

Diffuse Leptomeningeal Melanocytosis

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Abstract

Diffuse leptomeningeal melanocytosis is an extremely rare disorder, especially in the pediatric population. Its nonspecific symptoms make diagnosis challenging. However, imaging is typically abnormal and is used to help guide the ultimate histologic diagnosis. Affected patients have a poor prognosis, and treatment options are limited.

Keywords: brain, meninges, neoplasm

Case Summary

A previously healthy adolescent presents with progressive headaches, vomiting, and Charles Bonnet syndrome. MRI demonstrates diffuse leptomeningeal enhancement.

Imaging Findings

MRI of the brain demonstrated abnormal leptomeningeal signal on the right with focal areas of increased T1 signal, increased FLAIR signal, and diffuse enhancement. No focal lesions are present (Figure 1).

Diagnosis

Primary diffuse leptomeningeal melanocytosis (PDLM).

The differential diagnosis of progressively worsening headaches, vomiting, and visual disturbances in an adolescent includes subarachnoid hemorrhage, meningitis, neurosarcoidosis, metastatic melanoma to the meninges, and other primary brain tumors.

Discussion

PDLM is a benign central nervous system tumor derived from excessive proliferation of melanocytes of neural crest origin in the leptomeninges. It is one of four neoplasms that derive from melanoblasts. Other melanoblastic tumors include melanocytoma, melanoma, and primary diffuse melanomatosis—a malignant version of PDLM.¹ The estimated annual incidence of primary melanocytic lesions is 1 in 10 million.² PDLM is extremely rare, with only a few dozen reported cases in the literature and only one pediatric case reported in a PubMed database search.³ PDLM is strongly linked to hypohidrotic ectodermal dysplasia—a rare genetic condition marked by hypohidrosis, hypodontia, and hypotrichosis.⁴ PDLM may also be associated with neurocutaneous melanosis syndrome, Sturge-Weber, and neurofibromatosis type 1.^{4,5}

The disease presents a diagnostic challenge for clinicians, as the most common presenting symptoms are protean, and overlap exists with other inflammatory, autoimmune, and

neoplastic processes. Patients most commonly present with signs of elevated intracranial pressure, such as headache, vomiting, and changes in vision. Other manifestations may include seizures, hallucinations, ataxia, mental status changes, cranial nerve palsies, and neuropsychiatric symptoms.⁶ On examination, large, multiple benign pigmented nevi are commonly seen in the dermal tissue of affected individuals. One unique nevus associated with leptomeningeal involvement can often be seen, the nevus of Ota, which occurs on the face and eyelid unilaterally.⁷

