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# Langerhans Cell Histiocytosis Masquerading as Hodgkin Lymphoma

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**Conflicts of Interest:** Nil

## Abstract

Langerhans cell histiocytosis (LCH) is a rare clonal proliferative disorder characterized by the accumulation of abnormal Langerhans-type dendritic cells[1]. Although it is classified as a neoplasm, it exhibits a wide spectrum of clinical presentations, ranging from isolated lesions to disseminated, multisystem involvement. LCH primarily affects the paediatric population, with the majority of cases diagnosed in children under the age of 10. However, occurrences in adults, though less frequent, have also been documented. Recent research indicates that LCH arises from myeloid precursor dendritic cells, reinforcing its characterization as a neoplastic disorder rather than a solely reactive process.[2]

Clinically, LCH may involve both nodal and extranodal sites, including the skin, bones, lungs, liver, spleen, and pituatory. The disease is broadly categorized into two forms: single-system LCH, where only one organ or site is affected in which bone is the most common site following skin and lymphnode and Multisystem LCH, where two or more organ systems are involved primarily involving skin[3] and reticuloendothelial system.[4] Liver, spleen, and bone marrow are termed "risk organs" in LCH, as their involvement indicates an increased risk of mortality[5].The differentials for LCH includes lymphoma, Langerhans cell sarcoma, Erdheim-Chester disease (ECD) and Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy) can exhibit overlapping clinical and immunohistochemical features, such as S100 positivity. However, Rosai-Dorfman disease lacks expression of CD1a and langerin, and is characterized by the presence of large histiocytes demonstrating emperipolesis.[6]

In this report, we present the case of an 8-year-old child who presented with multiple enlarged lymph nodes in the cervical and inguinal regions. The clinical, radiological, and pathological findings, final diagnosis of LCH, are discussed in detail to highlight the diagnostic challenges and management considerations associated with this uncommon disease.

**Case report**

An 8-year-old child presented with a two-month history of multiple cervical and inguinal lymphadenopathies, associated with intermittent fever and generalized itching. Initial clinical evaluation raised suspicion of an underlying infective etiology. Ultrasonographic examination revealed multiple necrotic subcentimeter lymph nodes in the involved regions, suggestive of a probable infectious process. To further evaluate the nature of the lymphadenopathy, a fine-needle aspiration (FNA) was performed, followed subsequently by an excisional lymph node biopsy for histopathological examination and definitive diagnosis.

**Pathological Findings**

Although the ultrasonographic findings suggested a probable infective etiology, fine-needle aspiration (FNA) was done to further evaluate the nature of the cervical lymphadenopathy. FNA was performed on the larger lymph node measuring 2×1cm to obtain adequate cellular material for cytological assessment and to guide further diagnostic workup. FNA smears showed polymorphic population comprising of abundant eosinophils, lymphocytes, plasma cells and immunoblasts along with many scattered large bi and multinucleated cells having fine chromatin with no prominent nucleoli, nuclear groove or indentation with abundant cytoplasm gave diagnostic impression as suspicious of lymphoproliferative disorder favourable to Hodgkins lymphoma or LCH. Excisional biopsy and IHC was advised further.

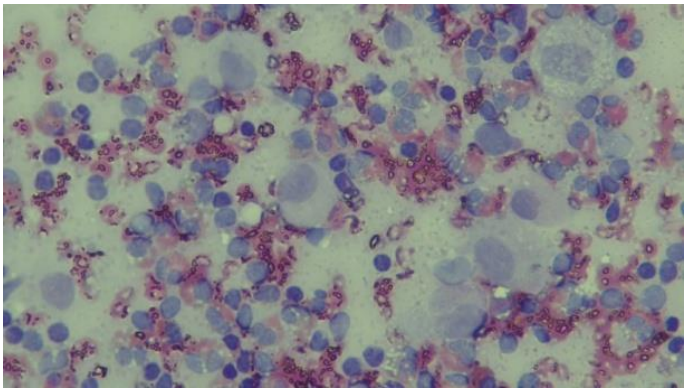


Figure A: Haematoxylin and Eosin stain from the FNA smears showing abundant eosinophils, histiocytes(black arrow head- coffee bean nuclei, orange arrow head- nuclear groove), immunoblasts, lymphocytes.

