

# Emergent presentation of Langerhans cell histiocytosis in a pediatric patient: Acute cerebellar involvement causing obstructive hydrocephalus requiring posterior fossa decompression

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## Abstract

Langerhans cell histiocytosis (LCH) is a disorder of the monocyte-macrophage system that can be unifocal or systemic. Here, we present a pediatric case who initially presented with osseous LCH but again presented 6 years later emergently with cerebellar symptoms, cerebellar mass and obstructive hydrocephalus. Patient underwent biopsy of the cerebellum which was path proven intracranial LCH.

**Key words:** Emergent decompression; intracranial Langerhans cell histiocytosis; obstructive hydrocephalus

## Introduction

Intracranial Langerhans cell histiocytosis (LCH) is a rare pediatric condition. Its etiology remains indeterminate. The four recognized patterns of LCH involving the head and neck in the order of frequency include osseous lesions, intracranial extra-axial changes (hypothalamic pituitary axis, pineal region), intracranial intra-axial lesions, and brain atrophy.<sup>[1]</sup>

Intra-axial lesions are uncommon, especially in the posterior fossa. The life-threatening complication of extensive vasogenic edema with brain stem compression is a very rare.

## Case Report

A 5-year-old female initially presented to the emergency department (ED) after trauma, which was thought to be responsible for left eye swelling and headaches. Persistent eye swelling and headaches led to hospital admission. Imaging work-up demonstrated lytic lesion in the left supraorbital region with associated soft tissue lesion on computed tomography (CT) scan of the head [Figure 1A]. There was increased uptake on bone scan [Figure 1B]. This mass was biopsied and the findings were consistent with LCH. The patient was treated with vinblastine with complete resolution of the lytic lesion 8 months after

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diagnosis. Patient was lost to follow-up subsequently due to social issues.

Patient represented to the ED at 11 years of age with worsening headaches, unsteady gait and blurry vision. Magnetic resonance imaging (MRI) at the time of admission demonstrated enhancing lesions in the cerebellum [Figure 2A]. Post-contrast T1 post-contrast sagittal image showed enhancing lesions [Figure 2B]. Diffusion weighted images showed multiple areas of diffusion restriction [Figure 3A]. Corresponding ADC map confirmed dark areas consistent with increased cellularity [Figure 3B]. Due to the mass effect from vasogenic edema in the posterior fossa, patient also had obstructive hydrocephalus. Patient underwent an emergent ventriculostomy drain placement and subsequently underwent stereotactic biopsy of the right cerebellar lesions. Follow up MRI brain performed 2 days later to evaluate the improvement in the compression of the brain stem in-fact demonstrated worsening cerebellar edema [Figure 4A]. There was significant brain stem compression [Figure 4B]. Pathology demonstrated findings consistent with LCH. Her condition started to deteriorate. This prompted emergent posterior fossa decompression via suboccipital craniotomy and C1 laminectomy. Complete laboratory and radiology work up including skeletal survey was performed. No osseous lesions were identified at the time of the second presentation. Patient was discharged

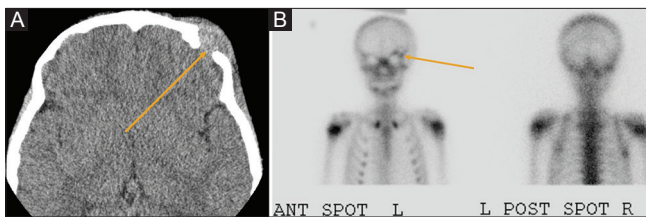
to inpatient rehabilitation service in stable condition approximately 2 weeks after admission. She completed 12 cycles of cytarabine and IVIG subsequently and tolerated them without incidence [Figure 5]. She was discharged from rehabilitation and she returned to school and resumed activities of daily living. She is in complete remission for 15 months. MRI of the brain performed as a follow up examination demonstrated no residual lesions.

## Discussion

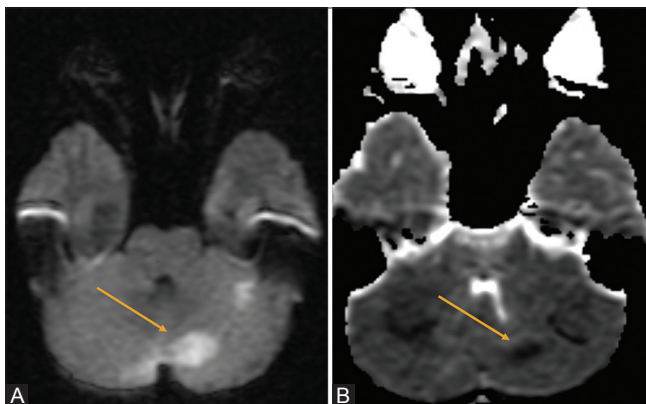
### Etiology and demographics

LCH is considered a reactive clonal disease of monocyte-macrophage system with an incidence of 0.2–2 cases/100,000 children under the age of 15 years of age.<sup>[2]</sup> It may present as a solitary focus typically involving the skeletal system or in systemic fashion affecting nearly any organ system. The lesions of this disease are characterized by Langerhans cells (CD1a+), which are cells of dendritic origin and normally function as antigen processing and presenting cells.<sup>[1]</sup> The etiology causing the reactive nature of these normal cells is not elucidated yet.

