Cerebellar astrocytoma with benign histology and malignant clinical course

Case report

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Juvenile cerebellar astrocytoma characteristically has a very benign course and good prognosis. A case is reported of juvenile cerebellar astrocytoma with massive craniospinal leptomeningeal spread prior to surgical intervention. The patient died 8 months after the onset of symptoms and only 5 weeks after presentation to the hospital. At postmortem examination, it was found that tumor encased the brain and spinal cord. The histology was benign. The literature on cerebellar astrocytoma is reviewed.

KEY WORDS • cerebellar astrocytoma • childhood brain tumor • subarachnoid metastasis • microcystic glioma

J U V E N I L E cerebellar astrocytomas characteristically have the best prognosis of all intrinsic gliomas of the brain. Based on histological features, two distinct groups of patients with "excellent" and "moderately good" prognosis have been described. The following case is unusual in that the histology placed the tumor in the most benign group, not accurately predicting the malignant clinical course. The literature on the relationship of the histology of juvenile astrocytoma with the clinical course is reviewed.

Case Report

This 8-year-old right-handed girl presented with an 8-month history of headache, projectile and paroxysmal vomiting, posturally related vertigo, and a 15-lb weight loss. In the 3 months before admission she became ataxic, worse on the right, and lost the ability to ride a bicycle or skip rope. A striking personality change developed: she became lethargic and disinterested in play, friends, or family. Diplopia in all directions of gaze developed a few days before admission. Birth, development, and prior medical history were all unremarkable.

Examination. She was an ill-looking child. Her height was 122 cm (in the 25th percentile); she weighed 20 kg (in the 10th percentile); her head circumference was 54.3 cm (above the 50th percentile). General examination was otherwise normal.

Neurologically, there was a positive cracked-pot sign. Apart from irritability and lassitude, her mental status was normal. There was gross papilledema; vision was 20/400 on the left, and 20/200 on the right. Right sixth, seventh, and eighth cranial nerve palsies were present. Right-sided dysmetria and dysdiadochokinesia were prominent. Tandem gait was impossible. Muscle power and tone were normal, but reflexes were symmetrically hypoactive, with bilateral Babinski reflexes.

Laboratory studies, including blood chemistry and urinalysis, were normal. Skull x-ray films showed diastatic sutures, an eroded sella turcica, and focal calcification in the posterior fossa. Computerized tomography (CT) revealed massive hydrocephalus and an enhancing right cerebellar hemispheric mass. A right ventriculoperitoneal shunt was inserted 3 days after admission. Intracranial pressure was measured at 50 mm Hg, with pronounced reduction of cerebral compliance. The ventricular fluid had a protein level...
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of 38 mg% and glucose level of 100 mg%; cytology did not reveal malignant cells.

Operation. The patient's condition improved, and 6 days later, at posterior fossa craniotomy, tumor was encountered throughout the subarachnoid space over the cerebellar hemispheres and in the fourth ventricle. Partial resection was accomplished.

The early postoperative course was uneventful, and 3600 rads of cobalt radiation was administered to the posterior fossa. However, over a 10-day period, a complete loss of cord function below T-4 developed. Myelography was not undertaken; the radiotherapy was increased to include the entire neuraxis (3750 rads). However, areflexic weakness of the left hand, and then the right, developed with severe head and neck pain, progressive breathing difficulty, and pharyngeal incompetence. She died of pneumonia 5 weeks after admission.

Pathological Examination. The operative tumor specimen resembled the postmortem tumor in histological appearance. Except for pneumonia, the general autopsy findings were unremarkable.

The only intraparenchymal tumor was in the right cerebellar white matter, presenting as a hard, yellow, granular mass continuous with gelatinous tumor in the fourth ventricle (Fig. 1). The lateral and third ventricles were tumor-free, but tumor extended into the subarachnoid space in the velum interpositum, distorting the fornix from the diencephalon (Fig. 2 left). Tumor coated the cerebral gyri, encased the optic nerves, mammillary bodies, and the entire brain stem, and insinuated itself between cerebellar folia (Fig. 2 right). The spinal cord was similarly encased in subarachnoid tumor along its entire length, compressing the cord in a nodular fashion at T-2 (Fig. 1 inset).

Histologically, the tumor was similar everywhere, with the exception that calcium was only present in the intraparenchymal cerebellar mass (Fig. 3 left). Architecturally, the variegated pattern from field to field was typical of a benign cerebellar astrocytoma of juvenile type: protoplasmic microcystic areas alternated with strongly fibrillated areas (Fig. 3 left). The nervous tissue parenchyma was nowhere invaded by subarachnoid tumor, although glial bridges were present (Fig. 4). The protoplasmic areas showed lakes of eosinophilic fluid, indented by microcysts (Fig. 3 right), which did not coalesce into macrocysts. Cyto logically, there were few atypical cells, with only occasional binucleate forms (Fig. 3 right). No mitoses could be found. Rosenthal fibers were present. Notably absent were any areas of high cell density, oligodendroglia, necrosis, pseudorosetting, or endothelial hyperplasia/hypertrophy.

