

Letter to the Editor

Primary diffuse leptomeningeal gliomatosis

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Primary diffuse leptomeningeal gliomatosis (PDLG) is a rare, fatal disease characterized by neoplastic glial cells throughout the leptomeninges without evidence of primary brain or cord tumor. Among 80 patients reported to date, only 3 were younger than 5 years [1, 2]. Affecting people with a wide age range, PDLG occurs with variable symptoms depending on the location of the lesions. Most of the cases documented until today were diagnosed after autopsy. In order to confirm the diagnosis, a biopsy from the pathological meninges is required. Primary diffuse leptomeningeal gliomatosis has a very poor prognosis. However, with an early diagnosis, patients treated with radio-chemotherapy can survive longer [3]. Herein, we report a case of a 5-year-old girl who presented with difficulty in walking for the last month. Her initial laboratory tests showed no abnormality. Herein, we report magnetic resonance imaging (MRI) findings of PDLG in the girl, who is the 4th youngest patient reported in the literature so far.

A 5-year-old girl presented with difficulty in walking for the last month. On physical examination the girl had atrophy in her lower extremities and deep tendon reflexes were absent. She was initially misdiagnosed with spinal muscular atrophy. However, the spinal muscular atrophy gene analysis result was negative. She had hydrocephalus a year ago and a suspicious history of meningitis at the age of 3. Her imaging reports were not available. No abnormality was found in her laboratory tests or family history. Magnetic resonance imaging of the cranium showed multiple superficially located small cystic lesions on the surface of the cerebrum, cerebellum and brainstem associated with thick nodular leptomeningeal-pial enhancement (Figures 1 A–C). Previously, a ventricular catheter was placed for hydrocephalus. Similar appearance was noted throughout the spine (Figures 2 A–C). There were diffuse small cystic lesions on the surface of the spinal cord together with thick leptomeningeal-pial enhancement and very intense enhancement around the cauda equina fibers. The MRIs showed findings of cystic lesions in the parenchyma distributed mainly in the superficial gray, perivascular spaces, and in the superficial portion of the cord.

There was no primary brain or cord tumor throughout the brain and spine. These imaging findings were suggestive of PDLG. Brain biopsy confirmed the diagnosis. She had only a few months to live after the diagnosis.

Primary diffuse leptomeningeal gliomatosis is glial tumor cell infiltration of the leptomeninges without any primary tumor in the brain parenchyma or spinal cord. It is thought to arise from the subarachnoid heterotopic glial nest cells. Subarachnoid heterotopic glial nest cells mostly

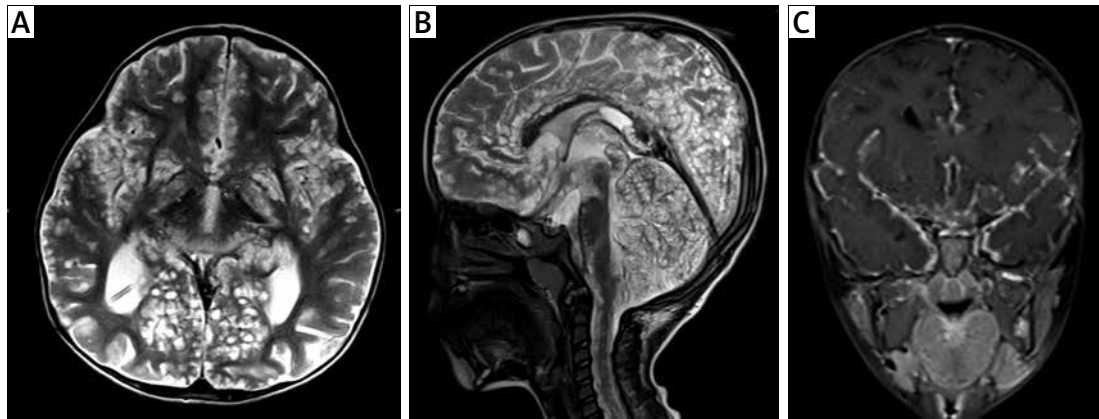


Figure 1. Axial (A) and sagittal (B) T2W and postcontrast fat saturated coronal (C) images show dilatation of lateral ventricles, a catheter image in the right lateral ventricle, tonsillar herniation, and diffuse small cystic lesions on the surface of the brain associated with thick nodular leptomeningeal-pial enhancement

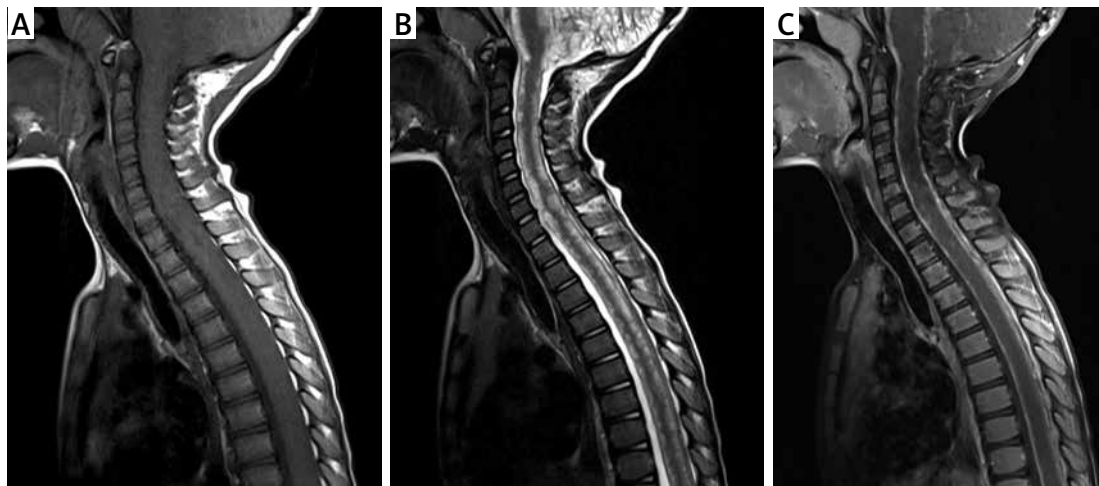


Figure 2. Sagittal T1W (A), T2W (B) and postcontrast T1W (C) images show diffuse small cystic lesions on the surface of the spinal cord together with thick leptomeningeal-pial enhancement and very intense enhancement around the cauda equine fibers

