilection for the temporal lobes, a favorable prognosis, and occurrence in children and young adults.³

Recently, tumors combining the features of both PXA and ganglioglioma have been reported.⁴⁻⁷ In addition, Sugita et al. described two PXAs with abundant vasculature and focal desmoplasia, which they have labeled "pleomorphic xanthoastrocytoma with desmoplastic reaction: angiomatous variant."⁸ We report a 27-year-old male with a frontoparietal lobe tumor with features of both angiomatous PXA and ganglioglioma. The significance of these findings in terms of both prognosis and tumor histogenesis is discussed.

Case Report

A 27-year-old right-handed Saudi male schoolteacher was admitted to the neurosurgery service at the King Faisal Specialist Hospital and Research Center (KFSH&RC), with a three-year history of intermittent, transient, mild, left-sided weakness. The symptoms were noted to be associated with a ball hitting his head ("heading") while playing soccer. Three weeks prior to referral to KFSH&RC, he had complained of headaches in the right frontoparietal region associated with vomiting. A CT scan and MRI of the head revealed a right medial frontal heterogeneous lesion consisting of both solid and cystic components with surrounding edema (Figure 1A). The solid component was enhancing. There was a suggestion of previous hemorrhage on the T₁ unenhanced MRI study.

The patient was started empirically on anti-tuberculosis medications and his symptoms apparently improved with the administration of dexamethasone.

Neurological examination on admission revealed a very mild left hemiparesis with extensor left plantar response. The patient was taken to the operating room in January 1996. Through a right frontoparietal paramedian craniotomy and intrahemispheric approach, a brownish-tan tumor was exposed. The tumor had a cystic-like film that was easily dissected from the left medial frontal lobe and thalamus. The deep-seated portion had blended with the cingulate gyrus. The tumor was pulsatile and compressible and there was yellowish discoloration of the surrounding brain, indicating previous hemorrhage. For reasons of safety, the wound was closed and a cerebral angiogram was performed which revealed a tumor with a dense arterial blush and evidence of neovascularity (Figure 1B). The patient was kept intubated overnight in the intensive care unit and was taken back to the operating room the next day. The craniotomy was reopened and a gross total removal of the vascular tumor was considered to be achieved, although a postoperative CT scan revealed a small amount of residual tumor. At twelve months postoperation, there has been no interval change in the size of this residual tumor.

Pathological Examination

The surgical specimen was fixed in buffered 10% formalin and embedded in paraffin. The following stains were used: hematoxylin and eosin (H&E); reticulin silver impregnation; Bielschowsky's silver impregnation; and elastic-Verhoeff-van Gieson (EVG). Immunohistochemical staining of the paraffin-embedded sections was performed by the labeled streptavidin-biotin (LSAB, DAKO) technique for glial fibrillary acidic protein (GFAP) (mouse monoclonal antibody, BioGenex, San Ramon, California, 2000x), neurofilament (70+200 kD) (mouse monoclonal antibody, Dako, Glostrup, Denmark, 2000x) and synaptophysin (rabbit polyclonal antiserum, Dako, 900x).

Histological examination of the resected tumor revealed a complex heterogeneous tumor. Portions of the neoplasm consisted of large, bizarre, pleomorphic cells with abundant eosinophilic or foamy cytoplasm (Figures 2A and 2B). Eosinophilic hyaline droplets and granular

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eosinophilic bodies were prominent (Figure 2C), as well as Rosenthal fibers. Other portions of the tumor consisted of collections of large cells with smaller nuclei, prominent nucleoli and cytoplasm containing basophilic material consistent with Nissl substance. In some regions the two components blended imperceptibly. There was also a less prominent, desmoplastic spindle cell component to the tumor (Figure 2D). The ganglion cells and neuritic processes showed positive immunohistochemical staining for neurofilament (Figure 2E) and synaptophysin. Staining for neuronal markers was most prominent in cells with the appearance of mature ganglion cells. The desmoplastic component showed dense staining with the reticulin (Figure 2F) and EVG stains, as well as with antiserum directed against GFAP. Focal neurofilament positivity was also noted in these areas. Some of the large, pleomorphic cells were also positive for GFAP, but the ganglion cells were negative. The entire neoplasm was invested with abundant vasculature. In places, the overall tumor architecture was effaced by a thin meshwork of thickened, hyalinized small vessels highlighted by the reticulin stain. Other areas contained larger caliber vascular channels. There was evidence of both acute and chronic hemorrhages with foci of hemosiderin, vascular calcification and perivascular lymphocytic infiltration. Despite the focal marked pleomorphism, mitotic figures, necrosis or endothelial proliferation were not present.

Discussion

Gangliogliomas are defined as neoplasms “composed of neoplastic astrocytes (rarely oligodendrocytes) and ganglion cells.”³ Histologic examination of the lesion in this case revealed a tumor that was essentially a ganglioglioma in which the glial component was an angiomatous pleomorphic xanthoastrocytoma. Preoperative imaging studies were consistent with either ganglioglioma or PXA, showing both solid and cystic components with enhancement of the solid areas. The superficial location of the lesion is particularly characteristic of a PXA. The suggestion of hemosiderin seen on the T₁ MRI images and the arterial tumor blush demonstrated by angiography revealed a highly vascular tumor with evidence of prior hemorrhage.

Malignant transformation in gangliogliomas is a rare phenomenon, most often involving the glial component of the tumor.³ The current WHO classification of brain tumors considers ganglion cell tumors to be grade I tumors, with surgical excision often being curative.⁹ The prognosis of PXAs is less certain, but is considered to be much better than expected, given the pleomorphism of the neoplastic astrocytes. However, recurrence and malignant progression have been documented.^{10,11} Regarding the grading of PXAs, the WHO considers these tumors to be grade II or III. In keeping with traditional practices, the grading and prognosis of gangliogliomas with a PXA

component should be considered that of the higher grade tumor.

Recently, Powell et al. used immunohistochemistry to demonstrate co-expression of neuronal and glial epitopes in PXAs.¹² Prior to the final preparation of this manuscript, we had the opportunity to observe the co-expression of GFAP, neurofilament and synaptophysin in large, bizarre “balloon” cells in a PXA that lacked apparent true differentiation into mature ganglion cells. Although expression of neuronal markers in the PXA cells of the current case was not demonstrated, it is possible that the development of a mature neuronal phenotype in this tumor could represent the completion of a process of differentiation gone awry in the bizarre, pleomorphic PXA cells in which dual expression of glial and neuronal epitopes is seen. If this is the case, the question is raised as to whether or not the state of increased “differentiation” evidenced by the presence of mature ganglion cells in these tumors indicates a better prognosis. The one case for which long-term follow-up is reported suggests otherwise,⁵ but further experience with these tumors is needed before any firm conclusions can be drawn.

In reporting two similar cases of angiomatous PXA, Sugita et al. reviewed the somewhat confusing subject of “angiogliomas” and reiterated the position of Rubinstein that this term be restricted to those tumors composed of both glioma and true hemangioblastoma.⁸ We agree that the vascularity in these tumors should be regarded as reactive rather than neoplastic, similar to the situation in angiomatous meningiomas. We also agree that desmoplasia may similarly be regarded as a reactive phenomenon. As noted in the history, the patient is an avid soccer player and reported a history of symptoms related to the practice of “heading” the ball. Although this practice has been associated with the development of a variety of acute and chronic neurologic syndromes,¹³ we believe that this is the first report of “heading” being possibly associated with chronic hemorrhage into a brain tumor. It would be interesting to speculate on the potential role of repeated, mild head trauma and hemorrhage in the development of both the intense vascularity and desmoplasia in this case.

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