Leptomeningeal dissemination of pilocytic astrocytoma via hematoma in a child

Case report

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A case of recurrent pilocytic astrocytoma with leptomeningeal dissemination (LMD) is described. A cerebellar tumor was diagnosed in a 3-year-old boy, in whom resection was performed. When the boy was 6 years of age, recurrence was treated with surgery and local radiotherapy. At age 13 years, scoliosis was present, but the patient was asymptomatic. Twelve years after initial surgery LMD was demonstrated in the lumbar spinal region without recurrence of the original tumor. This tumor also was subtotally removed. During the procedure, a hematoma was observed adjacent to the tumor, but the border was clear. Histological examination of the spinal cord tumor showed features similar to those of the original tumor. There were no tumor cells in the hematoma. The MIB-1 labeling index indicated no malignant change compared with the previous samples. Radiotherapy was performed after the surgery. The importance of early diagnosis and management of scoliosis is emphasized, and the peculiar pattern of dissemination of the pilocytic astrocytoma and its treatment are reviewed.

KEY WORDS • pilocytic astrocytoma • leptomeningeal dissemination •
MIB-1 labeling index • radiation therapy • scoliosis

Juvenile pilocytic cerebellar astrocytoma is a benign tumor that corresponds to histological Grade I.^{6,7,9} It is associated with 10- and 20-year survival rates of greater than 90% in patients who undergo total excision of the lesion.^{6,7,10,21} Many of these tumors are amenable to total resection, and the subsequent recurrence rates. Even in children in whom tumors are subtotally excised and radiotherapy is then performed, the 20-year survival rates are often between 70 and 80%.²¹

Histopathologically, an astrocytic tumor of low cellularity exhibits a biphasic pattern with varying proportions of compacted bipolar cells with Rosenthal fibers and loose textured multipolar cells with microcysts and granular bodies.⁹ Anaplastic transformation is unusual; some authors have suggested that it is induced by radiotherapy.^{9,20} A small percentage of these tumors manifest widespread dissemination either at presentation or later. Fur-

thermore, fewer than 10 cases of LMD from a pilocytic cerebellar astrocytoma have been reported;^{1,5,8-10,11,13,14,16,18-20} in five of these cases, the metastasis was spinal.^{1,5,8,9,10,12,14,16-18} The detection of dissemination of a histologically benign neoplasm raises fundamental questions regarding the biological features that account for tumor seeding, as well as practical concerns regarding the long-term outcome after treatment.¹⁵

When scoliosis is first diagnosed during childhood, it is classified into one of three categories: congenital, paralytic, or idiopathic. The congenital variety is a result of vertebral malformation present since birth. The paralytic type is suggested by a history of obvious neurological disease. A diagnosis of idiopathic scoliosis, on the other hand, must remain one of exclusion. It appears that when scoliosis is the main presenting feature in a case of a spinal cord tumor, its cause is often overlooked.^{3,4,15,17}

The case reported here is unusual in that, 12 years after surgery, a histologically benign astrocytoma disseminated to the spinal regions without pathologically malignant transformation or apparent regrowth of the primary tumor. In addition, intraoperative examination demonstrated a hematoma adjacent to the tumor. The goals of the present

Abbreviations used in this paper: CSF = cerebrospinal fluid; CT = computerized tomography; Gd-DTPA = gadolinium diethylenetriamine tetracetic acid; LMD = leptomeningeal dissemination; MR = magnetic resonance; VP = ventriculoperitoneal.

report are to emphasize the importance of MR imaging both at presentation and during the follow-up course in patients with these conditions, as well as to alert the clinician to consider a diagnosis of intramedullary tumor in patients in whom scoliosis is evident at an early stage.

