

Primary leptomeningeal oligodendrogliomatosis

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Abstract Primary leptomeningeal oligodendrogliomas (PLOs) are rare intracranial malignancies where tumors grow in the subarachnoid space without an obvious connection to the brain or spinal cord parenchyma. Adding to the three previously reported cases of PLO with no parenchymal involvement we report a fourth case of the same in this paper in a 50-year-old woman presenting with unremitting headaches. CT scan of her head revealed hydrocephalus and MRI revealed diffuse enhancement of her leptomeninges throughout her brain and spine, prominent over the basilar region. Biopsy obtained using a frameless stereotactic biopsy showed sharply defined cell borders, clear cytoplasm, and rounded nuclei consistent with an oligodendroglioma. Our case suggests that PLO can mimic diffuse forms of granulomatous meningitis and should be suspected in patients that clinically and

radiographically present like granulomatous meningitis but without blood or CSF markers for the same.

Keywords Oligodendroglioma · Primary leptomeningeal · Glioma · Basilar meningitis

Introduction

Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare condition where tumors grow in the subarachnoid space without an obvious connection to the brain or spinal cord parenchyma. PDLG is associated with rapid disease progression and mortality. The majority of these neoplasms are astrocytic, often high grade, and the diagnosis is usually made postmortem [1, 2]. Dissemination of oligodendrogliomas in the subarachnoid space (leptomeningeal oligodendrogliomatosis) is usually secondary to invasion of the leptomeninges or ventricular system by a primary intraparenchymal oligodendroglioma [3, 4]. In contrast to the well-documented primary leptomeningeal astrocytomas, primary leptomeningeal oligodendrogliomas (PLO) are rare with only three previously reported cases without parenchymal involvement [5–7]. We report a fourth case of PLO in this paper.

Case report

A 50-year-old woman, with a past medical history of resected cutaneous melanomas, was transferred in from an outside hospital with unremitting headaches. The patient's mental status was normal and she was neurologically intact at presentation with motor, sensory, cranial nerve and cerebellar examination within normal limits. She had a