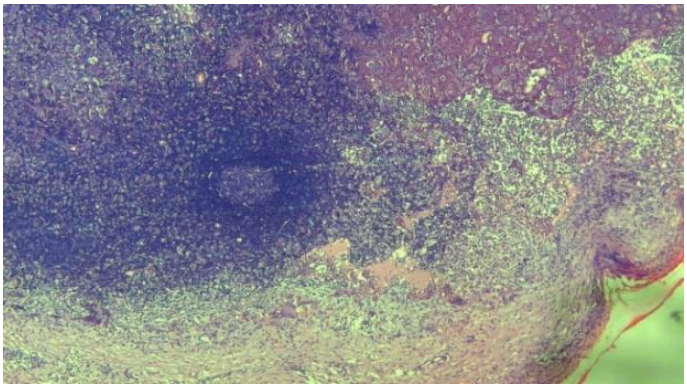
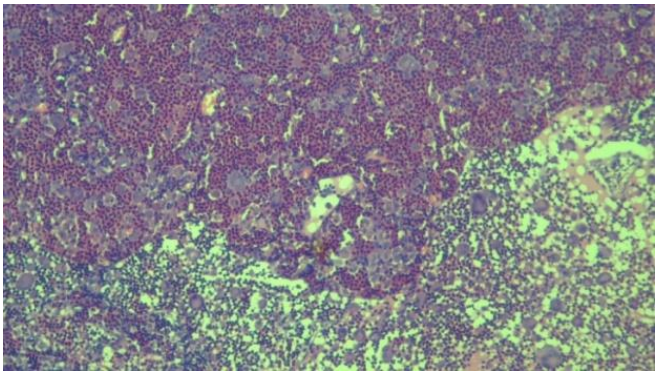


Figure B: Histomorphological picture showing abundant eosinophils with histiocytes in the subcapsular and lymphnode sinuses(Arrow head- abundant eosinophils with histiocytes)



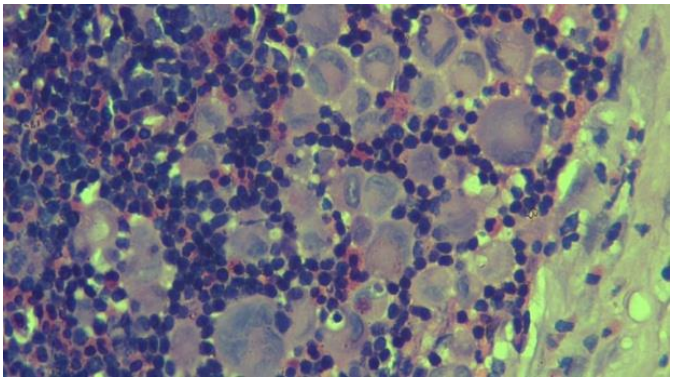


Figure C and D: H and E stained section shows multinucleated Langerhans cell histiocytes with abundant eosinophilic abscess (red arrow head- Multinucleated histiocytes).

Histopathological examination of the excised cervical lymph node revealed extensive effacement of the normal nodal architecture. Numerous multinucleated Langerhans cells were prominently noted in the subcapsular region. These cells were characterized by irregular nuclear contours, nuclear grooves, and abundant eosinophilic cytoplasm. Surrounding these cells were foci of eosinophilic abscesses composed predominantly of eosinophils and histiocytes, further contributing to the architectural distortion. To confirm the lineage of the atypical cells, immunohistochemistry (IHC) was performed. The Langerhans cells demonstrated strong nuclear and cytoplasmic positivity for S100 protein, a characteristic marker of dendritic lineage. Additionally, CD68, a marker of histiocytic origin, showed diffuse cytoplasmic positivity in the background histiocytes and CD1a showing membranous positivity. The combined histomorphological features and immunohistochemistry supported the diagnosis of Langerhans cell histiocytosis.

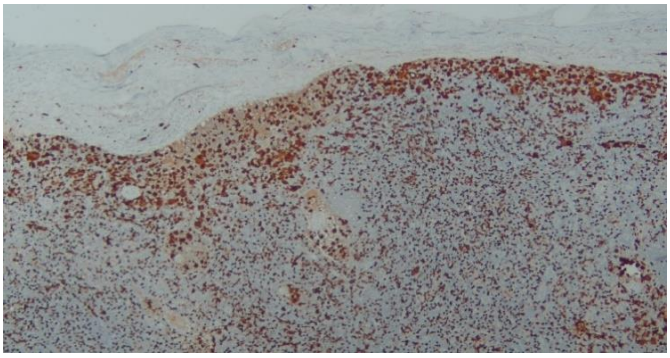


Figure E: S100 showing nuclear and cytoplasmic positivity in langerhans cell in subcapsular region