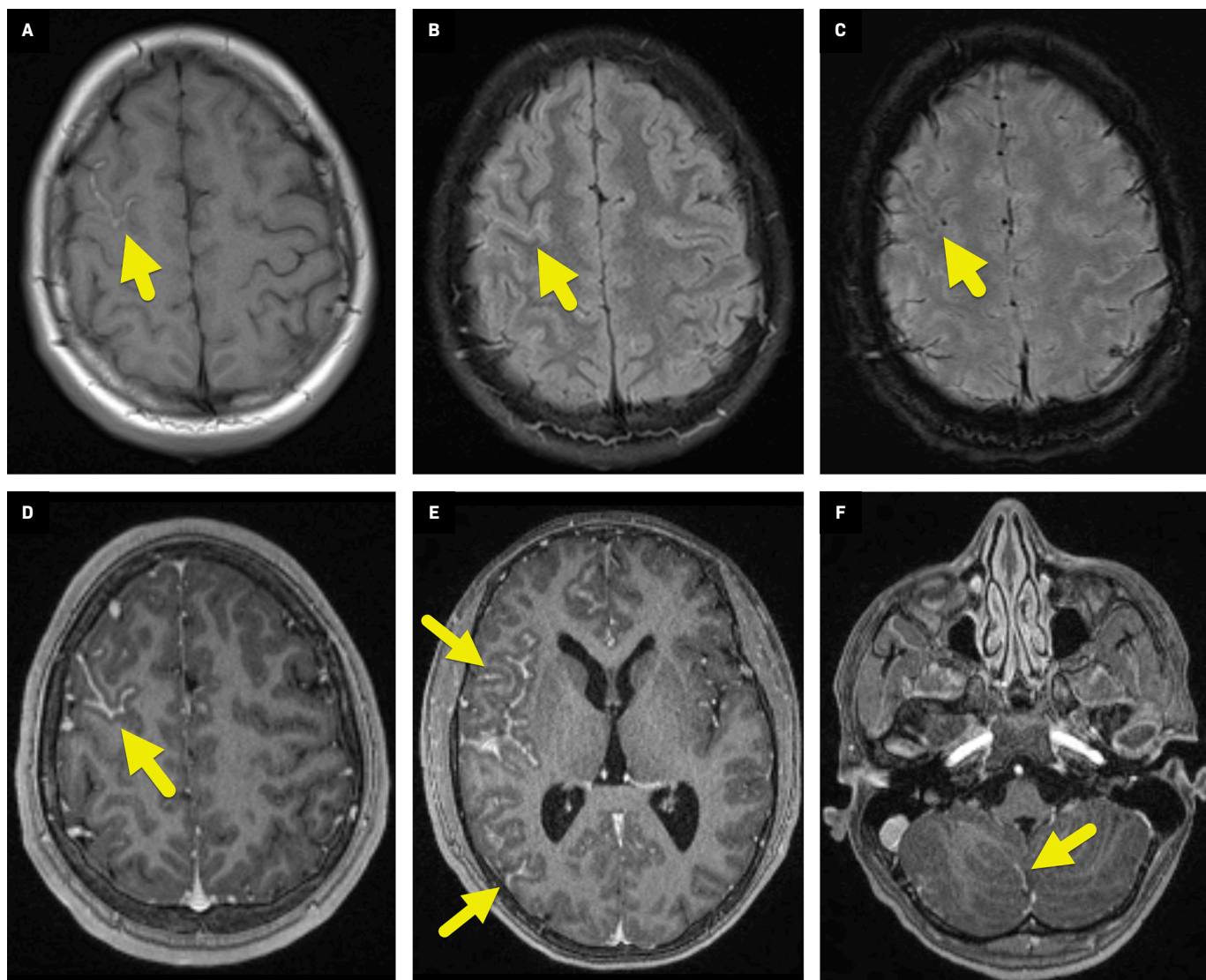
Imaging, immunohistochemistry, and genetic analysis play pivotal roles in diagnosing PDLM. On CT, PDLM may be seen as an iso- to hyperattenuating region along the meninges with variable contrast enhancement.⁶ On MRI, PDLM is best appreciated on pre- and post-contrast T1-weighted sequences. The lesion is hyperintense on pre-contrast imaging due to the paramagnetic effects of melanin. The lesion becomes more pronounced after the administration of contrast, where the classic leptomeningeal enhancement is highlighted.^{2,5}

While imaging can guide diagnosis, ultimate diagnosis requires a biopsy of the lesion.⁸ Histopathology examination confirms the presence of intracytoplasmic melanin. PDLM typically shows nonsignificant dysplasia and mitotic activity. Immunohistochemical analysis of PDLM highlights positive HMB-45,

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Figure 1. (A) Axial T1-weighted, (B) FLAIR, (C) susceptibility-weighted image, (D), (E), and (F) T1-weighted post-contrast images (from superior to inferior) show abnormal leptomeningeal signal (arrow). The signal is hyperintense on T1-weighted and FLAIR images. There is minimal decreased signal on the susceptibility-weighted image and focal areas of leptomeningeal enhancement consistent with diffuse leptomeningeal melanocytosis.



S-100, Melan A, and vimentin antibodies. Vimentin is a particularly important differentiator of PDLM. It is positive in PDLM and almost always negative in melanoma.⁶ Further histological discrimination of PDLM from melanocytoma, melanoma, and primary diffuse melanomatosis is currently not established.⁹

The prognosis for patients with PDLM is poor, with death typically occurring

within 3 years of symptom onset. The most common cause of death is progressive neurological deterioration and intractable intracranial hypertension, thought to be caused by increased cellular and protein density impairing cerebrospinal fluid output.¹⁰ Treatment is limited and primarily focuses on symptomatic relief via early ventriculoperitoneal shunting, surgical debulking, chemotherapy, and radiation.

Conclusion

PDLM is an extremely rare disorder, especially in the pediatric population. Its nonspecific symptoms make diagnosis challenging. However, imaging is typically abnormal and is used to help guide the ultimate histologic diagnosis. Affected patients have a poor prognosis, and treatment options are limited.

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