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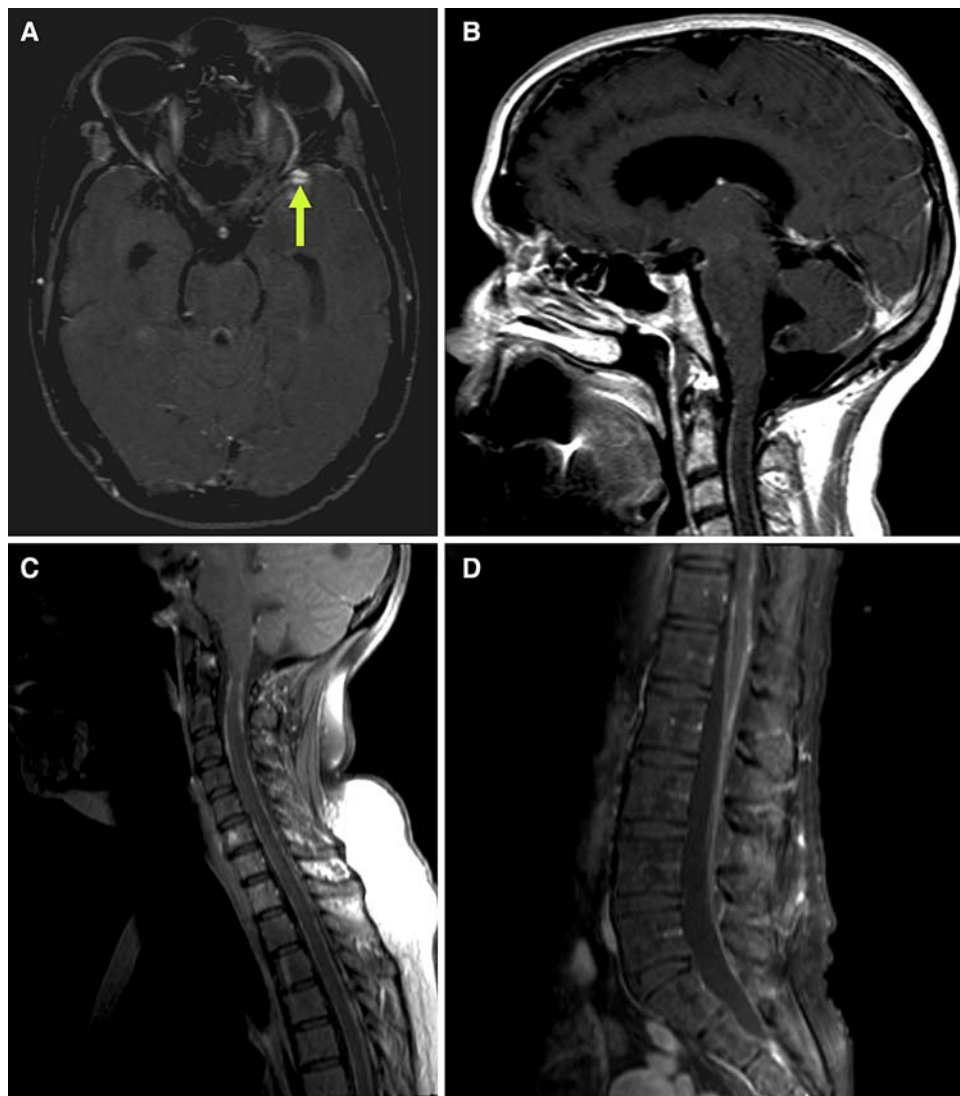
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10-pack-year history of smoking as well as a past medical history of pulmonary *Mycobacterium avium* intracellulare complex (MAC) infection treated with multiple antibiotics. CT scan of her head revealed hydrocephalus and MRI revealed diffuse enhancement of her leptomeninges throughout her brain and spine, prominent over the basilar region (Fig. 1a–d). There was a relatively discrete focus of this extra-axial process involving the left temporal area. Cerebrospinal fluid samples obtained from multiple lumbar punctures and a ventriculostomy were nondiagnostic of the nature of the leptomeningeal process (consistent with previous reports) [5] and showed glucose 50 mg/dL, protein 158 mg/dL, 127 RBCs/mm³, 18 nucleated cells/mm³ (36% lymphocytes, 58% monocytes, and 6% macrophages) with negative gram stain, acid fast bacilli stain and cryptococcal antigen. CSF cultures for bacterial and fungi were negative. Cytologic studies did not reveal a neoplastic

process. A work up with Positron Emission Tomography (PET) and CT scans of the chest, abdomen, and pelvis did not reveal a systemic malignancy. Ultimately the patient underwent a left peritoneal craniotomy and a frameless stereotaxic biopsy of her meningeal process. A ventriculo-peritoneal shunt was placed following which the patient underwent outpatient cranial irradiation and concomitant temozolamide chemotherapy for 42 days. Radiation dose was 3 Gy for the first three treatments then 1.8 Gy for an additional 23 treatments for a total whole brain dose of 50.4 Gy in 26 fractions. Treatments were completed with a 9 Gy “boost” in five fractions using an intensity-modulated radiation therapy (IMRT) technique. She then received three cycles of etoposide chemotherapy for progressive disease. The patient continued to deteriorate clinically and was transferred to hospice care where she expired 4 days later.

