



Diffuse Leptomeningeal Glioneuronal Tumor in an Adult: A Diagnostic Challenge

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Abstract

Here we report a rare case of diffuse leptomeningeal glioneuronal tumor (DLGNT) in a 35-year-old man, who was misdiagnosed twice as having tuberculosis meningitis and later racemose neurocysticercosis. His delayed diagnosis of DLGNT might be due to prevalence of tuberculosis in our country, similarity in magnetic resonance imaging finding of prominent leptomeningeal enhancement in different cisterns of brain, and extreme rarity of DLGNT in the adults. So, it should be differentiated clinically and radiographically from granulomatous or infectious conditions. Hence, a timely histologic diagnosis through a leptomeningeal biopsy of the brain and spinal cord in case of unusual leptomeningeal enhancement with uncertain laboratory findings is essential because cytological examination of the cerebrospinal fluid in DLGNT is known to be negative.

Keywords

- ▶ adult
- ▶ diffuse leptomeningeal glioneuronal tumor
- ▶ leptomeningeal biopsy

Key Message

DLGNT may occur in an adult. Neuroradiologists should be aware of the distinctive neuroimaging features of this entity to recognize it at an early stage.

Introduction

Diffuse leptomeningeal glioneuronal tumors (DLGNTs) are rare neoplasms, added as a provisional entity of glioneuronal tumors to the World Health Organization (WHO) 2016 classification of tumors of the central nervous system (CNS). They are characterized by extensive dissemination in leptomeninges of brain and spine, with or without intraparenchyma lesions. They have also been described as disseminated oligodendroglial-like leptomeningeal tumor (DOLT)

due to characteristic monomorphic clear cells with glial morphology reminiscent of oligodendroglioma in histology.^{1,2} Due to the limited number of reported cases, incomplete clinical follow-up, and the variability of outcome of this rare entity DLGNT has not been assigned a WHO grade.³ DLGNT is common in children and adolescents but rare in adults. The clinical diagnosis of this tumor is sometimes complicated due to the rather nonspecific imaging findings.⁴ Here, we present a case of DLGNT in a 35-year-old man, who was twice misdiagnosed as infectious pathology on radiology. Later, after worsening of symptoms, brain biopsy was performed and diagnosis was made. The current case highlights the importance of brain biopsy for cases presenting as multiple bilateral cysts in posterior fossa as well as well-defined lesion along the meninges of cervical vertebrae in magnetic resonance imaging (MRI).

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Case Report

A 35-year-old man admitted to our institution due to complaint of inability to walk without support since 1 month. One year prior to this presentation, he had complaints of vomiting, diplopia, slurring of speech, swaying to either side while walking (ataxic gait). There was no history of fever, but on systemic examination sign of meningeal irritation—neck rigidity was present. There was mild obstructive hydrocephalus with 4th ventricular dilatation and multiple conglomerate lesions in bilateral cerebellar hemispheres on MRI. On the basis of complaints and radiological imaging, a provisional diagnosis of obstructive hydrocephalus possibly caused by a granulomatous infectious etiology—tuberculous meningitis—was made. He underwent a ventriculoperitoneal shunt surgery in a peripheral hospital, leading to transient improvement in his gait disturbance. He had been treated with antituberculosis medication for the following 6 months but the patient's condition deteriorated. So on reevaluation of the patient's brain MRI, there were multiple variable-sized cystic lesions carpeting the surface of bilateral cerebellar hemisphere, vermis, both cerebellopontine angles along the walls of lateral ventricle and premedullary cistern, as well as diffuse leptomeningeal thickening. On MRI of spine, well-defined enhancing mass was seen at C7–T1 vertebral body level along anterior margin of cord 9 (►Fig. 1A, B). A diagnosis of granulomatous etiology—racemose neurocysticercosis—was made and the patient was treated with anti-parasitic drugs. But his symptoms aggravated; the patient became bedridden and was admitted in our institution. Hence, an imaging diagnosis was not considered sufficient and a biopsy was taken from posterior fossa by craniectomy. Grossly we received gray–brown soft tissue pieces collectively measuring 1.5 cm × 1 cm. Histopathological examination showed fragments of normal as well as expanded cerebellar folia having monomorphic oligodendrocyte-like cells with rounded nuclei and perinuclear halo as well few interspersed

ganglionic cells against a fibrillary matrix (►Fig. 2A, B). On performing immunostaining oligodendrocyte-like cells were positive for Glial fibrillary acidic protein (GFAP), Olig2, and S-100; negative for IDH 1 (R132H) [isocitrate dehydrogenase 1 (arginine to histidine at codon 132)]. Ganglionic cells showed positivity for synaptophysin. K_i 67 index was 3 to 4% [►Fig. 2C–F]. After evaluating the morphology mentioned earlier and immunohistochemistry, a diagnosis of diffuse leptomeningeal glioneuronal, low-grade, was made. Then patient was referred to the oncology department for further treatment.

