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Solitary intracerebral Langerhans cell histiocytosis. An unusual presentation

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ABSTRACT

Background: Langerhans cell histiocytosis is an uncommon proliferative histiocytic disorder which can affect any organ. It is common in children and can rarely occur in adults. In the central nervous system, the hypothalamic-pituitary axis is most commonly involved. Brain parenchyma is rarely affected.

Case summary: We report a case of a 13-year-old male who presented with chief complaints of headache and swelling over the right frontal region. On imageology, a clinical diagnosis of meningioma was considered. The tumor was excised and on histopathological examination diagnosis of Langerhans cell histiocytosis was considered

Conclusion: Intracranial Langerhans cell histiocytosis is a rare condition which can mimic primary neoplasms of the central nervous system such as glioma, meningioma and metastatic deposits on imageology. Histopathology is the gold standard for diagnosis.

Keywords
Langerhans cell histiocytosis, intracerebral, histiocytosis

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INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disease caused by clonal proliferation of myeloid precursors which differentiates into (CD)1a+/CD207+(Langerin) cells in lesion. [1] It commonly affects the children with incidence of 4 – 5 cases/ year/ million children with age less tha15 years. [2]

Incidence in adults is reported as 1-2/ million adults/ year. [3] LCH can affect any system or organ, but most frequently affects bone, lung, skin, spleen, liver, pituitary, lymph nodes, hematopoietic system and central nervous system. [4] Most common location of intracranial LCH is hypothalamic-pituitary axis and the brain parenchyma is rarely affected. [5] We are presenting a case of LCH involving brain parenchyma at the right frontal convexity and adjacent frontal bone which was clinically diagnosed as meningioma on imageology.

CASE REPORT

A 13 years old male patient presented with chief complaints of head ache and swelling over the right frontal region of head since 1 month, which was gradually increasing in size. There was no history of fever, trauma, ear or nose bleed/ vomiting/ blurring of vision, speech and

smell disturbances. General examination revealed pulse rate - 81/minute, blood pressure- 118/80mm Hg, respiratory rate – 141/min. Glasgow Coma Scale (GCS) scored 15 (E4V5M6). Haematological investigations were with in normal limits.

MRI with contrast study revealed well defined extra axial dural based altered signal intensity lesion measuring 3.2X1.6cms involving right frontal convexity, parasagittal location. The lesion is heterogeneously iso intense to grey matter on T1, T2, FLAIR showing peripheral restricted diffusion with no evidence of blooming. Peripheral post contrast enhancement with dural tail is present. Lesion is infiltrating lateral wall of superior sagittal sinus and mildly extending across midline to left side. Adjacent frontal bone is also involved by lesion. Based on the above findings radiological diagnosis of meningioma was considered.

Patient underwent right frontal craniotomy with excision of tumor. We received 2 grey brown soft tissue bits together measuring 1.3X0.5X0.5cms. Microscopic examination revealed lesion composed of sheets of histiocytes surrounded by eosinophils and lymphocytes (Figure 2). Histiocytes have moderate to abundant pale eosinophilic cytoplasm with elongated nuclei and indistinct nucleoli. Some of them show prominent nuclear grooves (Figure 3). Immunohistochemistry (IHC) showed histiocytes with cytoplasmic positivity for Langerin and membranous positivity with CD1a. Morphology and IHC favoured diagnosis of Langerhans cell histiocytosis

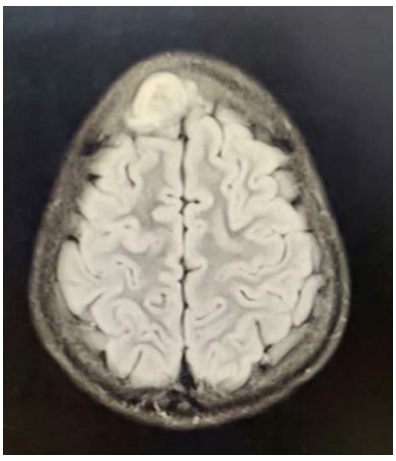

Figure 1. MRI scan showing well defined extra axial iso intense lesion broad base towards dura noted infrontal convexity showing peripheral enhancement.

