Rare disease

Pleomorphic xanthoastrocytoma with malignant transformation and multiple recurrences in an Iranian girl

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Summary

Pleomorphic xanthoastrocytoma (PXA) is a rare astrocytic tumour of the brain. Some PXAs are accompanied by anaplastic features and are difficult to manage because of frequent recurrences that lead to early death. Well-documented cases of malignant transformation in PXA and of anaplastic PXA are rare in the literature. The authors report a case of PXA with malignant transformation in the right temporo occipital lobe in a 13-year-old Iranian girl.

BACKGROUND

The pleomorphic xanthoastrocytoma (PXA) is a histologically alarming, yet biologically favourable, neoplasm that typically presents in later childhood or early adult life and exhibits a predilection for the cerebral hemispheres, particularly the temporal lobes.^{1 2} Although PXA appears malignant at first glance, mitosis and necrosis are absent and this is classified as a grade II brain tumour according to the WHO grading system. Classically, PXA has been considered as a tumour with relatively favourable prognosis.^{2 3} However, lethal malignant transformation in PXA has been reported in recent years⁴⁻⁹ and a concept called anaplastic PXA (WHO grade III) has been proposed.^{1 4 10 11} With a review of the literature, we present a case of PXA with malignant transformation who had repeated local recurrences, cerebral dissemination and eventually developed glioblastoma like on histology.

CASE PRESENTATION

This 13-year-old Iranian girl was admitted to the hospital with a 6 months history of headache, blurred vision, vomiting and seizure. There was no any other constitutional or focal neurological symptoms.

INVESTIGATIONS

MRI-without gadolinium revealed a 79×47 mm mass in right temporo occipital lobe. It was hypointense in T1 and hyperintense in T2 with internal cystic and solid component and severe pressure effect on right lateral ventricle, peripheral brain tissue oedema and mild mid line structures shift (figures 1 and 2). At surgery, the surgeon found a soft yellow mass with cystic cavities. The tumour excised partially and the patient discharged home on anticonvulsive drugs (sodium valporate). Tissue from the surgical specimen was fixed in neutral buffered formalin, then was paraffin embedded and routinely processed for histological examination. On microscopic examination the tumour was composed of spindle-shaped cells in fascicular array admixed with tumour giant cells with severe

nuclear abnormalities. The abundant cytoplasm of some of these cells were foamy or coarsely vacuolated, but more assumed a ground-glass, finely granular or hyalin quality. Due to histologic diagnosis of PXA without anaplasia, no further adjuvant radiotherapy or chemotherapy was performed. Five months later, the patient had a convulsive episode. MRI demonstrated huge mass in the mentioned area. Surgical exploration revealed a soft mass with cystic component. The histopathological examination showed a PXA with foci of necrosis, vascular proliferation and high mitotic activity. Neoplastic cells were positive for GFAP and 20 per cent of cells were positive for Ki67. The diagnosis was anaplastic PXA.

DIFFERENTIAL DIAGNOSIS

The histologically differential diagnosis of PXA includes glioblastoma multiforme (GBM), malignant fibrous histiocytoma, fibroxanthoma, xanthosarcoma, anaplastic pilocytic astrocytoma and ganglionic tumours. Immunohistochemistry detection of glial fibrillar acidic protein (GFAP) may support exclusion of non-glial neoplasms resembling PXA. However, GFAP expression in PXA may be faint or focal, although complete lack of GFAP has not been recorded.

TREATMENT

For obscure reason any adjuvant treatment was not proposed. Four months later the patient's symptoms recurred and she was operated for third time in our center. Again histopathologic diagnosis was anaplastic PXA. Postoperative images showed gross tumoural residue and the patient referred for radiation therapy and received 6000 cGy radiation dose with lateral parallel opposed fields with photon 9 MV. One month later repeated MRI showed partial response to radiotherapy, therefore temozolamide 150 mg/m² for 5 days every 28 days was started. After two courses images revealed that tumour size has not changed and unfortunately another lesion appeared in right frontoparietal lobe. Re surgery was recommended but not

Figure 1 MRI (axial plane) shows mass lesion with cystic and solid component and severe pressure effect on right lateral ventricle.

performed, due to the location and that the patient was generally good.

