Primary diffuse leptomeningeal oligodendrogliomatosis: A case report and literature review

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Abstract

Primary leptomeningeal oligodendrogliomatosis (PLO) is a rare low-grade intracranial and spinal canal subarachnoid neoplasm without an obvious primary neoplasm in the brain or spinal cord parenchyma. We present here the serial progression of radiological findings of this rare disease in a 2-year-old male child whose clinical status deteriorated over a period of 4 months with the main complaint of partial seizures. During this period, the MR findings progressed from mild hydrocephalus with minimal leptomeningeal enhancement to leptomeningeal multiple cystic lesions in the entire neuraxis including the spine.

Key words: Leptomeningeal gliomatosis; low-grade glioma; primary leptomeningeal oligodendrogliomatosis

Introduction

Primary leptomeningeal oligodendrogliomatosis (PLO) is a rare condition which shows near-normal MRI in the early presentation and slowly progresses to mild hydrocephalus with few cysts and leptomeningeal enhancement. Eventually, entire neuraxis is involved with multiple leptomeningeal cysts, progressive hydrocephalus, and pial surface edema. It is postulated that it arises from leptomeningeal heterotopias or already existing small undetected parenchymal primary. Sixteen cases of PLO have been reported in the literature.

Secondary leptomeningeal gliomatosis is a known entity that results from invasion of the subarachnoid space or ventricular system by a primary intraparenchymal glioma. PLO, however, has no obvious parenchymal primary that has been detected.

Chemotherapy and craniospinal radiation have shown good results. So, it is prudent to identify this rare condition in the early stage to initiate the treatment at the earliest.

Case Report

The case reported here is a child who was born by normal vaginal delivery in a tertiary care hospital with uneventful birth history. The child was asymptomatic till 2 years of age when he presented to the hospital with one episode of simple partial seizure, for which an MRI was done in March 2013 [Figure 1]. The MR findings were mildly dilated ventricles with periventricular T2 hyperintensity representing interstitial edema and prominent tiny cysts along the cerebellar folia. The principal diagnosis of neurocysticercosis

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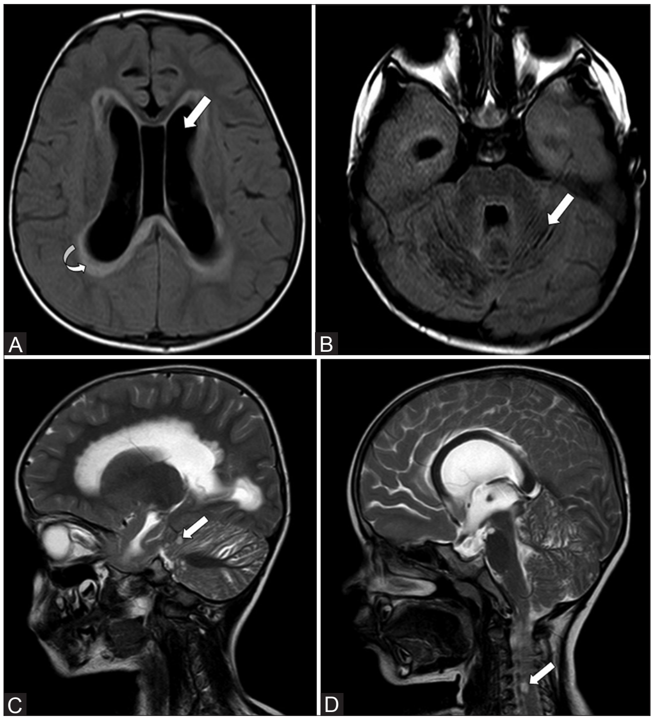

Figure 1(A-D): (A) MRI findings (March 2013) a: T2 FLAIR axial image shows moderate hydrocephalus (straight arrow) with cavum septum pellucidum with periventricular hyperintensity (curved arrow) (B) MRI findings (March 2013): T2 FLAIR axial image shows prominent cerebellar foliae (straight arrow) (C) T2 sagittal image shows few hyperintense cystic lesions in the cerebellum (straight arrow). The cyst appears to be intraparenchymal without perilesional edema (D) T2 sagittal image shows few hyperintense cystic lesions in the upper cervical cord in extra medullary location (straight arrow)

