Primary diffuse leptomeningeal oligodendroglioma

Case report

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The authors describe a case of a diffuse primary leptomeningeal oligodendroglioma in a 17-year-old girl who presented with raised intracranial pressure and hydrocephalus. She underwent imaging studies and a left frontotemporal craniotomy that revealed a cystic oligodendroglioma in the suprasellar cistern and spread of neoplastic cells to the spinal leptomeninges. The tumor showed little response to maximum radiotherapy and chemotherapy, and the patient died from complications of high-dose chemotherapy 2 years after diagnosis. Postmortem examination of the brain and spinal cord revealed diffuse meningeal infiltration by neoplastic cells and no evidence of an intraparenchymal origin. Glial heterotopias were noted at several sites along the brain base, adding circumstantial support to the theory that leptomeningeal gliomas are derived from ectopic glial tissue in the subarachnoid space.

KEY WORDS • oligodendroglioma • choristoma • glioma • meningeal tumor • meninges • chemotherapy

Primary leptomeningeal gliomas are rare tumors that grow in the subarachnoid space without an obvious connection to the brain or spinal cord parenchyma. The majority of these neoplasms are astrocytic and their possible origin from heterotopic nests of glial cells in the subarachnoid space has been investigated in previous reports. Widespread dissemination of an oligodendroglioma (“oligodendrogliomatosis”) in the subarachnoid space occurs, but it is usually caused by invasion of the leptomeninges or ventricular system by a primary intraparenchymal oligodendroglioma. In contrast to the well-documented primary leptomeningeal astrocytomas, primary leptomeningeal oligodendrogliomas have rarely been described. Accordingly, this report characterizes the clinical and autopsy features of one of these rare neoplasms.

Case Report

This 17-year-old previously healthy girl presented with a 12-month history of generalized, progressive headache and a 2-month history of nausea. The onset of nausea coincided with transient visual loss (10 to 15 seconds in duration) in the temporal field of the left eye, which occurred several times daily.

Examination. The only finding on neurological examination was bilateral papilledema. No other abnormalities were seen on general examination. Magnetic resonance (MR) imaging of the head revealed hydrocephalus, meningeal enhancement, and a cyst in the suprasellar cistern (Fig. 1 left). Meningeal enhancement was also evident on MR study of the spine (Fig. 1 center and right). The lumbar cerebrospinal fluid (CSF) pressure was raised (opening pressure 30 cm H₂O), the protein was elevated (7749 mg/L), the cell count was normal (leukocytes 2/mm³, red cells 384/mm³), and no neoplastic cells were seen on microscopic examination.

Operation. The patient underwent left frontotemporal craniotomy after placement of a ventriculostomy. A cystic structure was identified in the suprasellar cistern. The capsule of the cyst adhered to the adjacent fibrotic leptomeninges and could not be resected. The cyst contents, which were gray and friable, were removed. No connection was apparent between the cyst and the brain parenchyma.

Pathological Examination. The formalin-fixed surgical specimen was composed of a monomorphic glial neoplasm without areas of necrosis or vascular reactivity (Fig. 2). Glial fibrillary acid protein (GFAP) (polyclonal, 1:500 dilution) was strongly positive in the neoplastic cells.
dose of melphalan (40 mg/m²).

months postoperatively she received a single intravenous weeks between postoperative Months 14 and 19; 20

Left: old girl with a primary leptomeningeal oligodendroglioma. Right: Sagittal view of the thoracolumbar spine without (center) and with (right) gadolinium administration, showing diffuse meningeal enhancement.

Coronal view of the head after gadolinium administration reveal-

orally, Days 8 to 21), lomustine (110 mg/m² orally, Day 1), and vincristine (1.4 mg/m² per day intravenously, Days 8 and 29 (PCV chemotherapy)); the cycle was repeated after 6 weeks. This treatment was followed by 3620 cGy fractionated craniospinal radiation with a 1800-cGy boost to the suprasellar region. She was asymptomatic for a brief period but her headache worsened significantly in postoperative Month 13. She then received eight cycles of cisplatin (90 mg/m² intravenously, Day 1) and etoposide (VP-16)(150 mg/m² intravenously, Days 2 and 3) every 3