CASE REPORT

History. A 3-year-old boy was initially evaluated at an outside neurosurgical department for symptoms of increased intracranial pressure in 1989. Computerized tomography scanning performed at that time demonstrated a huge circumscribed tumor in the cerebellar vermis and obstructive hydrocephalus (Fig. 1A). A VP shunt was placed (Fig. 1B), and subtotal removal of the tumor was undertaken. The histological diagnosis was juvenile pilocytic astrocytoma. Adjuvant therapies were not administered, and the patient was discharged to out-patient care where no deterioration was reported. Three years after the initial operation, moderate regrowth of the tumor was revealed. In 1992, the patient was transferred to our hospital at his family's request and we excised the tumor subtotally. The histological diagnosis remained pilocytic astrocytoma (Fig. 2A). The MIB-1 labeling index was approximately 9% (Fig. 2B). At that time, a total radiation dose of 55 Gy was administered to the posterior fossa. During the 9-year period after the operation, the patient did well, and by 2001 no signs of recurrence were demonstrated on cranial MR imaging (Fig. 1C and D). When the boy was 13 years

Fig. 1. A: A nonenhanced CT scan obtained at the time of initial treatment (1989) when the patient was age 3 years, demonstrating a mass of moderate low density in the vermis, as well as obstructive hydrocephalus. B: Enhanced CT scan acquired after insertion of a VP shunt in 1989, revealing a well-enhanced circumscribed mass. C: Axial Gd-DTPA-enhanced T_1 -weighted MR image demonstrating no tumor recurrence, obtained in 2001 when the patient was age 15 years. D: Sagittal Gd-DTPA-enhanced T_1 -weighted MR image also demonstrating no tumor recurrence in September 2001.

Fig. 2. Photomicrographs of sections of the tumor resected in the cerebellar vermis in 1999. A: Typical histological features of juvenile pilocytic astrocytoma characterized by heterogeneous appearance of bipolar spindle-shaped astrocytes. No mitotic activity is evident. H & E, original magnification $\times 62$. B: Immunohistochemical staining for MIB-1. The MIB-1 labeling index is approximately 9%. Original magnification $\times 100$.

of age in 1999, the VP shunt malfunctioned after the peritoneal tube became obstructed. Reconstruction of the shunt system was undertaken, and the postoperative course was uneventful. Although there were no discernable lower-extremity impairment nor genital or rectal dysfunction, an abdominal radiograph demonstrated scoliosis that had not been radiographically apparent in 1992 (Fig. 3).

Examination. In July 2001, when the patient was age 15 years, he complained of pain in the right femur and increasing difficulty in urinating. After spinal MR imaging was performed at an outside institution, he was transferred to our hospital; a diagnosis of lumbosacral LMD was sus-

Fig. 3. A: Chest and upper abdominal radiograph obtained in 1992 when the patient was age 6 years demonstrating no scoliosis. B: Radiograph obtained at age 13 years, revealing scoliosis in the lumbar area.

Fig. 4. A: Sagittal T₁-weighted MR image of the lumbar spine obtained in September 2001, revealing an isointense mass in the L5–S1 region (white arrowheads). B: Sagittal T₂-weighted MR image of the lumbar spine demonstrating a high-intensity circumscribed mass in the L-5 region (black arrowheads). C: Illustration of the operative findings. After evacuating an easily aspirated mass (diagnosed as pilocytic astrocytoma), a circumscribed mass was demonstrated, which was diagnosed as a hematoma (black arrowheads). 1, nerve root identified through arachnoid membrane; 2, arachnoid membrane; 3, wall of the tumor; and 4, cavity of the tumor.

pected. Neurological examination at admission revealed no muscle weakness, sensory disturbance or laterality of deep tendon reflexes in the lower extremities. Pain on percussion, however, was demonstrated in the spinous process in the L2–4 area. Physiological examinations revealed decreases in both bladder and anorectal function. On T₁-weighted spinal MR imaging an isointense mass in the L5–S1 intradural area was revealed (Fig. 4A), and on T₂-weighted imaging a circumscribed cystic mass was observed in the L-5 intradural area (Fig. 4B). Whole-spine MR imaging revealed no other abnormal findings. Cytological examination of the CSF likewise showed no abnormal features.

Operation. To clarify the histological nature of the tumor and to ameliorate the symptoms, an L4–S1 laminectomy was undertaken.

The spinal dura was incised from L-4 to S-1 (Video Clip). We then identified the mass through the thick arachnoid membrane. After the arachnoid membrane was incised, we obtained a biopsy sample from the caudal side of the tumor. The tumor was soft and easily aspirated. We

identified nerve roots on both lateral sides of the tumor; these were tightly adherent to the wall of the tumor. Therefore, we decided to debulk the tumor but leave the wall.