was considered. The child was started on anticonvulsant therapy and albendazole for 7 days. Follow-up MRI after 1 month [Figure 2] showed progressive communicating moderate hydrocephalus with periventricular CSF seepage and diffuse leptomeningeal enhancement along the tentorium, prepontine, quadrigeminal and ambient cisterns, with increase in the number of cerebellar cystic lesions. Tuberculous meningitis with communicating hydrocephalus was considered as the primary diagnosis because of the endemicity. Other differentials included leptomeningeal tumor spread and cysticercal meningitis. CSF analysis was nondiagnostic for the nature of leptomeningeal disease and showed glucose 50 mg/dl, protein 58 mg/dl, 97 RBCs/mm^3, 12 nucleated cells/mm^3 (36% lymphocytes, 58% monocytes, and 6% macrophages) with negative gram stain, acid fast bacilli stain, and cryptococcal antigen. CSF cultures for bacteria and fungi were negative. Cytologic studies did not reveal a neoplastic process. During the course of illness, the child's mother noticed regression of certain previously attained milestones, such as inability to walk and loss of head control. Gradually, the frequency of seizures increased to every 10-12 days. Since the clinical status continued deteriorating, ventriculoperitoneal (VP) shunting was performed to relieve the hydrocephalus. A follow-up

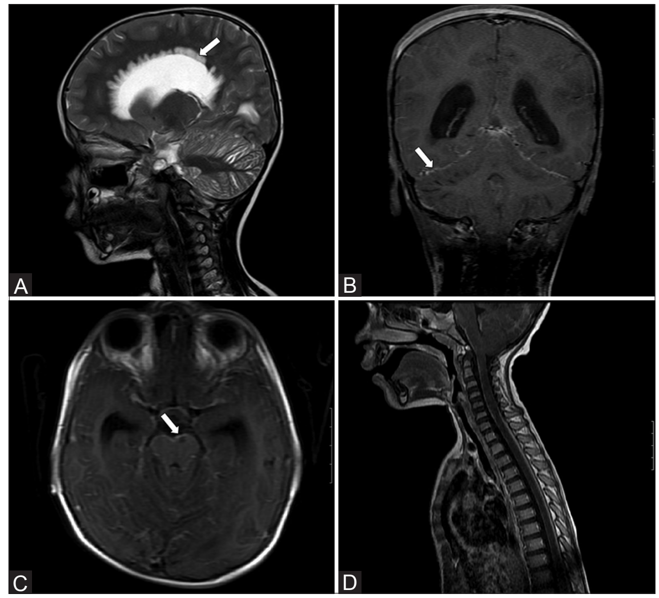

Figure 2(A-D): (A) MRI findings (April 2013): T2 sagittal image shows periventricular white matter hyperintensity (straight arrow) (B) T1-weighted post contrast images show diffuse leptomeningeal enhancement (staright arrow) (C) T1-weighted post contrast images show diffuse leptomeningeal enhancement (staright arrow) (D) MRI spine screening appears relatively normal and is given for comparison with the follow up MRI

contrast MRI brain and spine in June 2013 [Figure 3] showed resolution of hydrocephalus and appearance of multiple new T2-hyperintense small cystic lesions predominantly in the infratentorial region, and also involving the lateral ventricles, cerebral sulci, and the entire spinal canal. MR spectroscopy at TE 135 showed increased lactate and decreased NAA peaks. No significantly elevated choline peak was noted. Leptomeningeal biopsy [Figure 4] showed tumor cells with sharply defined cell borders, clear cytoplasm, and rounded nuclei, consistent with an oligodendroglioma (WHO grade II). The pathologic specimens were negative for 1p or 19q chromosomal deletions, pointing to the diagnosis of PLO. Patient expired despite intensive treatment.

Discussion

In 1954, Moore first described a diffuse form of a primary leptomeningeal astrocytoma (PLA).[1]

Primary diffuse leptomeningeal gliomatosis (PDLG) can be pathologically differentiated into two common types: PLA and PLO. Hence, the term PDLG can be interchangeably used with PLA or PLO. Compared to PLA, the incidence of PLO is very rare.[2-4] Radiologically, these two entities cannot be differentiated. Uncommonly, PDLG has been considered consistent with ganglioglioma and ependymoblastoma.[2,5] Histopathological type of PDLG has no significant prognostic importance and no treatment has proved successful.

