Diffuse form of primary leptomeningeal gliomatosis

Case report

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Primary leptomeningeal gliomatosis is rare, and the diffuse form is even rarer with only three cases reported in the literature. A fourth case is described in this report. Computerized tomography (CT) findings showed hydrocephalus with enhancement of the cerebral cisterns, and analysis of cerebrospinal fluid obtained by lumbar puncture showed many atypical cells. Based on these findings, a diagnosis of leptomeningeal tumor was made. There was some improvement in neurological and CT findings following radiotherapy and chemotherapy.

KEY WORDS - leptomeningeal gliomatosis □9 glioma □9 astrocytoma

THE diffuse form of primary leptomeningeal gliomatosis, in which glioma cells extend diffusely outside the parenchyma over a wide area of the central nervous system, is rare. Only three cases have previously been reported. The diagnosis of this condition can be difficult since few, if any, characteristic symptoms or laboratory findings have been identified. A fourth case of the diffuse form of primary leptomeningeal gliomatosis with some interesting computerized tomography (CT) findings is reported.

Case Report

This 15-year-old girl began to have occipital headaches in May, 1978, which gradually worsened. Approximately 1 year later, in June, 1979, she developed nausea and vomiting with progressive unsteadiness of her gait. She was admitted to our clinic on September 21, 1979.

Examination. On admission, general examination revealed no abnormalities. Neurological examination showed the patient to be alert with no motor or sensory disturbance, except for an unsteady gait, nystagmus on lateral gaze, an upward gaze palsy, and bilateral papilledema. Skull x-ray films revealed a slightly enlarged sella turcica and erosion of the posterior clinoid processes.

A plain CT scan showed symmetrical enlargement of the lateral ventricle and dilatation of the third ventricle (Fig. 1 upper). With contrast enhancement, diffuse bilateral enhancement of the cisterns was seen. No enhancement was seen within the brain or ventricles (Fig. 1 lower). Cerebral angiography revealed a vascular abnormality comprised of many fine vessels at the base of the brain. Cerebrospinal fluid (CSF) obtained from the lateral ventricle at the time of a shunt operation on September 26 was clear with two or three cells, a protein level of 10 mg/dl, and a glucose level of 68 mg/ml. No abnormal cells were seen. On October 6, CSF obtained by lumbar puncture showed xanthochromia, with a protein level of 99 mg/dl, a glucose level of 79 mg/ml, and many atypical cells.

Clinical Course. On the basis of these findings, a diagnosis was made of meningeal tumor extending widely over the surface of the brain. Subsequently, the patient's level of consciousness decreased, and tetraparesis appeared and worsened. She was given a daily intrathecal infusion of 20 mg ACNU (1-(4-amino-2-methylpyrimidine-5-yl)-methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride) to a total of 220 mg. From the 8th day of ACNU treatment, her level of consciousness and motor function improved. At this time, the CT enhancement of the cisterns decreased slightly. Two weeks following completion of ACNU treatment, however, the tetraparesis worsened and the cisternal enhancement became distinct.
Symptoms gradually improved again after the patient received irradiation with cobalt-60, 6000 rads, to the whole brain. At that time, CT showed a slight decrease in the enhancement effect. Irradiation of the spinal cord had also been planned, but was not instituted due to leukocytopenia.

The patient remained unchanged neurologically for approximately 1 year. In May, 1981, however, she became mute, her level of consciousness gradually declined, and she died from pneumonia on November 13, 1981. The entire course was 3 years and 6 months. A CT scan taken approximately 1 month prior to her death showed virtually no change in the enhancement of the cisterns.

Postmortem Examination. Systemic autopsy was undertaken 2 hours after death. The leptomeninges of the entire cerebrum and cerebellum were thickened, with a brown discoloration. At the sites where there had been enhancement on the CT scans, thickening of the leptomeninges was particularly notable. At the base of the brain and around the brain stem, particularly near the midbrain, a maximum thickness of 10 mm was found (Fig. 2 upper). The third and lateral ventricles were enlarged and filled with bloody CSF. There was no tumor within the brain parenchyma.

