

Solitary Langerhans cell histiocytosis of frontal lobe: a case report and literature review

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Abstract: The brain parenchymal Langerhans cell histiocytosis (LCH) without systemic disease or lytic skull lesions is extremely rare. We report a 23-year-old male presenting with new onset 1 hour seizure with loss of consciousness 20 days prior to admission, and recurrent seizure 2 weeks later. Brain magnetic resonance imaging (MRI) showed an irregularly mass with enhancement involving the right frontal lobe. Microscopically, the lesion was characterized by sheets of Langerhans cells in addition to reactive inflammatory elements. Immunohistochemically, Langerhans cells were positive for Langerin, CD1a and S-100 protein. The patient received no chemotherapy or radiotherapy after surgery. After 24 months of follow-up, no recurrence or other systemic lesions were observed. Although there is no standard treatment for solitary cerebral LCH, the prognosis generally appears to be good.

Keywords: Langerhans cell histiocytosis (LCH); histiocytosis; immunohistochemistry; pathology

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Introduction

Langerhans cell histiocytosis (LCH), characterized by clonal proliferation of Langerhans cells and focal aggregates of variable numbers of eosinophils, lymphocytes, neutrophils, foamy histiocytes and multinucleated giant cells, is a rare systemic disease that occurs frequently in children (1). LCH tends to involve the skeletons and surrounding soft tissue, presenting with osteolytic lesions. Unifocal central nervous system (CNS) involvement without systemic disease or lytic skull lesions is extremely rare. We report a case of solitary LCH of the right frontal lobe without osseous involvement, and review the relevant literatures.

Case report

A 23-year-old male presented with new onset 1 hour seizure with loss of consciousness 20 days prior to admission, and recurrent seizure 2 weeks later. The physical and neurological examinations were normal. His medical

history was unremarkable. No hereditary syndromes were disclosed. Brain magnetic resonance imaging (MRI) showed an irregularly mass of 4.1 cm × 3.1 cm × 3.5 cm involving the right frontal lobe, hypo-/iso-intense on T1-weighted image (*Figure 1A*), iso-/hyper-intense on T2-weighted image (*Figure 1B*) and fluid-attenuated inversion recovery (FLAIR). After the administration of intravenous contrast gadolinium-diethylene triamine pentaacetic acid (DTPA), the lesion showed moderate to intense homogeneous enhancement (*Figure 1C*).

A right frontal craniotomy was performed under general anesthesia on January 14, 2012. The lesion was located in the pallium of the precentral gyrus. The mass lesion was totally resected and sent for pathological evaluation. Grossly, the cross-section revealed a well-defined nodular lesion measuring 0.8 cm × 0.6 cm in grey matter, with gray-white and slightly tough appearance (*Figure 2A*). Microscopically, the lesion was limited to the grey matter. It was characterized by sheets of histiocyte-like cells in addition to reactive elements,

