Persistence and late malignant transformation of childhood cerebellar astrocytoma

Case report

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✓ A 5-year-old girl with juvenile pilocytic astrocytoma subsequently had multiple episodes of symptomatic recurrence over the course of 21 years of follow-up review. This lesion underwent histological transformation to an anaplastic small-cell neoplasm 21 years after the initial resection and diagnosis. Late transformation of benign childhood cerebellar astrocytomas to malignant astrocytic tumors is very rare; transformation to an anaplastic small-cell neoplasm has not been reported previously. This case and other reported cases in which juvenile pilocytic astrocytoma recurred after a long interval indicate the requirement of long-term follow-up review of these patients before assuming either a cure or arrest of the tumor's growth.

KEY WORDS □9 brain tumor □9 juvenile pilocytic astrocytoma □9 cerebellum □9 malignant transformation □9 recurrent tumor □9 anaplastic astrocytoma

JUVENILE pilocytic astrocytoma is the second most common intracranial tumor of childhood. Characteristically, these tumors have a benign biological behavior. Recurrence after initial resection, although uncommon, usually develops within several years after treatment.1,2 Late recurrence arising as long as 48 years after initial resection has been described, but this is exceedingly rare.1,2,5,9 Among reports of late recurrences are four cases in which there was malignant histological evolution of an initially benign tumor.1,2,5,9

We report here a fifth case of malignant transformation of a juvenile pilocytic astrocytoma that occurred 21 years after the initial diagnosis and treatment with resection and irradiation. Noteworthy features of this case are the documentation by biopsy of prolonged persistence of a biologically and histologically indolent neoplasm, and its eventual evolution to an anaplastic small-cell neoplasm.

Case Report

This 26-year-old woman was first brought for evaluation when she was a child of 5 years. At that time, she had developed gait ataxia, headaches, and episodic vomiting. Neurological examination revealed marked chronic papilledema, fine nystagmus to the left, and an enlarged head for her age. The family history, previous medical history, general physical examination, and laboratory studies contributed no information relevant to her symptoms. Ventriculography demonstrated a midline cerebellar tumor and complete obstruction of the fourth ventricle.

Course. In August, 1960, the patient underwent occipital craniotomy, and extensive removal of tumor was performed in a two-stage surgical procedure. At the time of the operation, the tumor was described as a soft, gray, midline mass with bilateral extension. This mass was incompletely resected, but decompression of the fourth ventricle and reestablishment of cerebrospinal fluid flow was achieved. The postoperative course was complicated by Pseudomonas species meningitis, meningeal scarring, hydrocephalus, and blindness. A ventriculoatrial shunt was placed, after which she received a course of cobalt irradiation (6500 rads) to the tumor bed.

The patient did well initially, but her subsequent...
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course was characterized by episodes of headache and gait ataxia occurring in 1967, 1970, and 1978, when she was 11, 13, and 22 years old, respectively. On each of these three occasions, the diagnosis of recurrent posterior fossa tumor was followed by surgical resection of recurrent tumor within the cerebellar vermis which resulted in relief of her symptoms.

In 1981, at the age of 26 years, she again developed occipital headache and progressive gait ataxia, with the additional symptoms of hearing loss in the left ear, anorexia, and dysphagia. A computerized tomography scan showed cystic and solid recurrence of tumor with tentorial spread. Posterior fossa exploration revealed tumor in the region of the superior vermis, extending upward to just beneath the tentorium. The tumor was gray, generally tough, and not well demarcated from gliotic cerebellum. Residual tumor in the region of the superior cerebellar peduncle was not resected.

The patient’s recovery from surgery was uneventful, and currently she is receiving additional radiation therapy and chemotherapy with BCNU (1,3-bis(2-chloroethyl)-1-nitrosourea).

Pathological Findings. Microscopic examination of the tumor initially resected in 1960 showed typical features of juvenile pilocytic astrocytoma, with predominantly spongy areas composed of diffusely infiltrating astrocytes, some fibrillary processes, numerous small blood vessels, and extensive microcyst formation (Fig. 1). Areas of compact tumor growth were sparse. The proliferating astrocytes appeared mature and had definite nuclear membranes, finely stippled chromatin, and occasional small nucleoli. Examination of tumor removed at subsequent craniotomies in 1967, 1970, and 1978 revealed histologically similar neo-

plasm, gliosis of surrounding brain parenchyma, and prominent dilated blood vessels with marked thickening and hyalinization of the vessel walls.

