

Synchronous multicentric pleomorphic xanthoastrocytoma with anaplastic features

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ABSTRACT

Pleomorphic xanthoastrocytoma (PXA) has been considered an astrocytic tumor with a relatively favorable prognosis. However, PXA cases having several recurrent patterns with poor prognosis have been reported in recent years, and a new concept of “PXA with anaplastic features” has been proposed. The present case was of a 55-year-old male who presented with weakness and numbness of right upper and lower limbs since 3 months along with difficulty in walking as well as difficulty in speaking since then. He also complained of headache since 9 months. The magnetic resonance imaging study revealed two nodular, homogeneously enhancing lesions, approximately 1 cm in size in the right cerebral hemisphere. Clinical and radiological examinations were suggestive of a metastatic neoplasm. A right frontal craniotomy was performed for excisional biopsy of both lesions. Histopathological findings showed that the tumor was PXA with strong pleomorphism, xanthomatous changes, extensive areas of tumor necrosis, and increased mitotic activity. From these findings, the histopathological diagnosis “PXA with anaplastic features” was given. Synchronous multicentric PXA presents unique challenges in that gross total resection would impose significant surgical morbidity; histological homogeneity among the lesions cannot be confirmed; and the well-described potential for anaplastic transformation may be increased with multiple lesions. The optimal treatment for patients with this rare and challenging diagnosis awaits further study.

Keywords: Anaplastic features, multicentric, pleomorphic xanthoastrocytoma, synchronous

INTRODUCTION

Pleomorphic Xanthoastrocytoma is a rare low-grade astrocytic neoplasm of young life and early adulthood, with superficial localization in the cerebral hemispheres.^[1] PXA cases having several recurrent patterns with poor prognosis have been reported in recent years, and a new concept of “PXA with anaplastic features” has been proposed. We herein report an extremely rare case of synchronous, multicentric PXA with anaplastic features in a 55-year-old male.

CASE REPORT

A 55-year-old male presented with weakness and numbness

of right upper and lower limbs since 3 months. Patient had difficulty in walking as well as difficulty in speaking since then. In addition patient complained of headache since 9 months. Patient had 2 to 3 episodes of vomiting since 3 days. On clinical examination, higher motor functions were normal. Memory of recent events was also normal. There was difficulty in vision for both eyes. Sensations were reduced in lower side of maxillary and mandibular region and there was difficulty in hearing in right ear. Pain sensations were reduced on right side. Tone and bulk were reduced in right upper and lower limbs. Clinical diagnosis of metastatic tumor in the brain was rendered. Patient underwent CT scan and possibilities of multicentric glioblastoma multiforme and metastatic deposits in brain were suspected. Patient underwent right frontal craniotomy with excisional biopsy of both lesions in the right cerebral hemispheres. Preoperatively the tumor was firm and moderately vascular. Gross examination revealed multiple grey–white soft tissue pieces measuring altogether 5 cm³. Microscopic examination revealed sheets of pleomorphic astrocytes showing focal fascicular arrangement and numerous tumor giant cells. These tumor cells were showing enlarged, hyperchromatic bizarre nucleus with prominent nucleolus and occasional intranuclear inclusions.

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The cytoplasm of these tumor cells varied from eosinophilic to hyaline to foamy [Figure 1]. Abundant PAS positive granular eosinophilic bodies were seen. Focal perivascular patchy lymphocytic infiltrate. There was dense reticulin staining around single or grouped tumor cells. There were extensive areas of tumor necrosis [Figure 2] and moderate number of mitotic.

DISCUSSION

Pleomorphic xanthoastrocytoma is a rare tumor accounting for less than 1% of all astrocytic neoplasms.^[1] Pleomorphic xanthoastrocytoma belongs to grade II of the World Health Organization (WHO) histological classification of tumors of the CNS and is therefore considered as a relatively benign entity among the astrocytic tumors. However, 9% to 20% of PXAs have been reported to undergo malignant transformation,^[2] and some of them exhibit anaplastic features at the first presentation.^[3] Pleomorphic xanthoastrocytoma with anaplastic features is a rarity.^[3,4] A review of the available PXA literature dating back to 1979 revealed only 16 cases of primary anaplastic astrocytoma till date.