Discussion

DLGNTs were first described by Beck and Russel in 1942 in four cases of “oligodendrogliomatosis of cerebrospinal pathway.”⁵ Gardiman et al termed it “diffuse leptomeningeal glioneuronal tumour” for the first time.⁶ It is characterized by diffuse growth of tumor tissue along leptomeningeal area, with similar cell morphology to that of oligodendrocytes. Lesions of this disease are principally located in the sub-arachnoid space; it is unclear whether it originates in the leptomeningeal compartment or a leptomeningeal extension of a subtle intraparenchymal disease.⁷ DLGNTs may originate from the isolated groups of glioneuronal progenitor cells entrapped in the leptomeninges during primitive migration which could be capable of divergent differentiation with neuronal, oligodendroglial, and astrocytic features or they may arise from leptomeningeal heterotopias formed of small nests of glial tissue found within the subarachnoid space and present in around 1% of healthy individuals.^{8,9}

This entity may mimic various nontumoral diseases due to slow evolution and variable nonspecific clinical manifestations. The challenge for radiologists is to be able to suggest the diagnosis during early stages of the disease, when hydrocephalus and diffuse leptomeningeal enhancement predominate the basal cistern and spine, as it may be a feature

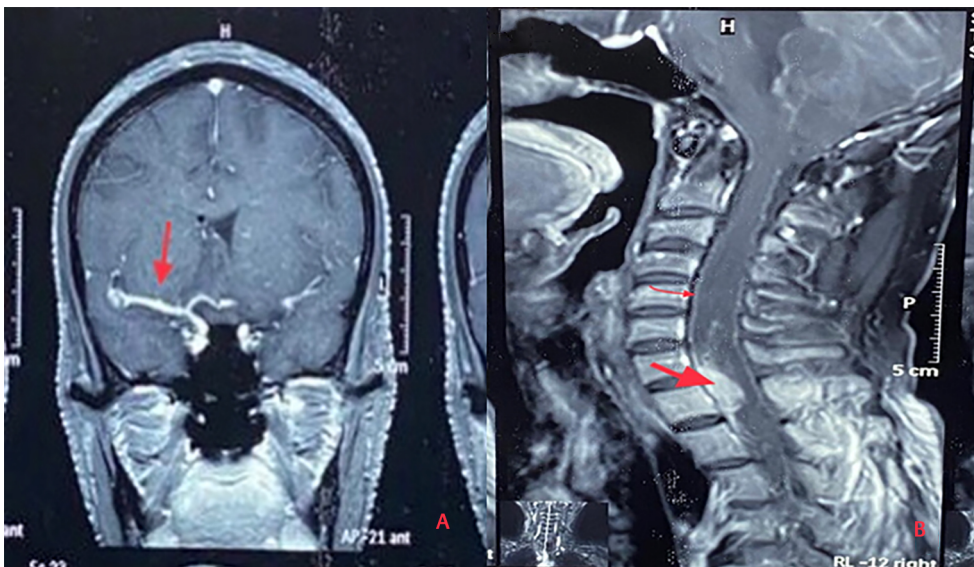


Fig. 1 (A) Coronal postcontrast magnetic resonance imaging (MRI) brain; arrow points to the diffuse thickening of leptomeninges. (B) Sagittal T1FS postcontrast image of cervical spine; arrow points to the cord expansion with enhancing mass at C7–T1 level.

