Metastatic juvenile pilocytic astrocytoma

Case report

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The authors report the case of a metastatic juvenile pilocytic astrocytoma of the hypothalamic region in a 10-year-old boy. Eight years after craniotomy and radiation therapy, the tumor spread via cerebrospinal fluid pathways to the left cerebellar tonsil and the lumbosacral region. Histological evaluation of both the original hypothalamic and the new lumbosacral masses showed features of a slow-growing juvenile pilocytic astrocytoma with no evidence of malignant transformation. The clinical implications and possible mechanisms of metastatic spread are discussed.

Key Words: juvenile pilocytic astrocytoma • metastasis • glioma • magnetic resonance imaging

Juvenile pilocytic astrocytoma, previously termed "spongioblastoma polare," occurs predominantly in children and young adults and accounts for approximately 60% of cerebellar astrocytomas in children. It is found most commonly in the cerebellum and hypothalamic region, and less frequently in the brain stem, optic nerves, and cerebral hemispheres. Clinically, juvenile pilocytic astrocytomas are characterized by a relatively benign course, although there have been several reports of malignant transformation. The treatment of choice is total excision. The postoperative survival rate is between 86% and 100% at 5 years, 83% at 10 years, and 70% at 20 years. Even patients with juvenile pilocytic astrocytomas of the hypothalamus, third ventricular region, or optic nerves can expect long-term survival, although these tumors often cannot be totally resected.

Metastatic spread of gliomas is rare. Most cases of metastasis involve anaplastic astrocytomas or glioblastomas multiforme. Low-grade cerebellar astrocytomas have also been reported to spread through cerebrospinal fluid (CSF) pathways; most of these tumors, however, were not classified as juvenile pilocytic astrocytomas. To our knowledge, only three histologically confirmed metastatic juvenile pilocytic astrocytomas have been reported. We describe the case of a hypothalamic juvenile pilocytic astrocytoma that underwent diffuse intracranial metastasis as well as pathologically confirmed subarachnoid spread.

Case Report

This 16-month-old boy presented with failure to thrive, and neurological examination showed reduced visual acuity and vertical nystagmus in the left eye.

First Admission. Axial computerized tomography (CT) scans revealed a solid, 3 × 3 × 3-cm contrast-enhancing mass in the hypothalamic region. He later underwent bifrontal craniotomy and subtotal resection of the lesion. The tumor was found to be filling the entire suprasellar region and extending into the left optic nerve canal. Medical therapy for panhypopituitarism was initiated at that time. Pathological examination of the resected tissue showed the presence of a juvenile pilocytic astrocytoma. Most of the tumor had a compact appearance, although some areas appeared to have undergone microcystic degeneration. Capillaries were prominent, and there was endothelial proliferation. No Rosenthal fibers, necrotic regions, or mitotic cells were seen.

Radiation therapy was begun 3 weeks postoperatively. During the next 6 weeks, the child received a total of 5700 rad of external beam irradiation. Follow-
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Fig. 1. Magnetic resonance T₁-weighted (TR 600 msec/TE 20 msec) image, sagittal projection, obtained after the administration of gadolinium in the 10-year-old patient. Note the enhancing masses in the hypothalamic region and the left cerebellar tonsil.

up CT scans showed no evidence of tumor during the 3 years after radiation therapy. However, when the child was 4 years old, a small mass in the hypothalamic region was noted on a CT scan produced by a newergeneration scanner. The lesion remained stable for 6 years and was considered most likely to represent scar tissue.

Second Admission. The patient was referred to our institution at the age of 10 years, after a CT scan showed an enlarging lesion in the hypothalamic region. A magnetic resonance (MR) image obtained after the administration of gadolinium showed an enhancing mass in the hypothalamus (Fig. 1). The tumor extended down into the sella and was centered to the left of midline. The optic chiasm could not be identified as a distinct structure, and the optic nerves beyond the optic canal were not enhanced and did not appear enlarged. In addition, a 2 x 2 x 2-cm gadolinium-enhancing lesion was seen in the left cerebellar tonsil (Fig. 1). These lesions were presumed to be metastatic, and a full spine MR image was obtained to check for further metastasis. It showed a gadolinium-enhancing spherical mass, 2.5 cm in diameter, in the thecal sac immediately posterior to the L5-S1 disc space (Fig. 2). More inferiorly in the caudal thecal sac, an area of enhancement was seen at the S2-3 level (Fig. 2). These lesions were thought likely to represent drop metastasis. There was no evidence of spread to the cervical or thoracic region. The patient had no symptoms of leg pain, weakness, sensory changes, or bowel or bladder dysfunction. His neurological examination was remarkable only for a baseline absence of vision in the left eye and a right temporal field defect in the right eye.

The patient then underwent an L-5 laminectomy for biopsy of the lumbosacral mass. The lesion was densely adherent to the nerve roots and dura. The final pathological diagnosis was a juvenile pilocytic astrocytoma with no evidence of malignant transformation. The tumor had both loose and compact areas, with bipolar cells and numerous Rosenthal fibers (Fig. 3). The histological appearance of this tumor was similar to that of the lesion removed 8 years earlier. After an uneventful postoperative course, the child was placed on a course of chemotherapy consisting of 6-thioguanine and 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU). The lesions in the hypothalamic region, cerebellar tonsil, and lumbosacral area have all remained stable or decreased in size after a follow-up period of 1½ years; the patient’s neurological function remains stable.