After removing the tumor, we identified another mass at the L-5 level, which seemed to be the cystic mass that had been observed on the previous T₂-weighted sagittal MR images (Fig. 4C). The content of this mass was a substantial hemorrhage. After evacuating and debulking the mass, we resected it almost totally.

Pathological Examination. Histologically, the tumor was essentially the same as the previous neoplasm (Fig. 5A), and no malignant changes had occurred. Immunohistological stainings showed the presence of glial fibrillary acidic protein (Fig. 5B) in the tumor cells. The MIB-1 index was approximately 9% (Fig. 5C), which was the same as that demonstrated by the previous study of the cerebellar tumor conducted in 1992. A diagnosis of pilocytic astrocytoma with LMD was determined for this tumor. The hematoma contained hemorrhagic and necrotic tissue (Fig. 5D) but no tumor cells.

Adjuvant Therapy and Postoperative Course. Radiotherapy (total dose of 55 Gy) was delivered to the lower lumbar region. The patient was discharged 2 months after admission, with no neurological deficit. Follow-up Gd-DPTA-enhanced T₁- and T₂-weighted MR imaging demonstrated no recurrence of the tumor and good postoperative outcome (Fig. 6A and B).

DISCUSSION

This case is unique in that the cerebellar tumor showed no local recurrence and the disseminated tumor had no anaplastic changes. Metastatic disease from a pilocytic astrocytoma is rare, estimated to occur in only 4% of patients.¹⁶ Pilocytic cerebellar astrocytoma with LMD without simultaneity has been reported in a total of eight patients, including the present one (Table 1).^{5,8,10,11,13,19}

Idiopathic Scoliosis: a Rare Manifestation of Intrinsic Spinal Cord Tumors

In most cases radiological evaluation of scoliosis is limited to conventional radiographs of the spine.¹⁵ In the present case, we should have noticed the idiopathic scoliosis 2 years previously. Scoliosis may indeed be the only presenting feature, and awareness of alternative diagnostic possibilities is important, primarily to prevent inappropriate correction of the deformity alone and, secondly, because early diagnosis and treatment can greatly improve the prognosis for patients with spinal cord tumors.^{3,4} Despite its rarity, the association of scoliosis with tumors of the spinal cord is important for many reasons. If the neurological deficit is slight, children are too often thought to suffer from idiopathic scoliosis and treated accordingly. This is more likely to occur because they are often of the same age group as the majority of children suffering from idiopathic scoliosis—that is, 8 to 14 years of age. Corrective treatment of the scoliosis may be harmful to the child. If, on the other hand, the child presents with an advanced neurological deficit, the possibility of a spinal cord tumor may not be considered because they are rare and difficult to diagnose in children.

Fig. 5. Photomicrographs of sections of the tumor resected from the lumbar spinal region in 2001. A: Piloid cells were found, which indicate that the lesion is the same pilocytic astrocytoma as that found in 1999. Tumor cells show no malignant change. Rosenthal fibers and eosinophilic granular bodies are also sparsely evident. H & E, original magnification $\times 62$. B: Immunoreactivity for glial fibrillary acidic protein. Original magnification $\times 62$. C: Immunohistochemical staining for MIB-1. The MIB-1 labeling index is approximately 9%. Original magnification $\times 62$. D: Hemorrhagic mass containing no tumor cells. H & E, original magnification $\times 50$.

Operative and Pathological Findings

Intraoperative examination, shown in the Video Clip, revealed that the hematoma was characteristic in that it was attached to the tumor and the borderline between them was clear. There were no vascular malformations or abnormal vessels. Histopathological examination showed no tumor cells. There has been one report about spontaneous hemorrhage due to juvenile pilocytic astrocytoma, but the authors concluded it was not related to the pathological findings.¹² When considering the mechanism, scoliosis may also become an issue. The pilocytic astrocytomas located in the cerebellar vermis and the lumbar spinal region were both diagnosed as having the same origin, and the spinal region astrocytoma resulted from LMD. There was no evidence of endothelial proliferation, necrosis, or mitosis to suggest malignant change.

Click here to view Video Clip. An intraoperative video clip showing the intradural procedure.