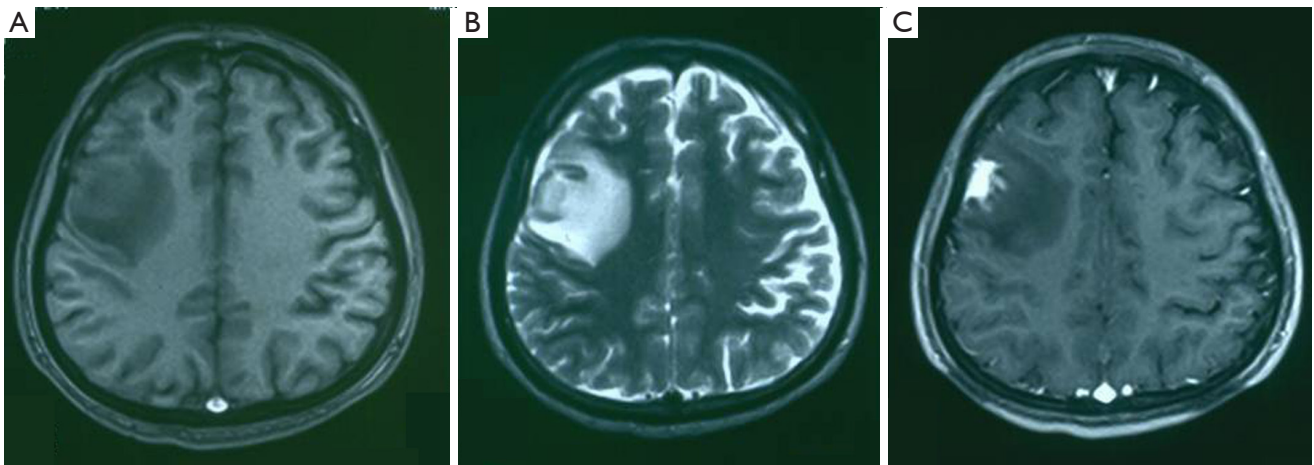


Figure 1 (A) Unenhanced MRI showed a slightly hypointense mass with surrounding hypointense edema on T1-weighted imaging; (B) and a slightly hyperintense nodular lesion approaching to the surface of the brain on T2-weighted imaging; (C) contrast enhancement T1-weighted MR imaging showed the nodular lesion enhanced obviously.

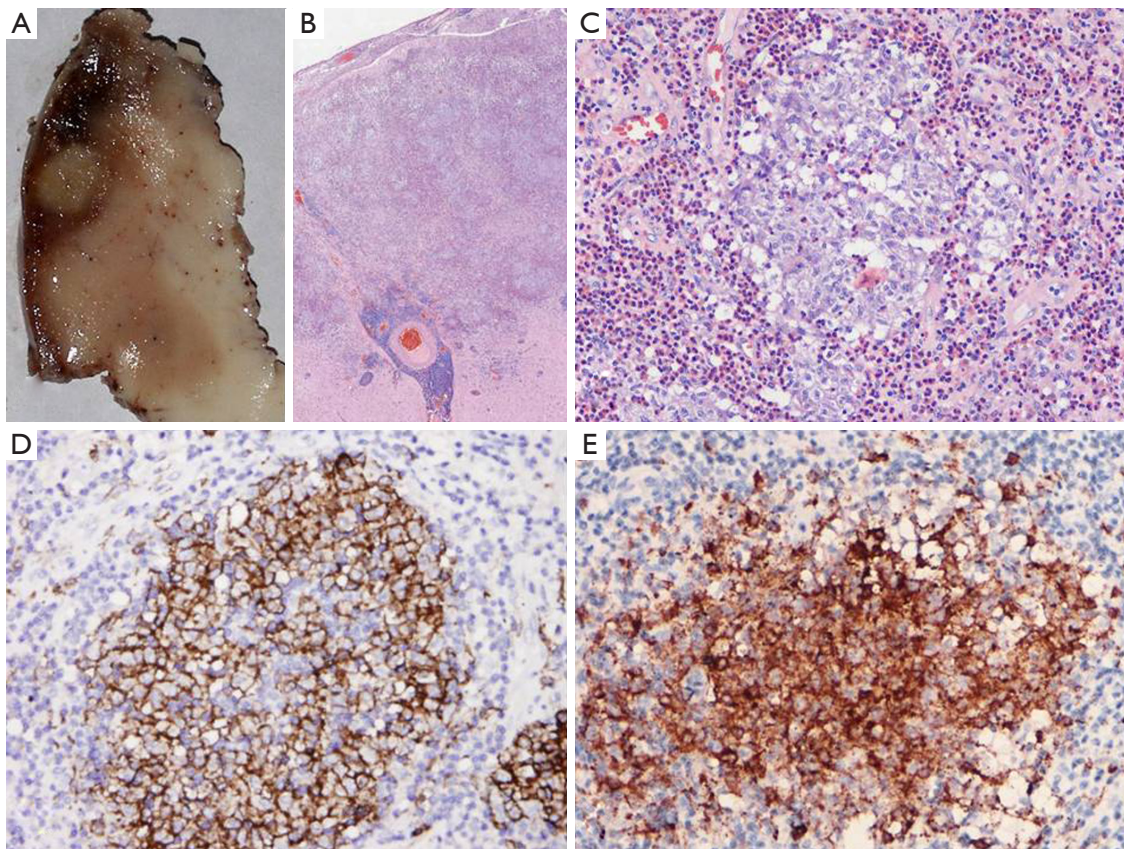


Figure 2 Grossly, the cross-section revealed a well-defined gray-white nodular lesion measuring 0.8 cm × 0.6 cm in grey matter (A). Microscopically, the lesion was limited to the grey matter. It is composed of sheets of Langerhans cells and reactive elements including eosinophils, neutrophils, macrophages, small lymphocytes, plasma cells, and so on (B, H&E, ×40) (C, H&E, ×400). Immunohistochemically, Langerhans cells were positive for CD1a (D) and Langerin (E).