lie around the brainstem and cervical spinal cord, being found in 1% of autopsies and 25% of patients with congenital malformations [3, 4]. Having a wide age range (3–49 years), PDLG occurs predominantly in children (mean age 18 years), and there is a slight predominance in males (M : F, 6 : 5) [5]. Histopathologically, PDLG occurs as astrocytoma of various grades, glioblastoma, ependymoblastoma, oligodendroglioma, primitive neuroectodermal tumor, gliosarcoma, and pleomorphic xanthoastrocytoma [5]. Mean survival time is 22 months, and 63% of patients die within 9 months after diagnosis [6]. Diffuse leptomeningeal glioneuronal tumor has been described recently; in this tumor, similar to PDLG, diffuse leptomeningeal infiltration without an intraparenchymal mass is present. Both can be either high or low-grade glioma. The main differential diagnosis is that diffuse leptomeningeal glioneuronal tumors should be positive for both neuronal and glial markers, while PDLG is negative for neuronal markers [6].

In PDLG, the clinical presentation is diverse, thus making diagnosis difficult. The most common symptoms are due to increased intracranial pressure, often with hydrocephalus, meningism, headaches, seizures and bilateral papilledema [4, 5]. Cerebrospinal fluid (CSF) analysis shows mild proteinosis, a normal-low glucose level and pleocytosis, thereby leading to the misdiagnosis of tuberculosis or fungal meningitis.

Hydrocephalus is the most common feature of tuberculous meningitis (TBM), particularly in children [7]. Basal meningitis with/without exudate, hydrocephalus, parenchymal enhancing lesions representing either granuloma or abscess, and infarction secondary to arteritis are the hallmarks of the disease. The CSF profile is insufficient in differentiation since both TBM and PDLG may have high opening pressure, lymphocyte pleocytosis, high protein and low glucose levels [8]. To diagnose TBM, showing tubercle bacilli in CSF culture and demonstrating acid-fast bacilli in CSF samples

are gold standard techniques. However, culture results and AFB in CSF are positive in a range of 5–87% and 10–87%, respectively. Therefore, in routine practice, TBM is usually excluded when the patient does not respond to anti-tuberculosis treatment. Since TBM may mimic PDLG according to symptomatology, laboratory results and imaging findings, a biopsy is mandatory for definite diagnosis of PDLG, especially when the patient is unresponsive to anti-tuberculous therapy. In the literature, one third of the patients with PDLG were treated for TBM initially [9].

Although very rare, when atypical cells are seen in CSF cytology, glial fibrillary acidic protein staining should be done [5, 10, 11]. The high rate of negative results in CSF analysis for malignant cells is explained by a desmoplastic reaction limiting the tumor cells to detach from the primary focus [11]. Also, positive cytology up to 66% was found in secondary gliomatosis cases [12].

Magnetic resonance imaging is essential for diagnosis. Common MRI findings of PDLG are diffuse-nodular thick and strong pial-leptomeningeal enhancement especially around the brain stem, cerebellum, ventricles and spinal cord, dilatation in ventricles usually accompanied with hydrocephalus, focal dilatation of cerebral sulci and lack of any tumoral lesion within the parenchyma or spinal cord [3]. However, there have been some cases in the literature that involved superficial parenchyma and Virchow-Robin spaces where the arachnoid and pia complex continues around small vessels. Multiple parenchymal cysts occur due to tumor cell infiltration and expansion of perivascular spaces with focal rarefaction of surrounding neuronal tissue [6–13].

Evaluated by nonspecific clinical symptoms, CSF results and imaging findings, a broad differential diagnosis list is revealed: tuberculous-fungal meningitis, brucellosis, sarcoidosis histiocytosis, leptomeningeal carcinomatosis, leptomeningeal dissemination of tumors (astrocytic tumors, oligodendroglioma, diffuse infantile ganglioglioma, central neurocytoma, ependymoblastoma, primary neuroectodermal tumor, melanocytoma and lymphoma) and idiopathic hypertrophic meningitis [11]. To confirm the diagnosis, a biopsy particularly from the contrast enhancing areas is mandatory. However, to achieve a diagnostic leptomeningeal biopsy is not easy since the disease consists of skipped lesions and has a predilection for the skull base rather than cerebral hemispheres where the biopsy is usually performed [11]. Therefore, multiple and repeated biopsy is strongly advised.

Since PDLG has diffuse involvement of leptomeninges throughout both brain and spinal cord, radiotherapy and chemotherapy are the only treatment options [14]. Antiepileptics can also be

used when necessary. The prognosis remains poor, especially in high-grade gliomatosis. Mean survival time after diagnosis is 4 months [11].

In conclusion, when a patient presents with intracranial hypertension symptoms and diffuse leptomeningeal thickening with contrast enhancement on MRI with no primary brain or cord tumor, PDLG or diffuse leptomeningeal glioneuronal tumor must be searched for, since early treatment with radiochemotherapy may prolong survival [3].

Conflict of interest

The authors declare no conflict of interest.

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