Otitis Media in an Infant - A Case Report of Langerhans Cell Histiocytosis

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ABSTRACT

Langerhans cell histiocytosis is a clonal proliferation of myeloid dendritic cells expressing a Langerhans cell phenotype. It can be unifocal or multifocal within a single system (usually bone) or it can be multisystem. Annual incidence in children is about 5 cases per 1 million. The disease is more common among individuals of European origin and Hispanics.[2] Here we describe a case of a 9-month-old male baby who presented with right sided ear discharge for 2 weeks and a mass protruding through the right ear. Radiological evaluation revealed a lytic lesion in the temporal bone which was histologically confirmed as a case of Langerhans Cell Histiocytosis.

Keywords: LCH, Otitis Media, Infant

*See End Note for complete author details

INTRODUCTION

Langerhans cell histiocytosis is a disorder characterised by histiocytic/dendritic cell proliferation with accumulation of dendritic cells and other inflammatory cells including eosinophils, giant cells, neutrophils, foamy histiocytes and accompanied by areas of fibrosis. It is the most common histiocytic disorder. Majority of the patients are younger than 30 years of age and males are often affected with the M:F ratio being 1.2:1.[1]

In the case of LCH, granulomatous lesions comprising langerin-positive histiocytes (CD207+) and an inflammatory infiltrate can arise in virtually any organ system but have a particular affinity for bone, skin, the lungs, and the pituitary. LCH has a widely variable clinical presentation, ranging from single indolent lesions to explosive multisystem disease.[4]

Patients with multisystem LCH are often infants presenting with fever, cytopenia, skin and bone lesions and hepatosplenomegaly. Children with liver, spleen or bone marrow involvement are at the highest risk for death from LCH and are therefore classified as having high-risk LCH. Although clinical outcomes have steadily improved over the past decades, standard-of-care chemotherapy (vinblastine, prednisone and mercaptopurine) fails to cure more than 50% of children with high-risk disease and majority have long term consequences like neurodegenerative syndrome.[4]

CASE PRESENTATION

A 9-month-old male baby presented with discharge from the right ear in the past 1 week which later turned mucopurulent for another week and was later on associated with a reddish polypoidal mass protruding from the right ear. There was no history of fever, shortness of breath, loose stools, dysuria or decreased activity. The baby was incessantly crying and there was associated rhinitis. The child was admitted in a local hospital where he was given intravenous antibiotics and other supportive measures.

After radiological evaluation, a clinical diagnosis of Right Acute Mastoiditis with Subperiosteal abscess was made, and was advised subperiosteal abscess drainage. The parents disagreed to do the procedure due to financial constraints and were later referred to our hospital.

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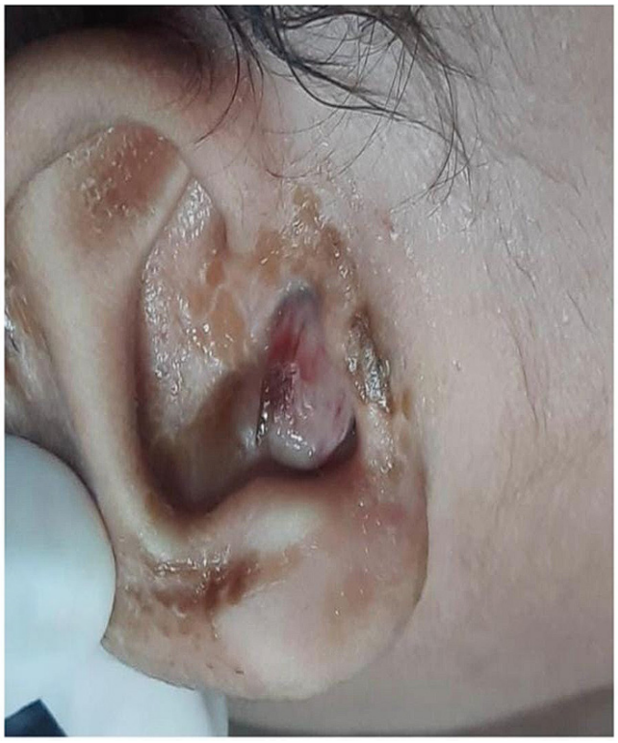

Figure 1. **Yellowish-brown Ear Discharge**

On examination of the right ear, there was a reddish polypoidal mass seen in the right external auditory canal, **(Figure 1)** yellowish-brown ear discharge was present. The child was active, alert and afebrile. General physical examination and systemic examination revealed no significant abnormality.

The child is developmentally normal and vaccinated upto age and there is no relevant past medical ,surgical or family history. Routine blood investigations showed Hb-9.1 g/dl,MCV - 65fl, MCH - 20.2pg, MCHC - 31.1g/dl, PCV- 29.3%, Total WBC count - 14400 cells/cumm, Differential count - N-37%, L-51%, E-1.7%, M-10% and Platelet count of 6.69 lakh/cumm. ESR was 2mm/hr. CRP was elevated - 23.9mg/L.

Peripheral smear revealed Hypochromic Microcytic Anemia and Thrombocytosis. Renal function tests, liver function tests, Serum electrolytes revealed normal study. Further tests like ECG, Chest Xray, USG Abdomen showed no significant abnormality.