including eosinophils, neutrophils, macrophages, small lymphocytes, plasma cells, and occasional multinucleated giant cells. The proliferating histiocytes were mostly large and round without significant atypia, and had abundant clear-to-eosinophilic cytoplasm and indented or convoluted nuclei with linear condensation of chromatin, resulting in a coffee bean appearance of nuclei (Figure 2B,C). Mitosis and necrosis were absent. The other characteristic finding was a reactive inflammatory infiltrate, with a prominence of eosinophils. Immunohistochemically, the histiocyte-like cells were positive for CD1a (Figure 2D), Langerin (Figure 2E) and S-100 protein, which confirmed their origination from Langerhans cells. Glial fibrillary acidic protein (GFAP), synaptophysin (SYN), epithelial membrane antigen (EMA), cytokeratin (CK) and vimentin were negative for Langerhans cells. The final diagnosis was LCH. The patient received no chemotherapy or radiotherapy after surgery. After 24 months of follow-up, no recurrence or other systemic lesions were observed.

Discussion

Isolated involvement of CNS without evidence of systemic disease and concomitant osseous involvement is very rare (2). Only 21 cases of solitary LCH involving brain parenchyma have been reported (3-22). Including the present one, we summarized all the 22 cases in our report. They consisted of 15 males and 7 females with a mean age of 28.5 years (range, 3-40 years). The findings suggested that the cerebral LCH tends to occur later than that of other systems. The temporal lobe was involved most commonly, followed by the frontal lobe and the parietal lobe.

Clinical manifestations of LCH varied with location and may also include nonspecific symptoms of mass effect. Headaches (21 of 22 cases), seizures (19 of 22 cases), and localizing signs, such as hemiparesis and sensory deficits, were most common. Intracerebral solitary LCH had no characteristic neuroimaging patterns. These lesions generally revealed as low-density masses with surrounding edema on CT, and occasional homogeneous contrast enhancement. MRI was variable in the cases reported. Some cases showed low- or iso-intensity on T1-weighted imaging and hyper-intensity lesions on T2-weighted imaging without gadolinium contrast enhancement, while the others demonstrated hyper-intensity on T2-weighted imaging with marked homogeneous enhancement after administration of gadolinium (23).

The final diagnosis should be made by pathological features. Histologically, the typical morphology of LCH appears to have a variable number of Langerhans cells

accompanied by reactive elements (2). In most cases, some Langerhans cells show the typical cytological features of indented or convoluted nuclei with linear condensation of chromatin, resulting in a coffee bean appearance of nuclei. The nuclear features are diagnostic, which may be used for distinguishing Langerhans cells from other types of histiocytes. Co-expression of CD1a and Langerin is most commonly used to confirm the diagnosis, and the positivity for S-100 protein is also helpful. Although ultrastructural demonstration of Birbeck granules is of great diagnostic relevance in the definition of this tumor type, Birbeck granules just exist in 2-69% of Langerhans cells (20,24). The brain parenchymal LCH often requires a broader category of differential diagnosis, including granulomatous diseases such as sarcoidosis, tuberculosis, non-LCH, histiocytosarcoma and lymphoma.

Optimal treatment for LCH with CNS mass lesions is not yet well defined. Ng Wing Tin *et al.* suggested that vinblastine, with or without steroids, could potentially be a useful therapeutic option in LCH with CNS mass lesions, especially for those with inoperable lesions or multiple lesions (25). Dhall *et al.* found that 2-chlorodeoxyadenosine is an active agent in patients with CNS LCH, with the possible exception of neurodegenerative disease (26). However, the preferred treatment for unifocal CNS LCH is surgical resection. Sometimes radiation and chemotherapy may be needed due to incompletely resection, especially in children. Along with the important role of chemokines in the pathogenesis of LCH has been gradually recognized, the agents aiming at cytokine, such as TNF- α , inhibition, are used to block the development process of LCH, which is expected to be the foundation of targeted therapy (27). Of all the 22 patients, 2 cases of recurrence have been reported, and one of them died from the disease (18). Recently, Laurencikas *et al.* reported that about one fourth of children with LCH had an MRI signature consistent with some degree of neurodegeneration. The finding highlighted the need for long-term follow up in patients with LCH-associated CNS neurodegeneration (28). Totally, the prognosis of solitary cerebral LCH generally appears to be good.

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