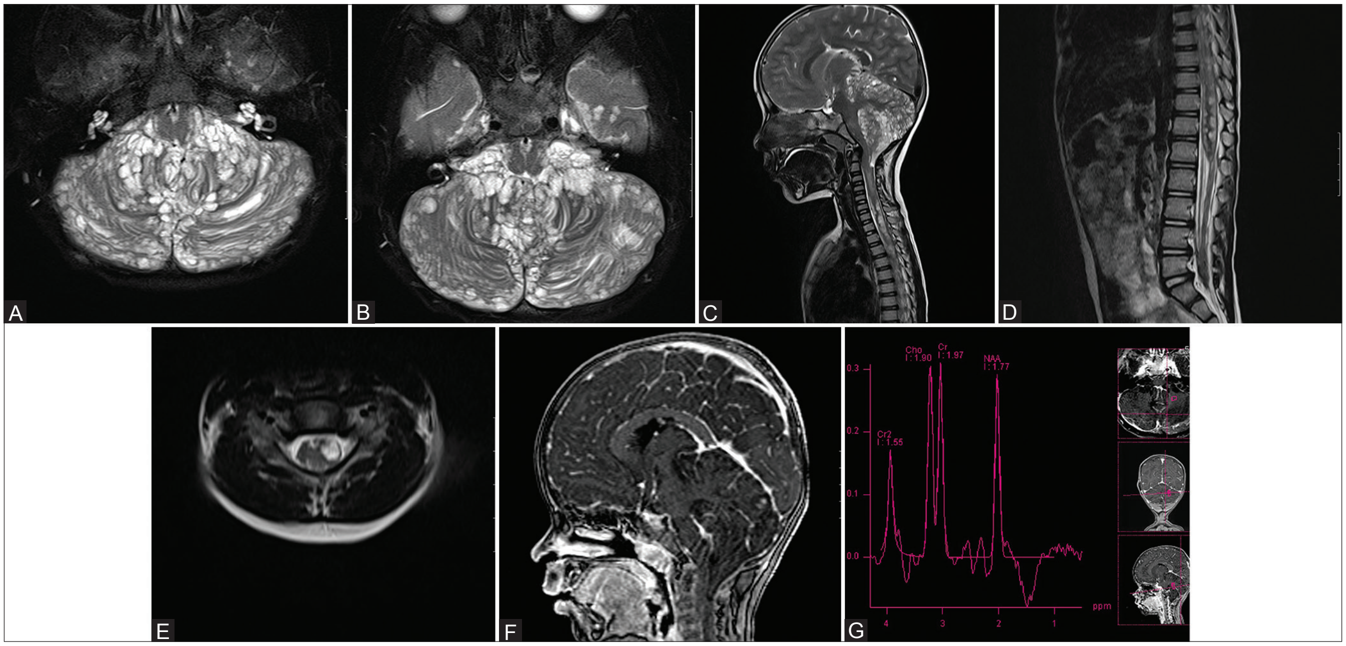

Figure 3(A-G): MRI findings (June 2013) (A-D): T2 axial and sagittal images show diffuse T2 hyperintense small cystic lesions more in the basilar region and cerebellar foliae and also involving the lateral ventricles, cerebral sulci and spinal cord extending upto the conus medullaris. (E) T2 axial image of the spinal cord shows the leptomeningeal cysts at the surface of the spinal cord. (F) T2 FLAIR sagittal image shows the cystic lesions are completely suppressible. (G) MR Spectroscopy at TE 135 shows increased lactate and decreased NAA peaks. No significant elevated choline peak

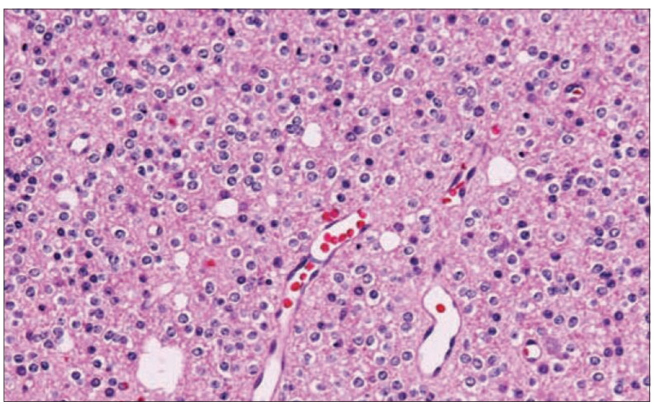

Figure 4: Leptomeningeal biopsy shows tumor cells with sharply defined cell borders, clear cytoplasm, and rounded nuclei consistent with an oligodendroglioma

Secondary leptomeningeal gliomatosis is a known entity that results from invasion of the subarachnoid space or ventricular system by a primary intraparenchymal glioma. Intraparenchymal as well as leptomeningeal lesions can be detected in the brain.