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Postoperative Course. The ventricular drain was re-

mended by the placement of a ventriculoperitoneal shunt. Because the CSF from the shunt reservoir was positive for neoplastic cells and the MR imaging indicated seeding of the spinal leptomeninges, the patient was treated with maximum chemotherapy and radiotherapy. Between postoperative Months 2 and 11 she received two cycles of procarbazine (60 mg/m² per day orally, Days 8 to 21), lomustine (110 mg/m² orally, Day 1), and vincristine (1.4 mg/m² per day intravenously, Days 8 and 29 (PCV chemotherapy)); the cycle was repeated after 6 weeks. This treatment was followed by 3620 cGy fractionated craniospinal radiation with a 1800-cGy boost to the suprasellar region. She was asymptomatic for a brief period but her headache worsened significantly in postoperative Month 13. She then received eight cycles of cisplatin (90 mg/m² intravenously, Day 1) and etoposide (VP-16)(150 mg/m² intravenously, Days 2 and 3) every 3 weeks between postoperative Months 14 and 19; 20 months postoperatively she received a single intravenous dose of melphalan (40 mg/m²).

During this rigorous treatment and despite continuing headaches, she functioned remarkably well and continued to attend classes at a university. However, her surveillance computerized tomography (CT) and MR studies showed persisting suprasellar and spinal enhancement, and the CSF repeatedly contained neoplastic cells. In view of the continued tumor growth she then received high-dose thio-

tepa (900 mg/m² over a 3-day period) in postoperative Month 25, which was followed by an autologous bone marrow transplantation. This treatment, however, was complicated by chest infection, adult respiratory distress syndrome, and thrombocytopenia. She died of a massive pulmonary hemorrhage 6 weeks after her last course of chemotherapy and 26 months after her initial presentation.

Autopsy Findings. The general autopsy showed pul-

monary hemorrhage; severe bronchopneumonia; sterile bacterial and viral lung cultures; peritoneal and pleural effusions; numerous petechial hemorrhages in the heart, bronchus, pancreas, and bladder; and infarcts of the spleen and left kidney.

The brain weighed 1360 g. Routine coronal (hemispheres) and horizontal (brainstem and cerebellum en bloc, spinal cord) slices were inspected. The basal meninges adjacent to the optic chiasm, tuber cinereum, mammillary bodies, and interpeduncular fossa were markedly thickened to 2 cm, opacified, and hemorrhagic (Fig. 3). A similar process affected the meninges around the pons, caudal cerebellum, and dorsal aspect of the spinal cord. The cerebral aqueduct and rostral fourth ventricle were lined with but not occluded by gelatinous gray material. The foramina of Magendie and Luschka were patent. The proximal end of the ventriculoperitoneal shunt tubing was correctly positioned in the right lateral ventricle; there was no hydrocephalus. The tissue slices were cut into thinner slices, 2- to 3-mm thick, but no gross evidence was found of focal disruption of the pial or ventricular surfaces to suggest a primary intraparenchymal source. No other central nervous system abnormalities were noted.

Multiple sections of the entire brain base and representa-

tive sections of the hemispheres, brainstem, and spinal cord were submitted for microscopic examination. The sections were stained with hematoxylin and eosin and solochrome; selected additional sections were also stained with hematoxylin and eosin alone or immunohistochemically for GFAP (polyclonal, dilution 1:500), vimentin (monoclonal, dilution 1:25), synaptophysin (polyclonal, dilution 1:250) (Dako Corp., Carpenteria, CA) and neurofilaments (68 kD–200 kD, monoclonal, prediluted; Diagnostic Products Corp., Los Angeles, CA).

The basilar meninges were fibrotic and showed mild chronic inflammation. The thickened meninges also contained numerous small collections of well-differentiated oligodendroglioma cells (Fig. 4 left) whose pattern of GFAP labeling was identical to that of the resected neo-

J. Neurosurg. / Volume 83 / October, 1995

FIG. 1. Magnetic resonance T₁-weighted images in a 17-year-old girl with a primary leptomeningeal oligodendroglioma. Left: Coronal view of the head after gadolinium administration revealing a cystic, enhancing mass in the suprasellar cistern. Center and Right: Sagittal view of the thoracolumbar spine without (center) and with (right) gadolinium administration, showing diffuse meningeal enhancement.

FIG. 2. Photomicrograph from the resected neoplasm showing the characteristic features of an oligodendroglioma, including marked perinuclear cytoplasmic vacuolation and monotonous rounded nuclei. H & E, original magnification × 270.
The tumor cells showed no immunolabeling with vimentin and the neural markers, synaptophysin and neurofilament. Tumor cells were found in the inferior horn of the right lateral ventricle, cerebral aqueduct, and fourth ventricle. Although the spinal leptomeninges were densely fibrotic, intraspinal tumor cells were restricted to the subarachnoid space around the cauda equina. An intraparenchymal origin of, or invasion by, the neoplasm was not found in any of the numerous basilar, brainstem, and spinal cord sections. Numerous heterotopic neuroglial excrescences and nests were present in the basilar meninges (Fig. 4 right). Many of the leptomeningeal blood vessels showed thickened and hyalinized walls, consistent with the effects of radiation.

