Pilocytic astrocytoma with spontaneous malignant transformation with intracranial and skeletal dissemination: case report and review of the literature


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SHORT REPORT

Pilocytic astrocytoma with spontaneous malignant transformation with intracranial and skeletal dissemination: case report and review of the literature

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ABSTRACT

Pilocytic astrocytoma is a benign low-grade tumor with a favorable prognosis. We present a 47-year-old lady with a posterior fossa pilocytic astrocytoma who underwent surgical decompression. She developed multiple early local recurrences. Along with malignant transformation of the cranial lesion, she developed skeletal dissemination within a very short time frame. There were no features or family history of neurofibromatosis 1. She did not receive radiotherapy or chemotherapy prior to the recurrences.

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Introduction

Pilocytic astrocytoma is a benign tumor in comparison to other gliomas with 80% survival rate after 10 years¹. Rarely their behavior changes and presents with early recurrence, multicentric disease, leptomeningeal dissemination or very rarely spontaneously malignant transformation with poor prognosis¹,². The risk of malignant transformation is not well ascertained however there may be a history of prior radiotherapy, chemotherapy or atypical histology¹. We report an adult patient with a cerebellar pilocytic astrocytoma with multiple early recurrences and spontaneous malignant transformation with cranial and diffuse skeletal dissemination. Both the behaviors in pilocytic astrocytoma are rare and our case is unique as both occurred together.

Case report

A 47-year-old lady presented with a headache, vomiting and gait ataxia of 16 months duration. On examination, she had a left side sixth nerve paresis and left side cerebellar signs. MRI showed a midline posterior fossa tumor of 4.6 × 5.3 × 4.5 cm, iso intense on T1, hyper intense on T2 weighted images, brilliantly and uniformly enhanced with contrast (Figure 1(A)) with hydrocephalus. She underwent a right ventriculoperitoneal shunt and later midline sub-occipital craniectomy and near total decompression of the lesion (Figure 1(B)). Histopathology revealed a biphasic tumor with microcystic change, many eosinophilic granular bodies and Rosenthal fibers (Figure 2(A–C)). The histological features were suggestive of pilocytic astrocytoma. Mitosis was sparse and the MIB-1 (proliferative marker) labeling index was 2–3%. The patient was discharged after 5 days.

After 6 months, she again presented with a headache and slurring of speech. MRI showed a large solid recurrence at the operative site of 4 × 3 × 3 cm (Figure 1(C)). She underwent re-exploration and near total decompression. She recovered well from surgery. Histology revealed features of Pilocytic astrocytoma. However, the cellularity was increased as compared to the previous surgery and mitosis was evident (Figure 2(D–F)). The MIB-1 labeling index was 7–9% and a histological diagnosis of atypical pilocytic astrocytoma was made. As MIB index was high she was kept on close follow-up.

Eleven months after the second surgery, she presented with one-week history of paraplegia. MRI brain and spine revealed local recurrence (Figure 1(D)) with an occipital lobe lesion (Figure 1(D)) as well as spinal dissemination. A thoracic (T5) level extradural mass lesion (Figure 1(E)) with significant cord compression along with multiple vertebral body signal changes on MRI were seen. The patient underwent D5 laminectomy and excision of the lesion. This specimen of histology revealed a cellular neoplasm composed of round to oval hyperchromatic primitive (undifferentiated) looking cells distributed in sheets. The tumors cells were GFAP and S100 positive and negative for synaptophysin, epithelial membrane antigen, cytokeratin, and CD99. The neoplasm was mitotically active and the MIB-1 labeling was high (Figure 3(G–K)). After 7 days, she underwent re-exploration and decompression of the posterior fossa recurrence along with right side occipital craniotomy and decompression of the metastatic lesion. The histology revealed a glial neoplasm with variation in cellularity and morphology. There were small foci resembling pilocytic astrocytoma with eosinophilic granular bodies (Figure 2(C)) and cellular areas composed of immature/primitive looking round to oval hyperchromatic cells which were positive for GFAP and S100 (Figure 3(A,D,E)). These cells were mitotically active with high MIB-1 labeling index (Figure 2(F)). Histological features were compatible with high-grade glioma suggestive of pilocytic astrocytoma with malignant transformation.

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Figure 1. (A) MRI contrast (axial) showed posterior fossa mass lesion with irregular enhancement. (B) Post op CT showed near-total decompression. (C) MRI contrast (axial) showed local recurrence of the tumor after six months. (D) MRI contrast (sag) showed local recurrence along with right side occipital lobe lesion after 11 months. (E) MRI spine contrast (sag) showed dorsal extradural lesion with enhancement. (E) MRI PET (FDG) showed areas of abnormal increase in FDG uptake in multiple bones of axial (involving ribs, pelvis, and entire spine) and appendicular skeleton (involving bilateral scapulae, the long bones of upper and lower limbs).