Discussion

In recent years, two new developments in our knowledge of juvenile cerebellar astrocytoma have taken place. The first is the correlation of the histology with a clinical subgroup of children who do less well than expected. The second is the revelation through individual case reports that the correlation of histology with prognosis does not always hold.

Although cerebellar glioblastoma occurring in childhood is recognized, our concern is with the histologically benign astrocytoma of the cerebellum. Cushing, in his classic series of 76 cases, first noted the often cystic nature of these tumors, and emphasized the need for identification and decompression of macrocysts, facilitating extirpation, relieving symptoms, and forestalling fatality. Some cysts entirely lined by tumor were described, but far more com-
monly the tumor was well localized to a mural nodule. Recently, it has been shown that the CT density of the proteinaceous cyst fluid is twice that of cerebrospinal fluid, aiding differentiation of arachnoid cysts and postoperative defects from tumorogenic cysts. Cush- ing also described the evolution of some tumor cysts, ending with extinction of the mural tumor. He mentioned two adults whose cerebellar symptoms became static. One had two xanthochromic cysts at operation, and in the other, the cyst was discovered at autopsy. This suggested to Cushing that the tumor could occasionally resolve spontaneously. More recently, the view that simple cysts of the cerebellum are "burnt-out" astrocytomas has been supported.

The classic histological features of benign cerebellar astrocytoma include fibrillated astrocytes, microcysts, Rosenthal fibers, calcium, often in oligodendrocytomatous areas, endothelial proliferation, and leptomeningeal invasion with glial bridging, the latter two features not connoting malignancy. Long-term studies, however, have suggested that a minority of patients do less well. These patients have recently been delineated histologically. Gilles, et al., found that in cases where microcysts, leptomeningeal deposits, Rosenthal fibers, and oligodendroglial foci clustered together (their glioma A), there was a 94% 10-year survival, and in cases where pseudorosettes, high cell density, necrosis, mitosis, and calcification clustered together (their glioma B), there was a 29% 10-year survival. They have constructed predictive linear dis-

Fig. 3. **Left:** Tumor and cerebellar white matter demonstrating calcospherites and variegated appearance with loose and densely fibrillated areas. PTAH, × 65. **Right:** Area of maximum cellular atypia (beneath the hypothalamus) demonstrating rare binucleate cells (B) with reniform to round nuclei. Collections of eosinophilic fluid are indented by microcysts. A Rosenthal fiber is seen (circled). H & E, × 360.

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Juvenile cerebellar astrocytoma, underwent malignant transformation 48 years later. Tyszkiwicz, et al., reported a 14-month-old child who lost the ability to sit and walk at 12 months, and died with three massive outgrowths up to 5.5 cm in diameter from a cerebellar glioma. The cell density was low, comprising chiefly fibrous astrocytes with oligodendrogial areas. There were few mitoses, a large number of capillaries, calcium, pseudorosettes, and necrosis, but no cysts. The tumor probably represents an aggressive, diffuse glioma B. Diffuse spread of astrocytic tumor via cerebrospinal pathways is also well known. Eade and Urich reported five metastasizing gliomas spreading via the cerebrospinal fluid in young patients, four apparently arising from the spinal cord and one from the thalamus. McLaughlin recorded five similar cases, four of thalamic origin and one arising in the cerebellar white matter. The latter, however, showed histological hallmarks of malignancy, with frequent mitoses and much tumor necrosis. Shapiro and Shulman reported three histologically benign cases of cerebellar astrocytoma which seeded the spinal cord, and believed that, due to the chronology of clinical events, this was part of the natural history of this tumor. Kepes, et al., recorded extensive invasion of the neck through the dura which was closed loosely at an initial operation. The initial tumor was histologically benign, and, in spite of radiotherapy, the tumor found at autopsy 40 months later had seeded the cranial and spinal leptomeninges, and was still histologically benign.

The case reported here represents an extreme degree of craniospinal leptomeningeal invasion of benign tumor rather than malignant transformation per se, as malignant histological features were totally lacking. Furthermore, this stage represented part of the natural history of this cerebellar astrocytoma, since tumor was seen covering the cerebellar hemispheres at initial surgery, prior to radiotherapy. Although radiotherapy has been recommended for cystic cerebellar astrocytomas, our case and that of Kepes, et al., demonstrate the ineffectiveness of radiotherapy in controlling the disseminating tenden-
cies sometimes present in the benign juvenile type of cerebellar astrocytoma.

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References

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