Discussion

A patient with a diffuse primary meningeal glioma has been described who presented with signs and symptoms of raised intracranial pressure that were attributable to growth of the neoplasm in the cranial and spinal leptomeninges. The monomorphic appearance of the cells and their limited pattern of GFAP immunolabeling were highly characteristic of an oligodendroglioma. Because most of the tumor was in the basilar meninges at presentation, it is assumed, but difficult to prove, that the spinal deposits originated from this site and traveled caudally in the CSF. The presence of tumor in the fourth and lateral ventricle may be explained by retrograde flow of CSF through the foramina of Magendie and Luschka as a result of the ventriculoperitoneal shunt.

Most reported cases of primary meningeal gliomas are astrocytomas or glioblastomas, which are either well localized and amenable to surgical excision or diffuse, unresectable, and eventually fatal; the present case is unusual in that it is a primary diffuse leptomeningeal oligodendroglioma.

A frequent criticism of any report of an apparent primary diffuse leptomeningeal glioma is that a small intraparenchymal source of the tumor has been overlooked. The minimum requirement for accepting a leptomeningeal origin in a glioma is a postmortem examination of the fixed spinal cord and brain, naked-eye examination of thin slices through the entire neuraxis, the submission and examination of sections from any areas in which there is even a hint of pial disruption by the tumor, and the exclusion of any case in which the pia or ependyma is breached by the neoplasm. If all of these requirements are met, as they have been in the present case, there is reasonable evidence that the glioma is a primary leptomeningeal neoplasm. Two other published cases of apparent primary diffuse leptomeningeal oligodendrogliomas have been described. In one, there was “invasion” of the right temporal lobe and the spinal cord was not examined; consequently, the suspicion remains that the neo-
plasm may have emerged from the temporal lobe, or a primary intraparenchymal spinal cord oligodendroglioma may have seeded the subarachnoid space. In the second case invasion of the brain was restricted to the perivascular spaces.20

“Leptomeningeal glial heterotopias” have been favored as the origin of primary leptomeningeal gliomas by many authors,6,7,9,13,14,18,22 based on light microscopic and ultrastructural similarities between the tumors and the heterotopias.1,6,7,14 These usually microscopic congenital anomalies occur in the subarachnoid space of approximately 1% of normal individuals and 25% of patients with congenital malformations.7 They originate as protrusions from the brain or spinal cord and are composed predominantly of astrocytes, but oligodendrocytes and ependymal cells are also found.7 However, heterotopic glial nests were not found in any of the previously reported cases of primary leptomeningeal gliomas. The coexistence in our patient of two rare phenomena in the basilar meninges, an oligodendroglioma and numerous glial heterotopias, may be more than coincidental and, at least, adds to the circumstantial evidence supporting the theory that meningeal gliomas are derived from leptomeningeal glial heterotopias.

Although microscopic examination of the oligodendroglioma did not reveal anaplastic features, its enhancement on CT and MR studies suggested, by analogy with hemispheric oligodendrogliomas, that it might be clinically aggressive,5 which is also to be expected with diffuse growth of a glioma in the leptomeninges. Accordingly, the patient was treated with maximum chemotherapy and radiotherapy; PCV was chosen as first-line chemotherapy because the former is frequently effective in aggressive oligodendroglioma6 and oligoastrocytomas.11 When this course of treatment failed, etoposide and cisplatin were chosen as second-line drugs; third-line chemotherapy consisted of melphalan because 55% of anaplastic oligodendrogliomas appear to show a response to this drug.3 With continued tumor growth, indicated by neuroimaging and tumor-positive CSF cytology, high-dose thiopeta with autologous bone marrow rescue was used in light of the recurrent oligodendrogliomas and mixed oligodendroglioma-astrocytomas with PCV chemotherapy. J Neurosurg 101:16–29, 1951

Conclusion

A case of a primary leptomeningeal oligodendroglioma has been reported that may have originated from coexisting leptomeningeal glial heterotopia. The neoplasm was resistant to maximum chemotherapy and craniospinal radiotherapy, and the patient died with autopsy evidence of residual tumor 3 years after the onset of her symptoms and 2 years after diagnosis.

References


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