Primary Diffuse Leptomeningeal Gliomatosis: Report of a Case Presenting with Chronic Meningitis

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Neoplastic meningitis occurs in approximately 5% of patients with cancer. Primary diffuse leptomeningeal gliomatosis is a rare condition whereby a glioma arises from heterotopic cell nests in the leptomeninges. We report here a case presenting with clinical features similar to those of chronic infectious meningitis without positive cerebrospinal fluid cytology. Neurological signs in our patient deteriorated progressively without responding to antitubercular, antiviral, or antibiotic therapy. Leptomeningeal biopsy sampling revealed the condition to be primary diffuse leptomeningeal gliomatosis.

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Neoplastic meningitis is diagnosed in up to 15% of patients with non-central-nervous-system primary cancers and 1~2% of patients with primary brain tumors.¹ Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare fatal condition that is characterized by a glioma from heterotopic cell nests in the leptomeninges, in which the cells infiltrate the meninges in the absence of an intraparenchymal tumor.³

Diagnosis of PDLG requires the fulfillment of three criteria: (1) no attachment of the tumor to the brain parenchyma, (2) no evidence of intra-axial lesions, and (3) the presence of leptomeningeal encapsulation of the tumor.²

Only 30 cases of PDLG have been reported,⁵ and only

1 of those cases had a positive cytology,⁴ suggesting that negative cerebrospinal fluid (CSF) cytology is common. We report here the first case of PDLG in Korea, which presented clinical features similar to those of chronic infectious meningitis.

CASE REPORT

A 22-year-old military officer was transferred to our hospital in a comatose condition and with progressive hydrocephalus that had developed 6 months before. Until 6 months before his first admission to hospital, the patient was in good health, but then several episodes of generalized tonic seizures occurred and he became

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stuporous and developed a fever above 38°C. An initial brain computed tomography (CT) scan taken at that time was not remarkable. CSF analysis revealed an opening pressure of 27 cm H₂O, pale yellow color, pleocytosis with 12 lymphocytes/mm³, and protein and glucose levels of 11350 mg/L and 10 mg/L, respectively. The following CSF investigations all produced negative results: bacterial culture, acid-fast blue staining, polymerase chain reaction for tuberculosis, varicella zoster, and herpes simplex, India ink staining, fungus culture, and viral culture. CSF cytology revealed many lymphocytes with a few atypical, insignificant lymphocytes. Following an initial diagnosis of viral or tuberculous meningoencephalitis, acyclovir and antitubercular medicine, including intravenous dexamethasone, were administered empirically. Despite this, the patient's intracranial pressure continued to increase, his mentality worsened, and he became comatose.

He was transferred to our hospital for further evaluation and treatment. On neurological examination it

was noted that his vestibulo-ocular reflex was impaired bilaterally. All four limbs extended in response to painful stimuli, with bilateral extensor toe signs. There was a severe neck stiffness. Brain magnetic resonance imaging (MRI) performed at 8 months after symptom onset revealed severe hydrocephalus and strongly enhanced leptomeninges with a leptomeningeal-enhancing nodular mass above the corpus callosum (Fig. 1).

Extraventricular drainage was performed to decrease the intracranial pressure and a leptomeningeal biopsy procedure was carried out by open craniotomy. Subsequent histopathological investigations revealed a marked hypercellularity and nuclear pleomorphism with geographic pseudopalisading necrosis (Fig. 2). There was no infiltration in the adjacent brain parenchyma, which confirmed the diagnosis of leptomeningeal glioblastomatosis.

His condition deteriorated progressively in spite of medical treatments, and the patient died due to brain herniation 9 months after symptom onset.

Figure 1. T1-weighted axial and sagittal brain MRI. There was extensive hydrocephalus and marked thickening of the meninges with prominent gadolinium enhancement, and a leptomeningeal-enhancing nodular mass above the corpus callosum.

Figure 2. Biopsy of the leptomeningeal mass above the corpus callosum. (A) Hematoxylin-eosin-stained meningeal tumor with marked hypercellularity, nuclear pleomorphism, geographic pseudopalisading necrosis, and venous endothelial hyperplasia ($\times 100$). (B) Positive glial fibrillary acidic protein staining of the tumor cells ($\times 200$).

DISCUSSION

The clinical manifestations in our patient resembled chronic infectious meningitis with negative CSF cytology, such as tuberculous meningitis or fungal meningitis.

Neoplastic meningitis is diagnosed in 4~15% of patients with solid tumors (carcinomatous meningitis), 5~15% of patients with leukemia and lymphoma (leukemic or lymphomatous meningitis), and 1~2% of patients with primary brain tumors.¹ The present patient had a leptomeningeal irritation sign, and the CSF study and brain MRI were compatible with the diagnosis of chronic infectious meningitis. However, his medical status deteriorated in spite of antibiotic and steroid therapy. A brain MRI revealed a leptomeningeal mass in the subarachnoid space above the corpus callosal area, and biopsy sampling confirmed the diagnosis of PDLG.

PDLG is a fatal primary brain tumor with malignant glial cell infiltration in the meninges without the presence of an intraparenchymal tumor.³ This patient met the three conditions of diagnostic criteria compatible with PDLG. This condition is usually confirmed only at postmortem during an autopsy. We performed a biopsy procedure, which revealed no involvement of the brain

parenchyma adjacent to the tumor, and this finding provided evidence that malignant glial cells were present only in the CSF space. That there was no invasion of the brain parenchyma was confirmed by brain MRI. A limitation of our report is that we did not perform an autopsy to confirm our diagnosis unequivocally.

According to a review of 15 previously reported PDLG cases, frequent symptoms of PLDG are intracranial hypertension (44%), cranial nerve palsies (56%), meningism (44%), and seizures (44%).³ Initial CT scan findings are frequently unremarkable except for ventricular dilatation, and the most common MRI finding is a leptomeningeal enhancement.³ With respect to CSF cytology, previous reports suggest that patients with secondary meningeal gliomatosis often have tumor cells, but that negative cytology seems to be a common finding in PDLG, and only 1 of 24 cases on record had a positive cytology.⁴ Our patient experienced increased intracranial pressure and a seizure at the onset of disease development. MRI revealed only dural enhancement and hydrocephalus with negative CSF cytology, which were similar to other reported cases.

In conclusion, we report here a case of a PLDG, which can be considered as a differential diagnosis for chronic infectious meningitis of unknown origin, and is intractable to the medical treatment.

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