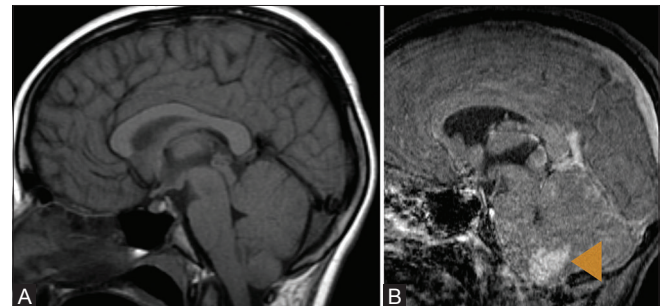
There are multiple patterns of neuraxis involvement with classic LCH, presenting as hypothalamic pituitary lesions and resultant diabetes insipidus. The second most common type of intracranial involvement is neurodegenerative pattern typified by bilateral cerebellar,



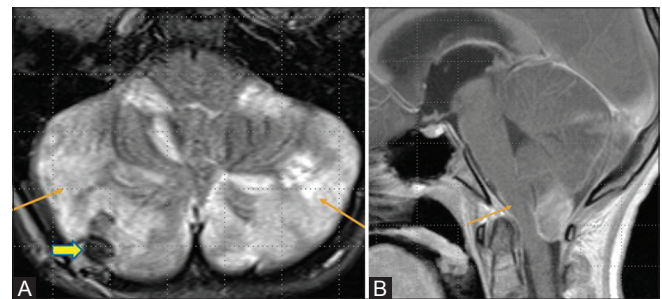
**Figure 1 (A and B):** (A) Axial noncontrast CT demonstrates well-defined lytic lesion in the left supra orbital region with associated soft-tissue component. (B) Tc 99m labelled MDP bone scan shows peripheral uptake surrounding the lytic lesion in the left orbit



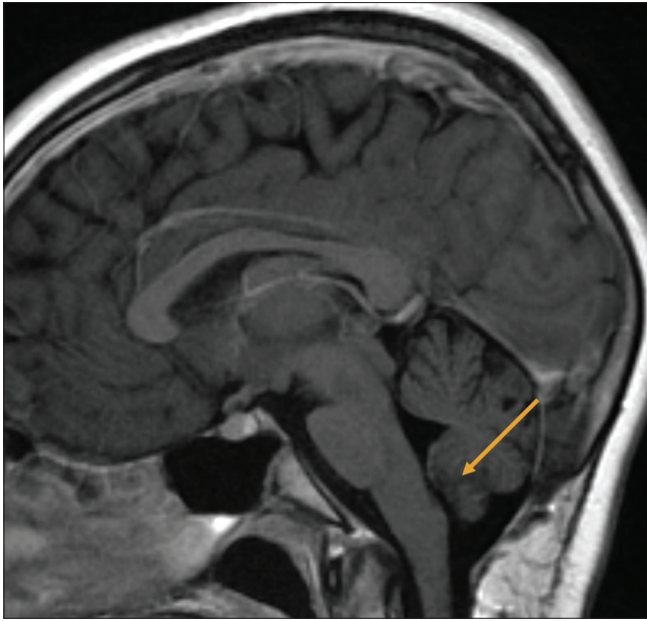
**Figure 3 (A and B):** (A) Diffusion-weighted image demonstrates multifocal areas of diffusion restriction in the cerebellum, (B) demonstrating corresponding decreased signal on ADC map



**Figure 2 (A and B):** (A) Precontrast T1 sagittal image demonstrates bulky cerebellar tonsil. (B) Post contrast T1 sagittal image study shows no abnormal enhancement of the pituitary stalk. However, there was an enhancing mass lesion in the cerebellum



**Figure 4 (A and B):** (A) Follow-up MRI performed 2 days after ventriculostomy and biopsy demonstrates worsening cerebellar edema (orange arrows). Biopsy tract (yellow arrow) was identified. Yellow arrow corresponds to biopsy tract. (B) Brainstem compression



**Figure 5:** Sagittal T1 post-contrast image demonstrates cerebellar atrophy and positive treatment response without contrast enhancement (orange arrow)

brain stem and basal ganglia involvement, which is rare and seen in approximately 4–10% of patients with LCH.<sup>[1]</sup> The neuropathological evaluation done by the CNS LCH Co-operative group has demonstrated that the neurodegenerative lesions do not include the typical CD1a+ cells but rather demonstrate profound neuronal and axonal degeneration in the background of CD8-reactive lymphocytes, resembling paraneoplastic encephalitis.<sup>[3]</sup>