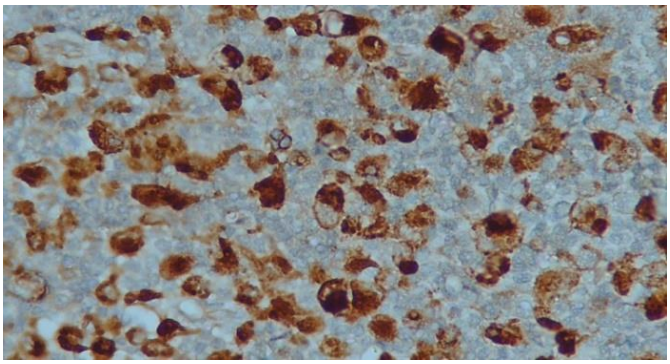


Figure F: CD68 showing cytoplasmic positivity.

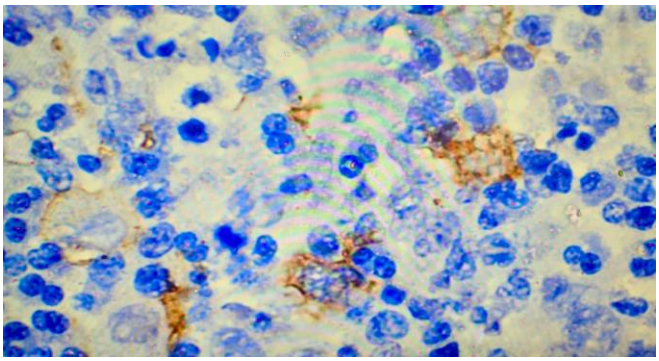


Figure G: CD1a showing membranous positivity.

**Discussion**

In the present case, the patient presented with cervical lymphadenopathy, a common presentation shared with various lymphoproliferative disorders, including Hodgkin and non-Hodgkin lymphomas. Imaging and clinical evaluation were non-specific, raising suspicion for neoplastic or infectious process. On histopathological examination, the lymph node architecture was completely effaced, and numerous large, atypical,

multinucleated Langerhans cells were observed in the subcapsular region, accompanied by eosinophilic abscess, a feature sometimes seen in LCH but not typical for lymphoma.

Given the significant architectural distortion and the presence of large atypical cells, the differential diagnosis initially included Hodgkin lymphoma and anaplastic large cell lymphoma, Rosai Dorfman disease (RDD) and Erdheim-Chester disease. However, immunohistochemistry played a crucial role in narrowing the diagnosis. Usually langerhans cells demonstrate immunoreactivity for S100 protein and CD1a, along with markers such as CD68, langerin, vimentin, p53, and bcl-2.[7] ECD typically presents in older adults and is histologically distinguished by the presence of lipid-laden histiocytes that lack expression of CD1a and S100, in contrast to the immunophenotype seen in LCH.[8] Where as RDD does not show expression in CD1a and Langerin.

In our case Langerhans cells showed strong nuclear and cytoplasmic positivity for S100 and cytoplasmic positivity for CD68. These findings, along with the characteristic morphology, were consistent with LCH. The inclusion of markers such as CD1a and Langerin (CD207) would further substantiate the diagnosis, as they are more specific to Langerhans cells, though not always available in routine panels.

This case highlights the importance of considering LCH in the differential diagnosis of lymphadenopathy with atypical histiocytes, especially when the clinical and radiological features suggest lymphoma. Misdiagnosis can lead to inappropriate treatment, as management strategies for LCH differ significantly from those for lymphomas. LCH may require systemic therapy or targeted treatment like BRAF inhibitors in BRAF V600E mutated cases.[9] whereas lymphomas are treated with cytotoxic chemotherapy or radiotherapy. Recent studies have identified BRAF V600E mutations in over 50% of LCH cases, as well as in individuals with Erdheim-Chester disease.[10]

**Conclusion**

Langerhans cell histiocytosis is an uncommon but important mimicker of lymphoma, particularly when it presents with lymph node involvement and architectural effacement. This case underscores the critical role of histopathological evaluation supported by immunohistochemistry in distinguishing LCH from hematolymphoid malignancies. clinching such presentations is essential to avoid misdiagnosis and to guide appropriate clinical management. Accurate diagnosis not only prevents unnecessary chemotherapy but also ensures timely and specific treatment of the disease. Recent discovery of somatic BRAF V600E mutations in more than half of LCH lesions confirms the neoplastic nature of this disease and provides a potential target for treatment by providing the BRAF inhibitor in LCH patients has shown promising results.[11]

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