DISCUSSION

PXA is a new tumour category that was first reported by Kepes *et al.*² This tumour is a rare tumour accounting for less than 1% astrocytic tumours.¹² PXA is now considered an astrocytic tumour of subpial origin in view of GFAP positive pathological findings.^{1 2} Patients are usually below 30 years of age, the tumours are located predominantly in the temporal and parietal lobes, they have cystic appearance and they are frequently superficially located. Epileptic seizures are a typical initial symptoms. The initial clinical, radiological and histological features of the present tumour were those of PXA. Histologically PXA appears malignant because of marked pleomorphism, but it is in fact a WHO grade II tumour with a favourable prognosis. However, in 1983, Weldon-Linne *et al*⁸ first reported a patient with recurrent PXA who then developed malignant transformation. From that time, patients with recurrent PXA have been reported to show malignant transformation.^{10 11 13} In 1997, Tonn *et al* reported two type of anaplastic PXA, primary, in which malignant tendencies are present from the first and secondary anaplastic PXA in which repeated recurrence results in malignant transformation.¹¹ Because in about our case all of the surgical resections were sub-optimal we could not determine whether this tumour was exactly primary or secondary type. However, rapid recurrences suggests that probably it is a primary type or it has a multicentric pattern. Early PXA literature with a short follow-up quoted a 6–9% rate of malignant transformation of typical PXA cases.¹⁴ PXA with anaplastic features at first presentation are more exceptional lesions (^{7 10 13 15–17}).

Figure 2 Same lesion in sagittal plane.

Histologic features of the malignant PXA, in addition to the featuring associated with conventional PXA, are mitosis, focal necrosis and endothelial proliferation.^{10 11 18} Our case is in accordance with these observations. Studies have reported that PXA can exhibit a synchronous multicentric pattern¹⁹ or result in multiple recurrences.⁹ Multifocal occurrence of PXA manifesting at different time frame is extremely uncommon but has been reported.²⁰

Because of the rarity of PXA with anaplastic features^{21 22} the standard postoperative radiotherapy or chemotherapy for PXA with anaplastic features has not been definitively established. Some studies showed surgery is the most important therapeutic approach,^{1 9 18 21} if anaplastic PXA is confirmed, the active adjuvant of radio and chemotherapy may be useful. One case has been reported in which the use of neoadjuvant vincristin and carboplatin was effective for controlling bleeding during surgery, presumably due to devascularisation.²³ The present patient underwent three operation to remove brain tumour. In each operation, partial resection was performed. Although when she referred for radiation therapy she had 14 years old, but she had 168 cm height and 64 kg weight that is such as an adult female in our country, therefore we decided to treat her according to physiological age. We decided to use concurrent temozolamide with radiation therapy such as other types of anaplastic astrocytoma in adults, similar to the manner that Tsutsumi *et al* used in a 16-year-old female,²⁴ but her parents insisted not to use chemotherapy agents unless radiation therapy could not be effective. When we repeated the MRI and they saw the results finally they agreed with chemotherapy but emphasised the use of drug without alopecia side effect. In previous studies some of chemotherapeutic regimens were used with some degrees of effectiveness, such as vincristine and carboplatin^{23 25} vincristine and cyclophosphamide, cisplatin, etoposide,²⁶ ACNU²⁷ and temozolomide.²⁸ Finally we started temozolomide such as Koga *et al* did so.²⁸

Unfortunately, after two courses a new lesion appeared without significant change in the size of previous lesion, therefore the drug was discontinued. Giannini *et al*¹ showed that PXA has a 70% 10-years survival time, and mitotic index and extension of resection appear to be the main predictor factors of recurrence and survival rate. Although the prognosis was relatively favourable, 15–20% of their patients experienced lethal recurrence or malignant transformation. In conclusion, the clinical course of the patient with PXA is not always favourable. A close follow-up is needed in order to detect any recurrence with malignant transformation. In the presence of malignant transformation local failure is the rule, but cerebrospinal fluid-borne so read is rarity.²⁹ The rarity of anaplastic PXA demands neuropathologic experience to find the correct diagnosis, since misinterpretation as other malignancies such as GBM might cause harmful therapeutically decision.

Learning points

- ▶ PXA is a rare astrocytic tumour of the brain.
- ▶ The clinical course of the patient with PXA is not always favourable.
- ▶ A close follow-up is needed in order to detect any recurrence with malignant transformation.
- ▶ In the presence of malignant transformation local failure is the rule.
- ▶ There are many controversies about effectiveness of adjuvant treatment.

Competing interests None.

Patient consent Obtained.

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