Primary leptomeningeal sarcomatosis

Case report

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This report describes a case of primary leptomeningeal sarcomatosis in a 50-year-old man who presented with progressive deficits involving multiple cranial nerves and spinal roots. Despite the clinical evidence supporting a diffuse process involving the leptomeninges, radiological, serological, and cerebrospinal fluid examinations failed to reveal the cause of the disorder. Consequently, surgical exploration and biopsy were required to obtain a pathological diagnosis. This case report illustrates the difficulty in diagnosing this disease and supports the use of open biopsy in patients with chronic meningeal disease when the diagnosis cannot be established by less invasive methods.

KEY WORDS • primary leptomeningeal sarcomatosis • sarcoma • meningeal tumor • chronic meningitis

Primary leptomeningeal sarcomatosis (PLS) is a rare malignant neoplasm that arises from and diffusely infiltrates the leptomeninges without forming large discrete tumor masses. As with other diseases that diffusely involve the meninges, PLS can produce variable clinical syndromes that resemble a variety of diseases including chronic infection, metastatic tumor, primary tumor, and sarcoidosis. Despite the use of high-resolution radiological imaging and cerebrospinal fluid (CSF) examinations, the ante-mortem diagnosis of PLS often remains elusive. Consequently, surgical exploration and biopsy of the leptomeninges are frequently required to obtain the pathological diagnosis. There is insufficient information regarding the efficacy of radiation and chemotherapy to determine the optimal treatment for this disease. The management of a patient with PLS prompted this report and review of the literature.

Case Report

This 50-year-old right-handed man was healthy until he developed a mild progressive hearing deficit 9 months prior to admission to the Yale-New Haven Hospital. He first sought medical attention 8 months before admission for the onset of right-sided focal motor seizures which occurred two to three times per day and responded well to phenytoin therapy. Four months prior to this admission, the patient was admitted to another hospital with intermittent delusions and hallucinations, acute bilateral visual loss, and marked auditory deterioration. He also complained of diffuse headache, intermittent nausea and vomiting, and mild left leg weakness. At that time, his general physical examination was unremarkable. His neurological examination was significant for the presence of bilateral dense scotomata, a left Marcus-Gunn pupil, mild bilateral abducens paresis, sensorineural deafness (total on the right and 50% on the left), and mild left leg weakness with normal reflexes and plantar responses. An extensive evaluation revealed the following: 1) stage I chronic lymphocytic leukemia (CLL); 2) an increased CSF protein level (133 to 166 mg/100 ml); and 3) normal radiographic studies of the head, including computerized tomography (CT) with and without administration of contrast material. The cause of the neurological signs and symptoms could not be determined, and he was discharged. The patient's condition continued to deteriorate over the next several months and he was admitted to our institution for further evaluation.
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Examination. On examination, the patient's higher cortical functions were preserved. Neuro-ophthalmological examination showed a moderate increase in his central scotomata, while the left Marcus-Gunn pupil and bilateral abducens paresis were unchanged. The fundi were normal except for mild optic disc pallor. An audiogram and brain-stem auditory evoked responses documented a total hearing loss on the right side and a 50% hearing loss on the left. The remaining cranial nerves were normal. With the exception of a mild distal left leg weakness, the motor and sensory examination in the limbs was normal. The reflexes were normal and there was no evidence of myelopathy or cerebellar dysfunction.

Multiple lumbar punctures revealed an opening pressure between 450 and 550 mm H:O. The CSF consistently showed a mildly increased protein level (50 to 80 mg/100 ml), a normal glucose content, and no pleocytosis. Studies for infectious agents, multiple sclerosis, and neoplastic cells were negative. Routine blood and serological studies were normal except for a mild peripheral leukocytosis related to his stage I CLL. Special studies for vasculitis, paraproteins, cryoglobulins, and blood viscosity were also within normal limits. Radiographic studies, including plain skull films, polytomograms of the skull base, high-resolution axial and coronal CT scans of the head with and without intravenous contrast material, and complete cerebral angiograms, were all normal. Magnetic resonance (MR) studies of the brain showed only a diffuse increase in the periventricular signal on T2-weighted images consistent with communicating hydrocephalus. Metrizamide myelography of the entire spine followed by selective CT scans showed irregular thickening of multiple roots of the cauda equina, especially of the lower lumbar and sacral roots. In the 2nd week of hospitalization, a lumbarperitoneal shunt with an 80-mm H2O pressure valve and filter was placed without subsequent improvement in the patient's symptoms or signs.

Operation. Since these studies did not reveal a diagnosis, an open biopsy was performed through a right frontotemporal craniotomy. The dura, leptomeninges, and cortex over the lateral aspect of the brain appeared normal. As the suprasellar region was approached by elevating the frontal and temporal lobes, the basilar arachnoid was found to be milky-white, thickened, and densely adherent. Further dissection revealed the entire suprasellar area to be involved with the abnormal tissue. The optic nerves appeared normal but the inferior aspect of the chiasm was swollen. Multiple biopsies were taken, one of which included the most severely involved portion of the chiasm. The patient had an uneventful postoperative course. Based on the pathological findings, a diagnosis of PLS was made.