Figure 2. (A) Microphotograph showing a hypo cellular glial neoplasm with microcystic change and an occasional giant cell [H and E x 100]. (B and C) Microphotograph showing a glial neoplasm with extensive Rosenthal fibres and eosinophilic granular bodies [H and E x 200]. (D–F) Microphotograph showing a relatively cellular neoplasm with microcystic change and prominent fibrillary interstitium and scattered eosinophilic granular bodies. Note the increased vascularity and a mitosis (asterisk) evident in Figure 500. [H and E x 200].
Dedifferentiation with metastatic deposits in the occipital lobe. The spine lesion also shows similar histopathological characteristics. The patient was subjected to PET (Fluro deoxy glucose MRI and it showed multiple lesions throughout the spine, ribs, pelvic bones and long bones (Figure 1f). The patient was referred for adjuvant radio and chemo therapy. She expired after 2 months of surgery.

**Discussion**

Generally, pilocytic astrocytomas are benign intracranial tumors occurring in the pediatric population with an excellent prognosis. In adults they are rarer and have not been studied as extensively but they do not seem to carry as good a prognosis as that seen in children. We have reported a unique case of adult pilocytic astrocytoma with a dismal prognosis. There are two features which stand out in this case; (a) malignant transformation and, (b) extra CNS diffuse skeletal metastasis.

Recurrence following surgery for adult PAs occurs in up to 30%, with malignant transformation in at least 50% of these recurrences. The risk factors for malignant transformation may be the adult age of onset of disease, partial resection, prior radiotherapy, the location of the lesion, molecular characteristics of the tumor, and degree of contrast enhancement on imaging. The intense degree of enhancement or high perfusion value at primary PA has been correlated with early recurrence and malignant transformation. Ellis et al. followed 20 adult cases of pilocytic astrocytomas and noted recurrence in 6 cases. The median time to recurrence was 16.5 months (range 11–46 months). Of the 4 which were re-operated three had undergone malignant transformation. Similar results have been reported in a series of 44 patients by Stuer et al.

Our patient was an adult, with a brilliantly enhancing posterior fossa lesion, who had initially undergone subtotal resection. We had not performed any molecular testing for BRAF: KIAA fusion proteins. She did not receive radiotherapy and had developed recurrence with malignant transformation at 17 months after first surgery.

The histological diagnostic criteria for malignant transformation of pilocytic astrocytoma are not well defined. WHO classification (2007) of CNS tumor set up the diagnostic criteria for anaplasia or malignant transformation in pilocytic astrocytoma. The features are multiple mitoses (>4) per (10) high power microscopic field, endothelial proliferation and with palisading necrosis, nuclear atypical. The degree of proliferation (MIB index) also determines the chance of malignancy. Few studies reported MIB index more than 2 is associated with early recurrence. The presence of necrosis, high MIB index correlates with poor survival when compared to the classic pilocytic astrocytoma. The histopathology of our case was in line with that discussed in the literature.

Neuroaxis dissemination is an intrinsic behavior of the malignant intracranial tumors. CSF is the main pathway for dissemination in the neuroaxis. The lesions usually present as a leptomeningeal spread in the spinal subarachnoid space or as solitary drop metastasis. Our case is unique as there was tumor recurrence with the widespread skeletal dissemination of the disease. Other than an occipital metastatic lesion (Figure 1D) there was no other lesion throughout the neuraxis. Haematogenous spread of the tumor cells may have accounted for it.

The overall outcome following management of classic PAs especially after gross total excision is good. The management of malignant transformation (MT) of pilocytic astrocytoma has not been standardized due to the rarity of such cases. Re-exploration with safe maximal resection followed by adjuvant radio- and chemotherapy are the mainstay of treatment. In spite of receiving radiotherapy and chemotherapy our patient developed spinal dissemination, had a rapid downhill course and expired 2 months after diagnosis of frank malignant transformation and metastasis.

**Conclusion**

To the best of our knowledge, this is the first case of a pilocytic astrocytoma to present with malignant transformation on subsequent recurrences with wide spread skeletal dissemination.
This case highlights the fact that there are lacunas in our understanding of the so-called “benign” pilocytic astrocytoma. Molecular characterization may help in better understanding and prognosticate such enigmatic tumors.

Disclosure statement

Authors do not have any conflict of interest or anything to disclose.

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