Tumor from the most recent craniotomy had some areas of compact proliferation of non-anaplastic astrocytes with phosphotungstic acid hematoxylin (PTAH)-positive glial processes (Fig. 2). This proliferation occurred within a gliotic stroma, and, again, there were prominent dilated blood vessels with thick hyalinized walls. However, there were also prominent broad areas in which the tumor was composed of

![Figure 1: Photomicrograph demonstrating compact and loose areas of tumor in the original biopsy specimen taken in 1960. H & E, × 16.](image1)

![Figure 2: Left: Photomicrograph of the most recent (1981) biopsy specimen showing nuclear pleomorphism and dense fibrillary background. H & E, × 320. Right: Area comparable to that shown left demonstrating abundant astroglial processes. PTAH, × 320.](image2)
dense aggregates of small cells with hyperchromatic rounded nuclei, prominent nucleoli, and frequent mitoses; several mitoses within a single high-power field were observed occasionally (Fig. 3). Staining with PTAH showed the presence of only small numbers of glial processes. There was no vascular or endothelial proliferation in these areas. No Homer-Wright rosettes or perivascular pseudorosettes were observed.

**Discussion**

Four previously reported cases of late recurrence of juvenile pilocytic cerebellar astrocytoma have documented transformation of the lesion to an anaplastic astrocytoma occurring 14 to 48 years after the initial resection. The rarity of such an event makes any such case unusual. The transformation of the lesion to a small-cell neoplasm in this case is without precedent within this select group of cases.

The histogenesis of the transformed neoplastic cells in this case is uncertain. Their appearance as small, round cells is suggestive of medulloblasts. In support of this possibility is our inability to find areas of transition between the small-cell neoplasm and adjacent areas of recognizable astrocytoma. A more conservative interpretation, which we prefer, is that this small-cell component represents a highly anaplastic astrocytoma with unusual morphology. This interpretation is supported by the demonstration of some glial processes by the PTAH stain and by the presence of this anaplastic tumor adjacent to astrocytoma with prominent glial processes. The difficulty in making an exact diagnosis in this case is in some ways reminiscent of an equally unique case, reported by Rubinstein, et al., of a cerebellar and brain-stem glioma arising in a 14-year-old girl; that lesion had concomitant features of a focal medulloblastoma and an infiltrating astrocytoma. There was no clinical evidence in our case to suggest that the anaplastic cells could represent metastasis from a systemic malignancy. We cannot exclude the possibility, however, that the anaplastic tumor is a second malignancy arising from an independent focus within the cerebellar astrocytoma.

Attempts to implicate previous radiotherapy, the effects of multiple surgical explorations, or other factors related to our patient's clinical course in the pathogenesis of this lesion would be speculative. It is known that intracranial fibrosarcomas and meningiomas may develop in humans after radiation therapy, and glioblastoma multiforme has been experimentally induced in monkeys that were exposed to ionizing radiation. The average time interval between therapeutic irradiation and the diagnosis of a subsequent intracranial tumor in humans has been estimated to be 20.8 years in the case of meningiomas, and most often ranges from 6 to 10 years in the case of fibrosarcomas. Studies of second malignancies in children after therapeutic irradiation for primary cancers arising outside the central nervous system (CNS) suggest a peak cancer frequency occurring 15 to 19 years following exposure to radiation. Our case does not fit the usual time sequence for development of postirradiation CNS malignancy, but the small numbers of such cases reported, as well as the different histopathology in our case, make the possible influence of prior irradiation uncertain. It is noteworthy that the patients reported by Bernell, et al., did not receive radiation therapy.

This case of late malignant transformation of a

![Fig. 3. Left: Photomicrograph showing the most densely cellular portion of the latest (1981) recurrent tumor. Note presence of small, round to oval, dark-staining nuclei and scattered background cytoplasmic processes. H & E, × 320. Right: Area comparable to that shown left reveals occasional PTAH-positive processes. PTAH, × 320.](image-url)
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juvenile pilocytic cerebellar astrocytoma and the similar cases reported previously represent a rare transformation of a common tumor. Nonetheless, they emphasize that, because the natural history of these tumors may follow such a course, decades of follow-up review are necessary to obtain an accurate assessment of the lesion.

References


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