Pathological Examination. The lateral cerebral cortex was histologically normal and the underlying white matter showed only mild glial cell proliferation. The optic chiasm and basilar arachnoid biopsies (Fig. 1) were entirely composed of dense interlacing fascicles of cells showing hyperchromatic, ovoid to elongated, medium-sized nuclei, eosinophilic cytoplasm, and ill-defined cell borders. Numerous mitotic figures were present. The neoplastic cells were individually enmeshed by a prominent reticulin network. Immunostaining for glial fibrillary acidic protein was negative, as were special stains for acid-fast bacilli (Ziehl-Neelsen), fungi (Grocott), and bacteria (Brown-Brenn). Based on the histopathology and the gross appearance of the meninges, a diagnosis of PLS was made.

Discussion

In this case, PLS was diagnosed in a middle-aged man who presented with chronic progressive auditory and visual deficits, mild left leg weakness, and intracranial hypertension without ventriculomegaly. The more common causes of a diffuse, indolent, leptomeningeal process include chronic infections (tuberculous, fungal, and syphilitic), metastatic tumors (lymphomas, leukemias, and carcinomas), and sarcoidosis. The diagnosis of stage I CLL in this patient proved to be an incidental finding. Unlike the acute leukemias, CLL very rarely involves the central nervous system (CNS) and then only in the more advanced stages. Primary brain neoplasms such as medulloblastoma, glioma, ependymoma, and primary CNS lymphoma can diffusely infiltrate the meninges and on rare occasions present with chronic meningeal signs. Even rarer causes of diffuse leptomeningeal neoplasia stabilized for 4 months but then rapidly deteriorated, and he died 5 months after the diagnostic biopsy.

Fig. 1. Photomicrograph of a specimen obtained by biopsy of the leptomeninges over the optic chiasm showing sarcomatous changes. H & E, × 125.
are the primary leptomeningeal tumors, which include diffuse meningeal melanoblastosis, gliomatosis, and sarcomatosis.14,5,8

The World Health Organization classification of brain tumors2 separates meningeal sarcomas with a diffuse, leptomeningitis-like pattern (PLS) from discrete forms of meningeal sarcomas. In large series, sarcomas comprise about 1.2% of all intracranial neoplasms, with PLS accounting for approximately 10% of intracranial sarcomas.9,17 The variety of terms that have been used to describe this tumor (primary sarcoma of the leptomeninges, diffuse tumor of the leptomeninges, sarcomatose meninge diffuse primitive, diffuse mesotheloma of the leptomeninges, diffuse meningeal fibroblastoma, diffuse meningiomatosis, meningeal meningiomatosis)6,20-22 stem from the controversy over the embryological origin of the meninges, the rarity of the tumor, and the difficulty in its diagnosis. The inadequacy of histopathological techniques and the fact that most diffuse meningeal tumors are not of meningeal origin led Black and Kernohan to disregard cases reported prior to 1927. Based on the embryological studies of Weed, which suggested that the leptomeninges are of mesodermal origin, most neuropathologists accept the term “primary leptomeningeal sarcomatosis.”

Experimental work suggests the possibility of a viral etiology for PLS. Rabson and Kirschstein15 developed an experimental model of meningeal sarcomatosis by intracerebral injections of polyoma virus into hamsters. Vandepitte and Brucher26 were able to produce the same tumor in rats by intravenous, subcutaneous, or intracerebral inoculation of the same virus.

To date, approximately 57 relatively well-documented cases of PLS have been reported. Some authors claim a male preponderance and a predilection for infants and children.5,8,13 However, others report a more even sex and age distribution.2,5 The clinical course is usually rapid, with most patients dying 1 to 6 months after the onset of symptoms.5,11 The clinical manifestations are variable but can be divided into three clinical categories:1 1) a polyneuropathy form; 2) a cerebral form with symptoms suggestive of a brain tumor; and 3) a spinal form with signs of compressive myelopathy.

Antemortem diagnosis of PLS is difficult. In previous cases, radiographic studies have been nonspecific or negative. Some cases have had myelographic abnormalities similar to our patient.5,13 Computerized tomography scans of the head were performed in the two most recent case reports in the English literature6,11 and, as in this case, did not demonstrate the tumor. To our knowledge, MR imaging has not been previously reported in patients with PLS; however, it also failed to reveal the tumor in this case. The CSF has been abnormal in all cases in which it was examined and typically shows an elevated protein level, a low glucose content, and a variable pleocytosis.5,11 Because these changes are nonspecific, cytological studies are necessary and in some cases highly suggestive of PLS.1,5,6,12,21 As in our case, most of the antemortem diagnoses of PLS have required open biopsy.5,13 While radiation therapy has been the recommended treatment, the limited survival time of patients with PLS makes its efficacy difficult to assess.

References

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