Mechanism of the LMD

A long interval between the first radiologically detected signs and the beginning of clinical symptoms is one of the characteristic features in this type of LMD. Generally, seeding of an anaplastic astrocytoma or glioblastoma heralds the end stage of disease. The growth character, biological behavior, and clinical course of the disseminated pilocytic astrocytoma were clearly different from those of

malignant glioma.² Several mechanisms have been proposed to explain the spread of intracranial tumors by CSF pathways. It has been hypothesized that malignant transformation, cellular anaplasia, surgical manipulation, natural history, or multiplicity may contribute to the spread of the tumor. Specifically, recent studies of cell adhesion molecules have helped to clarify the mechanisms that allow adhesion: in recent studies involving CD44 investigators have found that this adhesion molecule may play a role in astrocytic invasion and adhesion.¹⁴ Recurrent and disseminated pilocytic astrocytoma may not preclude long-term survival, because it rarely shows malignant transformation. Shapiro and Shulman¹⁸ reported three of 72 patients with histologically benign cerebellar astrocytomas in whom the tumor seeded the spinal subarachnoid space without malignant transformation.¹⁸ They noted that the seeding was not indicative of a rapidly fatal course and believed that this was part of the natural history of this tumor.

Treatment Controversy

Radical resection of the tumor, either alone or in conjunction with radiotherapy and chemotherapy, has been recommended as initial treatment.⁹ The treatment of the disseminated tumor, however, remains controversial. In our patient we found LMD without the presence of histological anaplastic transformation. Furthermore, after resection, radiotherapy alone was an effective treatment for the cerebellar tumor, and it has been efficacious for the

Fig. 6. A: A sagittal gadolinium-enhanced T₁-weighted MR image of the lumbar spine obtained in December 2001, revealing a slightly enhanced wall. B: Sagittal T₂-weighted MR image of the lumbar spine demonstrating a high-intensity region suggestive of postoperative change.

spinal dissemination. The selection for the treatment was made because of a high MIB-1 labeling index for pilocytic astrocytoma and because the tumor was a circumscribed mass. Additionally, we did not choose to administer intrathecal therapies because of the absence of abnormal CSF results. Radiotherapy may be important in the anaplastic change of low-grade astrocytoma in children. Auer, et al.,¹ demonstrated the ineffectiveness of radiotherapy in controlling dissemination. Recently, it has been reported that chemotherapy including cyclophosphamide, carboplatin, and etoposide may be beneficial in the management of this tumor and can delay the need for radiotherapy.¹⁰ If chemotherapy is beneficial, radiotherapy can be held in reserve. To evaluate the effectiveness of radiation, we will undertake a further follow-up review in which Gd-DTPA-enhanced MR imaging is performed.

In conclusion, although seeding from a cerebellar pilocytic astrocytoma rarely occurs, it is difficult to predict the occurrence of dissemination even by histological ex-

amination. Therefore, careful follow-up review involving both cranial and spinal Gd-DTPA-enhanced MR imaging is important even in cases of histologically benign pilocytic astrocytoma.

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References

1. Auer RN, Rice GPA, Hinton GG, et al: Cerebellar astrocytoma with benign histology and malignant clinical course. Case report. **J Neurosurg** 54:128–132, 1981
2. Awad I, Bay JW, Rogers L: Leptomeningeal metastasis from supratentorial malignant gliomas. **Neurosurgery** 19:247–251, 1986
3. Banna M, Pearce GW, Uldall R: Scoliosis: a rare manifestation of intrinsic tumours of the spinal cord in children. **J Neurol Neurosurg Psychiatry** 34:637–641, 1971
4. Citron N, Edgar MA, Sheehy J, et al: Intramedullary spinal cord tumours presenting as scoliosis. **J Bone Joint Surg Br** 66: 513–517, 1984
5. Civitello LA, Packer RJ, Rorke LB, et al: Leptomeningeal dissemination of low-grade gliomas in childhood. **Neurology** 38: 562–566, 1988
6. Garcia DM, Latifi HR, Simpson JR, et al: Astrocytomas of the cerebellum in children. **J Neurosurg** 71:661–664, 1989
7. Geissinger JD: Astrocytomas of the cerebellum in children. Long-term study. **Arch Neurol** 24:125–135, 1971
8. Jamjoom AB, Jamjoom ZA, al-Rayess M: Intraventricular and leptomeningeal dissemination of a pilocytic cerebellar astrocytoma in a child with a ventriculoperitoneal shunt: case report. **Br J Neurosurg** 12:56–58, 1998
9. Kleihues P, Cavenee WK: **Pathology and Genetics of Tumours of the Nervous System**. Lyon: IARC Press, 2000
10. Mamelak AN, Prados MD, Obana WG, et al: Treatment options and prognosis for multicentric juvenile pilocytic astrocytoma. **J Neurosurg** 81:24–30, 1994
11. McCowage G, Tien R, McLendon R, et al: Successful treatment of childhood pilocytic astrocytomas metastatic to the leptomeninges with high-dose cyclophosphamide. **Med Pediatr Oncol** 27:32–39, 1996