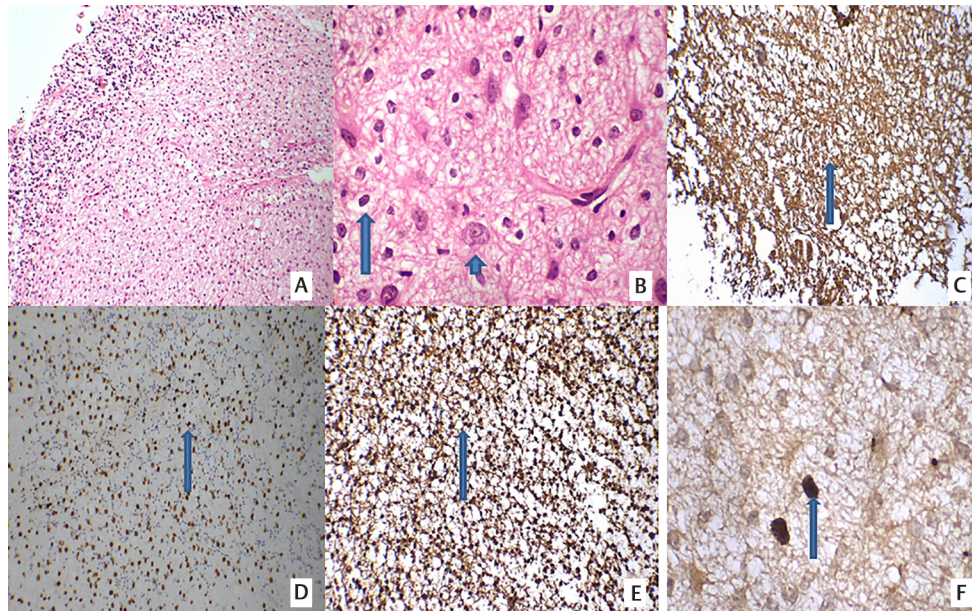


Fig. 2 (A, B) In microphotograph expansion of cerebellar folia by oligodendrocyte-like cells, neuronal cells, and thin vasculature, pointed by arrows (H&E; $\times 100$, $\times 400$). (C–F) Arrows showing immunostaining positivity for GFAP, Olig2, S-100, and Ki67, respectively ($\times 100$). GFAP, Glial fibrillary acidic protein; H & E- hematoxylin & eosin.

of granulomatous lesions including neurosarcoidosis, fungal meningitis, and secondary leptomeningeal carcinomatosis arising from primary brain tumors, tubercular meningitis, neurocysticercosis.¹⁰ Neuroimaging profile is characteristic in advanced disease where innumerable small pseudocystic implants are observed along the surface of the brain, mainly in the posterior fossa and spine, as reported in our case.⁶ The initial clinical improvement observed in our case was related to the implantation of a ventricular shunt. From an anatomicopathologic point of view, one should be aware that these T2 or fluid-attenuated inversion recovery hyperintense pseudocystic lesions along the surface correspond to tumor cell infiltration with focal rarefaction of surrounding neural tissue.¹

Diagnosis of DLGNTs can only be confirmed through biopsy, since cerebrospinal fluid frequently merely shows increased protein levels or rarely lymphocytosis. Absence of tumor cells in the cerebrospinal fluid cytology is explained by the entrapment of tumor cells by the desmoplastic tissue induced by the tumor.¹⁰ Microscopic evaluation of biopsy unveils a neoplastic population of oligodendroglioma-like cells with low-mitotic activity. Moreover, glioneuronal nature of the tumor can be specified through immunopositivity for glial markers such as GFAP and Olig2 as well as neuronal markers such as synaptophysin or Neu N as in our case.^{5,6} Due to low incidence, the degree of malignancy and prognosis of DLGNT are unclear as the factors that determine clinical outcome remain elusive, highlighting the need to develop targeted therapeutic strategies. However, few studies demonstrated the efficacy of chemotherapy (a combination of thioguanine, procarbazine, cyclonexyl-chloroethyl-nitrosourea or lomustine, and vincristine [TPCV (thioguanine, procarbazine hydrochloride, lomustin & vincristin)] or carboplatin and vincristine) and radiotherapy for this entity.¹¹ Early treatment of this low-grade tumor is

associated with a higher likelihood of stable disease, hence the reason for early diagnosis.¹⁰

To summarize, DLGNTs are rare, low-grade glioneuronal tumors, predominantly in the children and adolescents. They are characterized by the presence of multiple nodular cystic-like lesions scattered over the brain and spinal cord surface. Neuroradiologists should be aware of the distinctive neuroimaging features of this entity to recognize it at an early stage. Indeed, this should not to be confused with an infectious or inflammatory condition, as early diagnosis is linked to better prognosis.

Conflict of Interest

None declared.

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