Primary leptomeningeal gliomatosis, however, has no radiologically detected parenchymal focus. It is postulated that primary leptomeningeal gliomatosis arises from leptomeningeal heterotopias[6] or from local or metastatic spread from undetected small intraaxial primary tumor.[7]

Sixteen cases of PLO have been reported in the literature.[8-19] These cases were summarized by Michotte *et al*.[20]

The age distribution covers a wide range from 2 years[8] to 78 years, the peak incidence being in children less than 10 years of age. No sex predilection is noted.

The diagnostic criteria of PLA were first given by Cooper and Kernohan as: No apparent attachment of extramedullary meningeal tumor to the neural tissue, no evidence of primary neoplasia within the neuraxis, and the existence of distinct leptomeningeal encapsulation around the tumor[21]. PLAs may have two well-established anatomic and clinical forms: Nodular form, first described by Bailey and Dietrich as "a solitary or focal leptomeningeal gliomatosis, defined by limited tumor masses in cranial or spinal leptomeninges,"[9,22] and a diffuse form, first reported by Korein as "an extension, outside the nervous parenchyma, of glial tumor cells over a wide area of the CNS."[23] The classical appearance of extra-axial multiple tiny cystic lesions is mentioned in the literature in the subsequent reported cases.

In this case, gradual radiological progression was observed. Initial findings were mild communicating hydrocephalus, periventricular interstitial edema, few tiny leptomeningeal cystic lesions, and mild leptomeningeal enhancement, suggestive of an infective etiology. Later, frank multiple small leptomeningeal cysts with a diffuse leptomeningeal distribution in the brain as well as spinal column were noted. MR spectroscopy at TE 135 showed increased lactate and decreased NAA peaks. No significantly elevated choline peak was noted. In the initial presentation, neurocysticercosis was considered as the principal diagnosis, though intracystic eccentric nodule was not observed. Subsequent progression of the disease showed leptomeningeal enhancement with communicating hydrocephalus, for which the differential diagnoses of tuberculous meningitis, leptomeningeal tumor spread, and cysticercal meningitis were considered.

Cysts in neurocysticercosis show intracystic eccentric nodule appearing as pea in a pod and perilesional edema in inflammatory stage which is not seen in our case. Also, basal meningitis with hydrocephalus due to neurocysticercosis is rare.

Tuberculous meningitis is the closest differential, but leptomeningeal cysts are very rare. CSF examination typically shows increased proteins, decreased glucose concentration, and lymphocytosis in tuberculous meningitis, which were not observed. Even though CSF culture for *Mycobacterium* was negative, empirical anti-tubercular and anti-inflammatory drugs were started to assess the response. As there was no improvement with treatment, patient was subjected to tissue examination.

Histopathology showed tumor cells with sharply defined cell borders, clear cytoplasm, and rounded nuclei, consistent with an oligodendroglioma (WHO grade II).

Optimal treatment is debated as the disease is a rare entity. Chemotherapy and craniospinal radiation have shown good results. Bourne *et al*. reported stable disease after chemotherapy with cisplatin, vincristine, cyclophosphamide, and etoposide,[24] while Franceschi *et al*. recently described treatment of this condition with temozolomide.[25] In general, this disease has a poor prognosis. However, 6-7 years of good-quality life have been reported following palliative therapy. To the authors' knowledge, only six cases of these rare tumors have been treated with adjuvant chemo-radiotherapy.[26-31]

To conclude, PLO has a sequential progression from few tiny leptomeningeal cysts to florid disease. So, if the clinical picture shows mild hydrocephalus with tiny cysts and mild leptomeningeal enhancement without scolex or ring enhancment or significant perilesional edema, then PLO can be considered. Patient needs close follow-up and leptomeningeal biopsy can be done if feasible. Awareness, early detection and treatment of the disease are imperative to reduce the morbidity.

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Conflicts of interest

There are no conflicts of interest.

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