TABLE 1

Summary of reported cases with LMD of cerebellar pilocytic astrocytoma without simultaneity*

Authors & Year	Age (yrs), Sex†	Treatment of Primary Tumor	Timing of LMD (yrs)	Disseminated Sites	Treatment of LMD	Follow Up
Civitello, et al., 1988	8, F	total resection	6	hypothalamus, basal cistern, spinal cord	lomustine, VCR, spinal RT	alive at 17 mos
Mishima, et al., 1992	6, M	total resection, 40-Gy RT (local)	6	4th ventricle, T3–4	total resection, 40-Gy RT (local)	alive at 24 mos
Pollack, et al., 1993	4, M	total resection	4.75	basal cisterns, ventricles	carboplatin, VCR	alive at 17 mos
Mamelak, et al., 1994	11, M	total resection, 54-Gy RT	0.33	T10–11	none	alive at 46 mos
McCowage, et al., 1996	5, F	total resection	3	C-2 conus medullaris	cyclophosphamide	alive at 10 mos
Jamjoom, et al., 1998	8, M	VP shunt	2	multiple intracranial	30-Gy RT (whole brain)	alive at 5 mos
Tamura, et al., 1998	6, M	total resection	4	C7–T1	30-Gy RT (whole spine)	alive at 76 mos
present case	3, M	subtotal resection, 55-Gy RT (local)	12	L3–S1	subtotal resection, 55-Gy RT (local)	alive at 5 mos

* RT = radiotherapy; VCR = vincristine.

† Reflects age at initial diagnosis.

12. Mesiwala AH, Avellino AM, Roberts TS, et al: Spontaneous cerebellar hemorrhage due to a juvenile pilocytic astrocytoma: case report and review of the literature. **Pediatr Neurosurg** **34**: 235–238, 2001
13. Mishima K, Nakamura M, Nakamura H, et al: Leptomeningeal dissemination of cerebellar pilocytic astrocytoma. Case report. **J Neurosurg** **77**:788–791, 1992
14. Morikawa M, Tamaki N, Kokunai T, et al: Cerebellar pilocytic astrocytoma with leptomeningeal dissemination: case report. **Surg Neurol** **48**:49–52, 1997
15. Nokes SR, Murtagh FR, Jones JD III, et al: Childhood scoliosis: MR imaging. **Radiology** **164**:791–797, 1987
16. Pollack IF, Hurtt M, Pang D, et al: Dissemination of low grade intracranial astrocytomas in children. **Cancer** **73**:2869–2878, 1994
17. Samuelsson L, Lindell D: Scoliosis as the first sign of a cystic spinal cord lesion. **Eur Spine J** **4**:284–290, 1995
18. Shapiro K, Shulman K: Spinal cord seeding from cerebellar astrocytomas. **Childs Brain** **2**:177–186, 1976
19. Tamura M, Zama A, Kurihara H, et al: Management of recurrent pilocytic astrocytoma with leptomeningeal dissemination in childhood. **Childs Nerv Syst** **14**:617–622, 1998
20. Versari P, Talamonti G, D'Aliberti G, et al: Leptomeningeal dissemination of juvenile pilocytic astrocytoma: case report. **Surg Neurol** **41**:318–321, 1994
21. Wallner KE, Gonzales MF, Edwards MSB, et al: Treatment results of juvenile pilocytic astrocytoma. **J Neurosurg** **69**: 171–176, 1988

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