Discussion

LCH is an uncommon disease involving hypothalamic-pituitary axis in brain, but involvement of the brain parenchyma is infrequent. According to the reviewed literature less than 30 cases have been reported in Pub med data base. [5] The etiology of LCH is still unknown. The histiocytic cells in this lesion stain positive for CD1a and S100 and also form Birbeck granules which is similar to that of Langerhans cells, a specialized dendritic cells found in mucosa and skin. But these cells do not exhibit morphology of dendritic cells. [6]

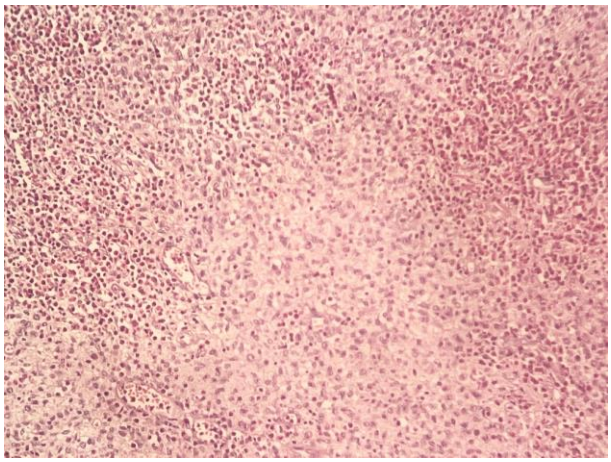

Figure 2. Lesion composed of sheets of histiocytes surrounded by eosinophils and lymphocytes (H&E,X100).

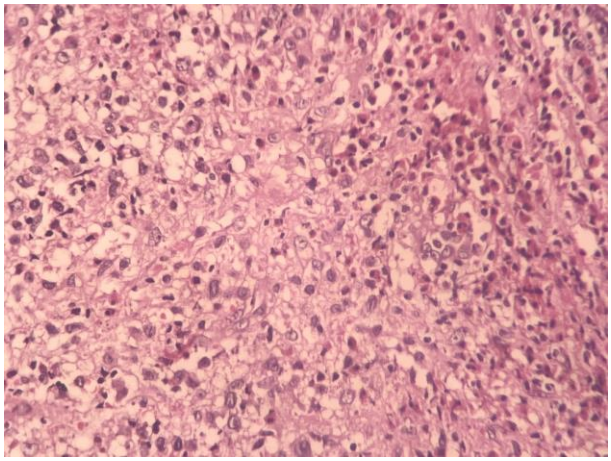

Figure 3. Lesion composed of sheets of histiocytes surrounded by eosinophils and lymphocytes. Histiocytes have moderate to abundant pale eosinophilic cytoplasm with elongated nuclei and some of them are showing nuclear grooves (H&E,X400).

LCH is a disease entity composed of 3 distinct clinical syndrome with indistinguishable histology characterized by presence of Langerhans cells which stain positively with S-100 and CD1a. Clinical syndromes include Hand Schuller-christian disease,

Letterer-Siwe disease and Eosinophilic granuloma. Hand-Schuller-christian disease is characterised by extraskeletal involvement of reticuloendothelial system and multifocal bone lesions. Lettere-Siwe disease is characterized by disseminated involvement of reticuloendothelial systems and has fulminant course in children with age less than 2 years. Eosinophilic granuloma are seen in 5 – 15 years old patients and are limited to bone.

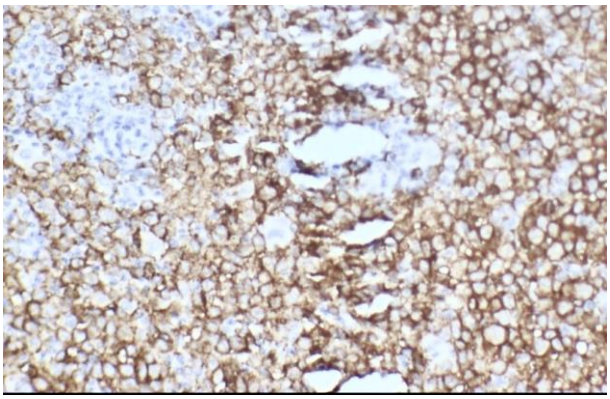

Figure 4. Immunohistochemistry showing membranous positivity with CD1a (CD1a,X400).