Pleomorphic xanthoastrocytoma is an astrocytic neoplasm with a relatively favorable prognosis, typically encountered in children and young adults, with superficial location in the cerebral hemispheres. Characteristic histologic features include (1) fascicular arrangement of the neoplastic astrocytes; (2) pleomorphic astrocytes with bizarre cytologic features; (3) lipidization of the neoplastic astrocytes; (4) perivascular patchy lymphocytic infiltrates; (5) dense reticulin staining around single or grouped tumor cells; and (6) eosinophilic granular bodies. The neoplastic astrocytes in the PXA can show neuronal differentiation. Mitotic index and Ki-67 are important prognostic predictors. World Health Organization

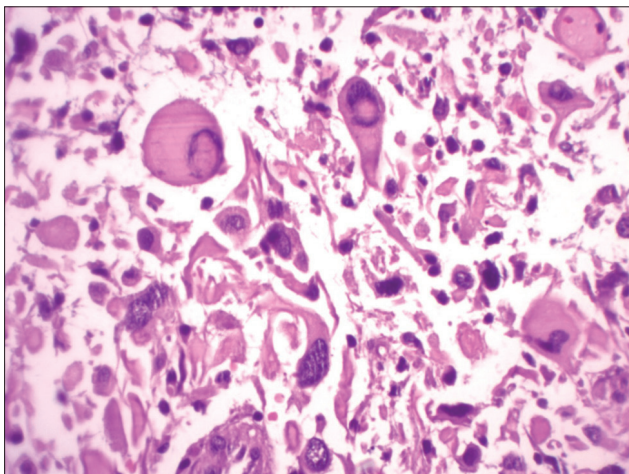


Figure 1: Photomicrograph showing large cells with bizarre hyperchromatic nuclei, intranuclear pseudoinclusions, vacuolated cytoplasm, and eosinophilic granular bodies (H and E, 40×)

recommends the designation “PXA with anaplastic features” to denote PXA featuring high mitotic activity (≥ 5 mitoses per 10 HPF) with or without accompanying necrosis. The designations “anaplastic PXA” and “PXA grade III or IV” are currently not recommended by WHO.

The presence of necrosis in PXA is also an uncommon and a significant feature. Pleomorphic xanthoastrocytomas may show regions of necrosis at diagnosis or after many years of follow-up, a feature that is recognized by the WHO as qualifying for the diagnosis of “pleomorphic xanthoastrocytoma with anaplastic features.” It predicts the poor prognosis. Leptomeningeal dissemination is not an uncommon pattern of recurrence for PXA with anaplastic features.^[5] The well-described potential for anaplastic transformation may be increased with multiple lesions. Leptomeningeal dissemination of PXA, with or without anaplastic features, commonly presents as multiple nodular lesions, in contrast to the diffuse dissemination seen in high-grade astrocytomas.^[6] In these cases, the differential diagnosis needs to exclude other malignancies, for example, glioblastoma or malignant fibrous histiocytoma. Immunocytochemical detection of GFAP may support exclusion of non-gial neoplasms resembling PXA. However, GFAP expression in PXA may be faint or focal, although complete lack of GFAP has not been described.^[7] Typically, classic PXAs are low-grade astrocytomas as they are less aggressive than cytologic features would suggest. Several reported studies showed that mitotic index, necrosis, and Ki-67/MIB-1 index are important outcome predictors.^[8] Pleomorphic xanthoastrocytoma with anaplastic features can show transformation in to glioblastoma.^[9]

Some PXAs are accompanied by anaplastic features and are difficult to manage because of frequent recurrences that lead to early death. Conventional chemotherapy and radiotherapy are not curative for PXA with anaplastic features.^[10] In addition, synchronous multicentric PXA presents unique

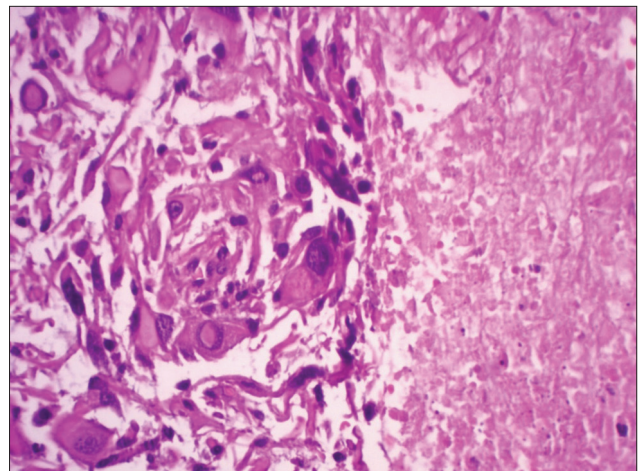


Figure 2: Areas of necrosis adjacent to viable tumor tissue (H and E, 40×)

challenges in that gross total resection would impose significant surgical morbidity; histological homogeneity among the lesions can not be confirmed. Koga *et al.*^[10] have reported a case of PXA with anaplastic features in which they controlled disseminated tumor nodules in the brain and the spinal cord for a relatively long period by repeated stereotactic irradiation. The optimal treatment for patients with this rare and challenging diagnosis awaits further study.

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