The surface of the spinal cord was diffusely brown with hemorrhage evident on the surface below the thoracic spinal region (Fig. 2 lower). Within the parenchyma of the spinal cord, no macroscopic evidence of tumor was found. Other than bronchopneumonia of the right lung, no abnormalities were identified in other organs.

Histopathologically, atypical cells were found to have infiltrated diffusely into the leptomeninges, and neovascularization was also evident in some areas. These cells had round hyperchromatic nuclei. The cytoplasm was relatively rich, with astrocytic processes. Mitoses were not seen, but there were many macrophages filled with hemosiderin. These atypical cells were confined to the leptomeninges and had not significantly infiltrated the parenchyma of the brain or the spinal cord, or the ventricular walls (Fig. 3). Glial fibrillary acidic protein (GFAP) staining of the cytoplasm and processes of the tumor cells, using an enzymatic immunoassay technique, was positive. Based on these findings, a final diagnosis of primary leptomeningeal gliomatosis (astrocytoma grade II) was made.

Fig. 1. Plain (upper) and contrast-enhanced (lower) computerized tomography scans obtained at the time of admission showing hydrocephalus and diffuse enhancement in the basal cistern.
Diffuse leptomeningeal gliomatosis

Discussion

Secondary leptomeningeal gliomatosis, in which a glioma of the brain or spinal cord infiltrates the leptomeninges, has frequently been reported.\(^2,4,5,8,12,16\) It is said that such lesions account for approximately 20% of malignant gliomas examined at autopsy.\(^6\) In contrast, primary leptomeningeal gliomatosis, which is thought to arise from heterotopic neuroglial tissue of the leptomeninges,\(^3,6\) is rare. A total of only 16 such cases have been reported\(^1,3,5,7,9-11,14,15\) (Table 1). Of these 16 cases, 13 were so-called "solitary tumors" developing as limited tumor masses. Only three cases have been reported of the diffuse form, in which the tumor developed extensively along the leptomeninges, as in our case.

In order to make a diagnosis of primary leptomeningeal gliomatosis, it is necessary to confirm that the tumor is not present within the parenchyma of the brain and spinal cord. In addition, macroscopic and histopathological findings must show that the tumor proliferating in the leptomeninges is, histologically, a glioma. It is therefore required that autopsy of the entire central nervous system be performed for definitive diagnosis.\(^13\) In our case, these criteria were met.

In the solitary form of primary leptomeningeal gliomatosis, clinical symptoms consist predominantly of various focal signs.\(^1,3,7,10,14\) In the diffuse form, focal signs are not characteristic, while convulsions, increased intracranial pressure, delirium, confusion, and various other psychiatric symptoms are common. Thus, diagnosis may be extremely difficult, and patients are often believed to have tuberculous or aseptic meningitis until the presence of the tumor is confirmed at autopsy.\(^9,11,15\)

In our case, the CSF findings were important in the diagnosis since tumor cells were discovered in the CSF obtained by lumbar puncture. In the previously reported cases, no tumor cells were found. The CT findings in the diffuse form of primary leptomeningeal gliomatosis have been reported in only one patient.\(^9\) In that report, the only abnormal finding was hydrocephalus on the plain CT scan; no abnormalities were seen with contrast enhancement. In our case, in addition to hydrocephalus on plain CT scanning, the contrast-enhanced...
TABLE 1
Summary of 17 reported cases of primary leptomeningeal gliomatosis*