#### Clinical and imaging findings

The clinical presentation of central nervous system (CNS) involvement can be varied and were classified in four patterns by Grois *et al.* in 1998, which included: (1) hypothalamic-pituitary axis involvement leading to diabetes insipidus; (2) site-dependent symptoms from space occupying lesions causing seizures or headaches; (3) symptoms such as ataxia, tremors, dysarthria from involvement of the cerebellar-pontine pathways; and (4) patients with overlap of these symptoms.<sup>[2]</sup>

The imaging findings of LCH can be classified into one of four categories, as described by Prayer *et al.* (1) lesions of the craniofacial bones and skull base with or without soft tissue extension; (2) intracranial, extra-axial change (circumventricular organs i.e. hypothalamic-pituitary axis and meninges); (3) intracranial, intra-axial lesions; and (4) parenchymal atrophy.<sup>[3]</sup>

The most common intracranial findings involve around circumventricular organs (CVO) involving the area postrema, hypothalamic-pituitary region, pineal region and perivascular spaces. It is thought to be secondary to the lack of blood-brain barrier.<sup>[3]</sup> In addition, the

lesions of the CVO region resemble the other lesions found in the other organ systems.<sup>[4]</sup> The involvement of the hypothalamic-pituitary region is in the form of thickening (>3 mm) of the infundibulum with or without loss of normal posterior pituitary bright spot.<sup>[4]</sup> Furthermore, atrophy of the infundibulum is also noted in several patients. Pineal gland involvement is seen in the form of enlargement or cystic changes in the gland.<sup>[3]</sup>

The neurodegenerative pattern involves the dentate nuclei, cerebellar gray matter, pontine pathways and basal ganglia is the second most common pattern of intracranial involvement.<sup>[4]</sup> The signal changes involving the infratentorial gray matter include T1 and T2 hyperintense areas.

The basal ganglia involvement is represented by T1 hyperintense signal; however, on T2-weighted images, these could be hypo, iso or hyperintense.<sup>[3]</sup> In addition, there is typically diffusion restriction involving T2 hyperintense lesions with variable postcontrast enhancement.<sup>[3]</sup> The neurodegenerative pattern is also associated with white matter leukoencephalopathy-like changes due to massive neuronal loss and subsequently Wallerian degeneration.<sup>[4]</sup>

#### Treatment and prognosis

The treatment protocols and duration of treatment of LCH is usually systemic and depends on the organs of involvement.<sup>[5]</sup> The CNS lesions are treated with drugs that cross the blood-brain barrier including cladribine, cytarabine, dexamethasone, IVIG and infliximab.

In addition to the MRI findings involved with hypothalamic pituitary axis, the other intra-axial findings do not necessarily correlate with clinical symptoms and vary widely from asymptomatic to severe neurological dysfunction. It is thought that, despite the prevalence of intracranial involvement, the findings are underreported due to lack of routine imaging in patients without clinical symptoms.<sup>[6]</sup>

More recently, the long-term course of neurodegeneration in LCH demonstrated vast heterogeneity in imaging and clinical presentations.<sup>[6]</sup> Some patients with CNS lesions demonstrate no clinical symptoms whereas others demonstrate mild behavioral, psychiatric or movement-related changes. Overall, the pattern of neurodegeneration manifesting clinically may take years from onset of imaging changes.<sup>[6]</sup>

#### Differential diagnoses

The differential for MRI findings is wide and varies with the regions of involvement. The involvement of the hypothalamic-pituitary region can be seen with other granulomatous disease such as sarcoidosis, lymphoma, hypothalamic gliomas and non-LCH histiocytosis such as



xanthoma disseminatum, multicentric reticulohistiocytosis, Erdheim–Chester disease and sinus histiocytosis with massive lymphadenopathy. The gray white matter changes can be seen with ADEM, gangliogliomas, and infarction. The parenchymal WM changes can also be seen with MS, ADEM, metastasis and sarcoidosis. The extraparenchymal intracranial lesions can be seen with leukemia, lymphoma, meningiomas and choroid plexus papillomas.

#### Teaching points

- LCH classically manifests as bony lesions, extra-axial lesions and as pituitary-hypothalamic or pineal lesions. However, when presented with demyelinating lesions and signal changes in deep gray nuclei, especially in pediatric patients, LCH needs to be considered
  - Early diagnosis leads to appropriate patient management including biopsy and medical treatment. Surgical supportive management may include decompressive procedures
  - Typically, the intra-axial lesions demonstrate altered signal intensities in either white matter or deep gray matter. There may be atypical imaging findings such as multifocal mass-like involvement with adjacent mass effect and areas of diffusion restriction. These changes may be secondary to active demyelinating disease such as ADEM superimposed on the actual disease process
- Early tissue diagnosis and decompression procedure is the key to successful management in these patients.

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#### Conflicts of interest

There are no conflicts of interest.

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