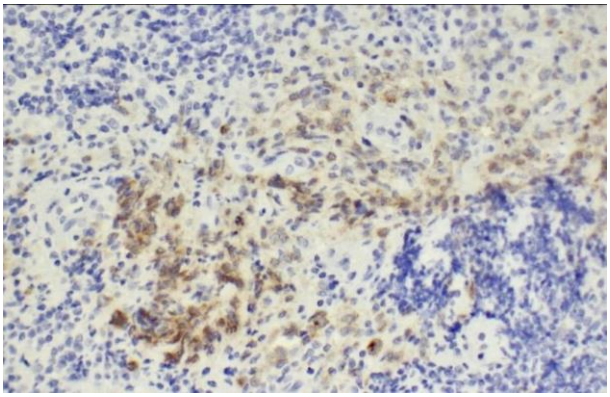

Figure 5. Immunohistochemistry showing cytoplasmic positivity with Langherin (Langherin,X400).

Pathogenesis of LCH is controversial. Cell of origin of LCH is not the Langerhans cell, but a myeloid dendritic cell which expresses CD1a and CD207. Some studies suggest that LCH is a reactive disorder as there was increase in levels of various cytokines in the blood of patients, which indicates possibility of immune response. There were also upregulation of genes associated with T cell recruitment and regulatory T cell expansion. [7] However recent evidences suggest that LCH is a myeloid neoplasia. Many studies have suggested that the oncogenic BRAF V600E mutation was found in high percentage LCH cases in children. Cases with these mutations were having increased relapse. [8,9] LCH patients with BRAF mutations are associated with more aggressive form of disease and poor short term response to therapy. [10]

According to the literature, intracranial LCH are mostly part of systemic disease and only 40% of intracranial LCH are solitary, isolated to brain. [11] Patients presented with headache, polyuria and polydipsia indicating diabetes insipidus in patients with tumors infiltrating posterior pituitary, gait disturbances or ataxia, nausea and/or vomiting, visual impairment and seizures. Other rare symptoms were lethargy, anorexia, and chronic eczema. [12]

Imaging characteristics of LCH on Magnetic Resonance Imaging (MRI) are isointense on T1 weighted MRI and iso to hyper intense on T2 weighted images. On post contrast MRI, lesion is diffusely and homogenously enhancing. On Contrast Tomography (CT) imaging, lesion appears isodense and presents as destructive lesion when involving bone. [12]

Histopathological examination of the lesion is required for the diagnosis. Differential diagnosis of LCH are juvenile Xanthogranulomatosis, Erdheim Chester disease and Rosai Dorfman disease. Juvenile xanthogranulomatosis is a benign lesion often affecting the skin. Histiocytic cells in this lesion are CD68 positive, negative for S-100 and CD1a. They also do not have Birbeck granules. Erdheim Chester disease is characterised by fibrosis surrounding the histiocytes which are positive for CD68 and CD 163 but are negative for CD1a. In Rosai Dorfman disease, multinucleated histiocytes with emperipolesis are seen. Histiocytes in this lesion are S-100 positive and negative for CD1a or CD207. [13]

No specific treatment has been suggested but therapeutic measures implemented were surgical resection, with low dose radiotherapy and combination chemotherapy. [11] Prognosis depends on initial presentation of disease. If the presentation is low risk with isolated involvement of skin, lymphnodes, or pituitary gland, then the mortality is low and is less than 5%. If presents as high-risk disease involving liver, spleen, bone marrow or skeleton, mortality is 50% or more with more wide spread disease. [14]

Conclusion

Intracranial LCH is a rare condition which can mimic primary CNS neoplasms such as glioma, xanthogranuloma, meningioma on imaging and should be considered as one of the differential diagnosis in children. Histopathological examination is the gold standard for diagnosis. Standard treatment protocol is not available due to limited data.

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