<table>
<thead>
<tr>
<th>Authors, Year</th>
<th>Age (yrs), Sex</th>
<th>Location</th>
<th>Type</th>
<th>Symptoms</th>
<th>CT Scan Finding</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bailey, 1936</td>
<td>39, M</td>
<td>lt frontoparietal</td>
<td>solitary</td>
<td>convulsion, aphasia</td>
<td>—</td>
<td>astrocytoma</td>
</tr>
<tr>
<td>Cooper, et al., 1951</td>
<td>40, F</td>
<td>T-2</td>
<td>solitary</td>
<td>back pain, paraplegia</td>
<td>—</td>
<td>ependymoma grade I</td>
</tr>
<tr>
<td></td>
<td>32, M</td>
<td>T10-L5</td>
<td>solitary</td>
<td>low-back pain, paraplegia</td>
<td>—</td>
<td>astrocytoma grade II</td>
</tr>
<tr>
<td></td>
<td>48, M</td>
<td>conus medullaris, cauda equina</td>
<td>solitary</td>
<td>pain of lower limbs</td>
<td>—</td>
<td>fibrillary astrocytoma</td>
</tr>
<tr>
<td>Abbott &amp; Glass, 1955</td>
<td>18, F</td>
<td>L-3 &amp; conus medullaris</td>
<td>solitary</td>
<td>bilateral sciatica</td>
<td>—</td>
<td>ependymoma grade I</td>
</tr>
<tr>
<td>Korein, et al., 1957</td>
<td>43, F</td>
<td>rt cerebral hemisphere</td>
<td>solitary</td>
<td>convulsion, pt hemiparesis</td>
<td>—</td>
<td>astrocytoma grade II</td>
</tr>
<tr>
<td>Daum, et al., 1963</td>
<td>36, F</td>
<td>lt Sylvian fissure</td>
<td>solitary</td>
<td>convulsion, rt hemiparesis</td>
<td>—</td>
<td>astroblastoma</td>
</tr>
<tr>
<td></td>
<td>39, M</td>
<td>lt Sylvian fissure</td>
<td>solitary</td>
<td>homonymous hemianopsia</td>
<td>—</td>
<td>oligodendroglioma</td>
</tr>
<tr>
<td></td>
<td>37, F</td>
<td>rt frontoparietal</td>
<td>solitary</td>
<td>convulsion, pt hemiplegia</td>
<td>—</td>
<td>glioblastoma multiforme</td>
</tr>
<tr>
<td></td>
<td>41, M</td>
<td>lt frontal</td>
<td>solitary</td>
<td>rt hemiplegia</td>
<td>—</td>
<td>glioblastoma multiforme</td>
</tr>
<tr>
<td>Sumi &amp; Leffman, 1968</td>
<td>32, M</td>
<td>rt frontal</td>
<td>solitary</td>
<td>convulsion</td>
<td>—</td>
<td>oligodendroglioma</td>
</tr>
<tr>
<td></td>
<td>61, M</td>
<td>cerebral hemispheres &amp; base of brain</td>
<td>solitary</td>
<td>hallucination, confusion, visual disturbance, convulsion, weakness of pt leg</td>
<td>—</td>
<td>astrocytoma</td>
</tr>
<tr>
<td>Scully, et al., 1978</td>
<td>57, F</td>
<td>C8-T2</td>
<td>solitary</td>
<td>lt arm pain</td>
<td>brain atrophy</td>
<td>mixed astrocytoma &amp; ependymoma</td>
</tr>
<tr>
<td>Horoupian, et al., 1979</td>
<td>49, F</td>
<td>rt frontoparietal</td>
<td>solitary</td>
<td>convulsion, pt hemiplegia</td>
<td>contrast-enhanced mass</td>
<td>astrocytoma</td>
</tr>
<tr>
<td>Ho, et al., 1981</td>
<td>55, M</td>
<td>whole brain &amp; spinal cord</td>
<td>diffuse</td>
<td>confusion, dizziness, blurred vision, occipital pain</td>
<td>hydrocephalus</td>
<td>astrocytoma</td>
</tr>
<tr>
<td>Kitahara, et al., 1985</td>
<td>15, F</td>
<td>whole brain &amp; spinal cord</td>
<td>diffuse</td>
<td>hydrocephalus, enhancement in cisterns</td>
<td>—</td>
<td>astrocytoma grade II</td>
</tr>
</tbody>
</table>

* CT = computerized tomography.

enhanced CT scan showed widespread enhancement of the subarachnoid space. These findings remained virtually unchanged throughout the course of the disease.

Due to the fact that the leptomeningeal gliomatosis was not diagnosed during life in the three previously reported cases, no therapy other than a shunt operation for the hydrocephalus was undertaken. Death followed shortly after admission (5 weeks, 2 months, and 18 months). In contrast, based upon a correct diagnosis in our case, radiotherapy and chemotherapy were performed, and some improvement, although transient, was observed in the level of consciousness and the tetraparesis, with a slight decrease in the enhancement on CT scanning.

References
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...ingeval astrocytoma mimicking a meningioma. Arch Pathol Lab Med 103:676–679, 1979

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