Discussion

Pilocytic astrocytomas have been categorized into adult and juvenile types. Adult type is characterized by a uniform histological appearance consisting of closely packed and interwoven broad bundles of bipolar fibrillated cells. These cells seldom undergo microcystic degeneration, and they have no distinct relationship with blood vessels. These tumors are seen in older patients and are more likely than juvenile pilocytic astrocytomas to undergo malignant transformation. Juvenile pilocytic astrocytomas most commonly develop during the second and third decades of life. They have a more varied histological appearance than adult pilocytic astrocytomas and consist of thin elongated cells positioned in parallel arrays that tend to sheathe blood vessels longitudinally. Microcystic degeneration is common in these tumors, although malignant transformation is rare.
Diffuse spread of gliomas via CSF pathways is a rare occurrence in anaplastic gliomas. In a review of 405 patients with supratentorial glioblastomas and 630 patients with anaplastic gliomas, the incidence of spinal cord metastases was 1.6% during radiation therapy and 1.2% during chemotherapy. Eade and Urich reported five malignant gliomas that metastasized via CSF pathways (four from the spinal cord and one from the thalamus). Finally, leptomeningeal dissemination was noted on follow-up studies in five of seven anaplastic astrocytomas of the posterior fossa in children.

Low-grade gliomas do not often metastasize. In a review of 314 consecutive primary intracranial tumors in children, Packer, et al., found that none of 36 low-grade cerebellar gliomas and only two of 58 extracerebellar low-grade gliomas underwent leptomeningeal dissemination. Shapiro and Shulman reported three low-grade cerebellar astrocytomas that seeded the spinal cord, and Auer, et al., described another low-grade cerebellar astrocytoma that underwent craniospinal leptomeningeal spread. However, in none of these reports were the tumors classified as juvenile pilocytic astrocytomas.

Metastasis of a juvenile pilocytic astrocytoma is extremely rare. Kocks, et al., reported a juvenile pilocytic astrocytoma arising in the optic chiasm and metastasizing via CSF pathways to the lumbar region 4 years after craniotomy. The tumors from the two locations showed similar histological features with no evidence of anaplastic transformation. The spinal lesion was treated with local irradiation. McLaughlin reported five extracerebellar astrocytomas with piloid features; autopsy showed that all five had spread to the ventricles and three had spread to the lumbar region. The histological findings indicated a juvenile pilocytic astrocytoma in only two of these cases. One of these two patients (Case 5) had a hypothalamic juvenile pilocytic astrocytoma, which autopsy revealed had spread diffusely throughout the intracranial but not the spinal CSF pathways. It contained protoplasmic areas with widely scattered mitotic cells. The other patient (Case 4) had a cerebellar juvenile pilocytic astrocytoma, which autopsy showed had spread to the lumbar subarachnoid and basal cisterns. The tumor was characterized by numerous mitotic cells and necrotic regions. The other three tumors had piloid areas, but two of them were predominantly oligodendrogliomas and the other was a poorly differentiated gemistocytic astrocytoma. All five patients died within 20 months of the onset of symptoms and within 2 months of surgery.

Juvenile pilocytic astrocytomas appear to metastasize by local invasion of the leptomeninges and subsequent spread through CSF pathways. Surgically induced dissemination of cells may also contribute to metastasis. Progressive loss of tissue-specific proteins in neoplastic cells may make the cells antigenically neutral, thus releasing them from normal local restraints and allowing metastasis. Surgical dissemination of tumor cells may have occurred in our patient, although his craniotomy was performed 8 years before the metastases were discovered. In addition, hypothalamic juvenile pilocytic astrocytomas may be more likely than other juvenile pilocytic astrocytomas to metastasize via CSF pathways because of their proximity to the subarachnoid space and third ventricle and their low likelihood of being totally resected.

Two histological characteristics common in gliomas that spread via the CSF pathways are oligodendrogliomatous areas and nuclear pleomorphism in which the nuclear membrane is folded. At least one of these features was present in each of the five cases reported by McLaughlin. Endothelial proliferation and mild cellular pleomorphism are common findings in juvenile pilocytic astrocytomas and do not indicate a poor prognosis, as they do in other tumors. However, frequent
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mitosis, necrosis, or infiltrative growth and formation of secondary structures should cause re-evaluation of the diagnosis of a juvenile pilocytic astrocytoma. 11 Although our patient's tumor did not have any of these characteristics, it gave rise to documented metastases.

The possibility of sampling error should be considered. The initial craniotomy involved nearly total resection of the hypothalamic juvenile pilocytic astrocytoma, whereas the subsequent lumbar laminectomy consisted of only a biopsy. It is possible that the lumbar lesion had more histological features of malignancy than we detected. However, leptomeningeal spread of a juvenile pilocytic astrocytoma after malignant transformation has been reported only once, and the diagnosis of this metastasis was based on clinical evidence without histological confirmation. 12,13 de Keizer, et al. 12 reported a juvenile pilocytic astrocytoma of the optic nerve that contained areas of highly anaplastic astrocytoma and showed intraocular seeding. Because no previous biopsy had been performed, however, it is not clear whether this was a case of malignant transformation. Thus, in the small number of reported juvenile pilocytic astrocytomas undergoing late malignant transformation, 14-16 the incidence of metastases is probably the same as in other anaplastic gliomas.

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References