Fig. 1 Postcontrast T1 W MRI of brain (a, b), cervical (c) and lumbar (d) spine show diffuse enhancement of her leptomeninges throughout her brain and spine. Arrow in the axial brain image (a), points to the biopsy site



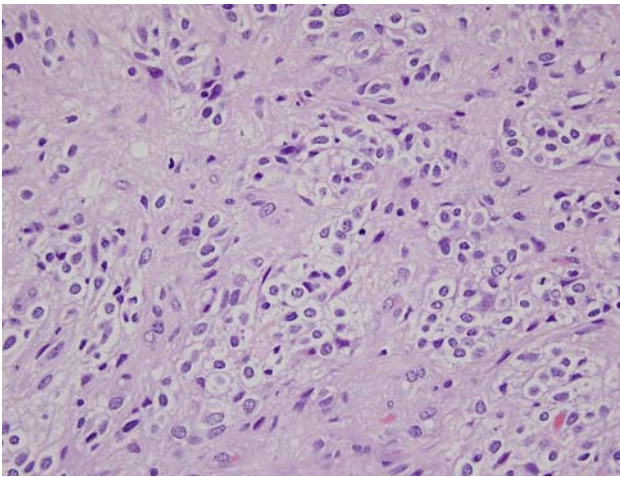


Fig. 2 Hematoxylin-eosin stained biopsy specimen under high magnification shows tumor cells with the sharply defined cell borders, clear cytoplasm, and rounded nuclei

Results

Biopsy findings showed tumor cells with sharply defined cell borders, clear cytoplasm, and rounded nuclei consistent with an oligodendroglioma (Fig. 2). The pathologic specimens were negative for 1p or 19q chromosomal deletions. These findings were present when read at our institution as well as that of a large center where the tissue specimen were sent for histopathologic confirmation. The tissue did not stain with immunohistochemical stains for systemic cancers (such as cytokeratin).

Discussion

The dissemination of parenchymal glial tumors into the leptomeninges has been recognized since the early twentieth century [8]. PDLG by contrast is a rare condition in which a glioma primarily involves the leptomeningeal space without obvious extension into the central nervous system parenchyma. The tumors likely arise from heterotopic nests of glial tissue in the subarachnoid space [9]. Patients with PDLG can present with a variety of clinical symptoms, but the most common presenting symptoms are due to raised intracranial pressure [10].

Cooper and Kernohan in a pathologic study of heterotopic cell rests and leptomeningeal gliomas found no attachment of the extramedullary tumor to the underlying parenchyma, no evidence of a primary neoplastic process within the neuraxis, and many of the tumors were encapsulated by a leptomeningeal sheath [9]. Chen et al. proposed that a diagnosis can only be established after a complete neuroanatomical examination, which includes

postmortem examination of the brain and spinal cord, a gross inspection of representative thin sections from the entire neuraxis, and a microscopic examination of all areas that raise the suspicion of pial disruption during gross examination [7]. These criteria rely on autopsy data to determine a postmortem diagnosis; hence making a clinical diagnosis continues to remain difficult. Due to the non-specific and variable clinical presentation many cases have been diagnosed and managed as tuberculous meningitis with the diagnosis of PDLG made only at late stages or postmortem [1, 2]. Since the characteristic MRI finding is that of a diffuse contrast enhancing process chronic meningitis needs to be ruled out. Therefore, a biopsy is necessary in the work up of the patient. Due to the paucity of reported cases in the literature the optimum treatment plan for PDLG or PLO is unknown. Our decision to use cranial radiation and chemotherapy was empiric after discussion with the patient as well as experts from our and outside institutions.

In contrast to the relatively well-documented primary leptomeningeal astrocytomas, primary leptomeningeal oligodendrogliomas are rare with only three reported isolated leptomeningeal cases with no parenchymal involvement [5–7]. Our case adds to the literature documenting the occurrence and features of PLO. With the definite documentation of intact chromosomes 1 and 19, our case provides insight towards the spectrum of molecular findings associated with this condition, and its prognostic implications with respect to chemotherapy. Since PLO can mimic diffuse forms of granulomatous meningitis, it should be suspected in patients that clinically and radiographically present with symptoms of granulomatous meningitis but without blood or CSF markers for the same. Ultimately the diagnosis rests on obtaining a biopsy and histologic confirmation.

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