HRCT Temporal Bone revealed a soft tissue density in the middle ear cavity mea. 3.5x2.4x3.5cm, with characteristic post-contrast enhancement and with necrotic areas causing near total destruction of the right mastoid bone, destruction of the right facial canal, right lateral semicircular canal and extending into the right external auditory canal and right retro auricular region - possibly Complicated CSOM with granulation tissue and cholesteatoma formation and Left-sided uncomplicated CSOM **(Figure 2).**

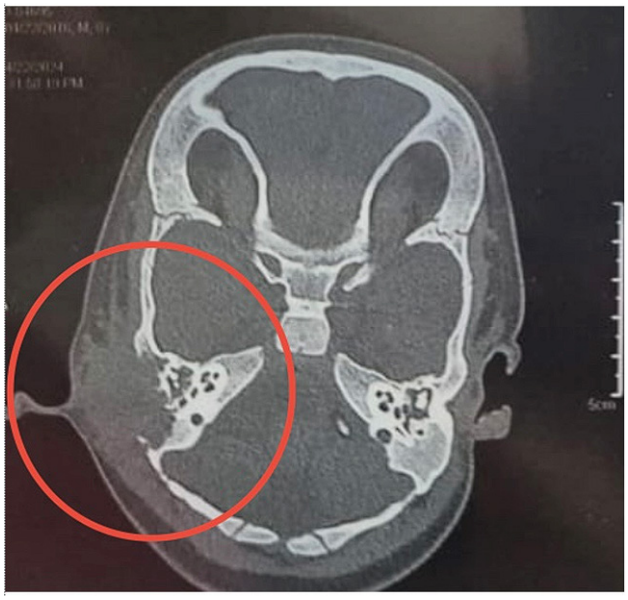

Figure 1. **HRCT Temporal Bones - Soft tissue density in the right middle ear cavity causing erosion of the mastoid bone**

MRI Brain with MR Venogram (Plain And Contrast), revealed a large destructive lesion measuring 3x2.4x2.6cm, in the right temporal bone with epicentre in the mastoid associated with moderately enhancing lobulated soft tissue thickening and causing destruction of posterior wall of external auditory canal and filling the canal, erosions of lateral walls of tympanic cavity and sigmoid sinus. No intracranial extension seen.

The lesion is causing smooth anterior indentation and luminal narrowing of the distal sigmoid sinus. No luminal encroachment or thrombosis seen **(Figure 3).**

Few enlarged bilateral posterior cervical nodes with short axis diameter upto 1cm was seen.

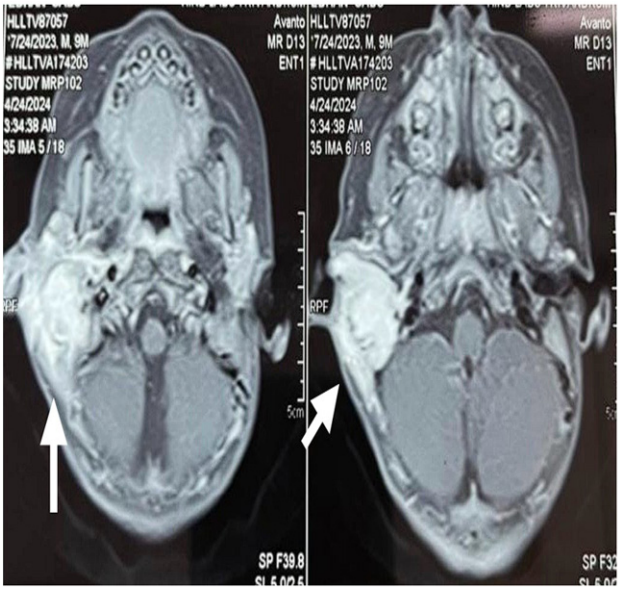

Figure 3. **MRI Brain showing a large lytic lesion in the temporal bone with adjacent soft tissue enhancement**

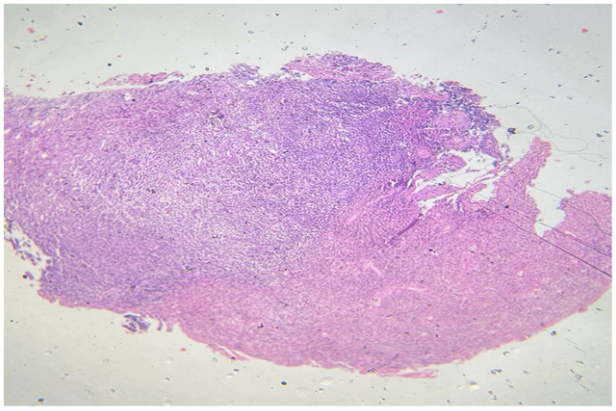

Figure 4a. **Scanner view**

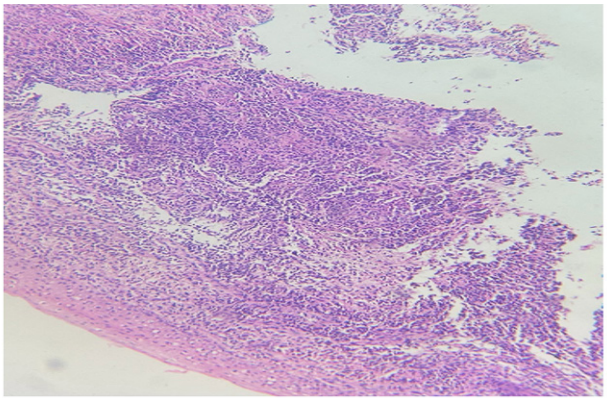

Figure 4b.**100x, showing diffuse pattern of the neoplasm**

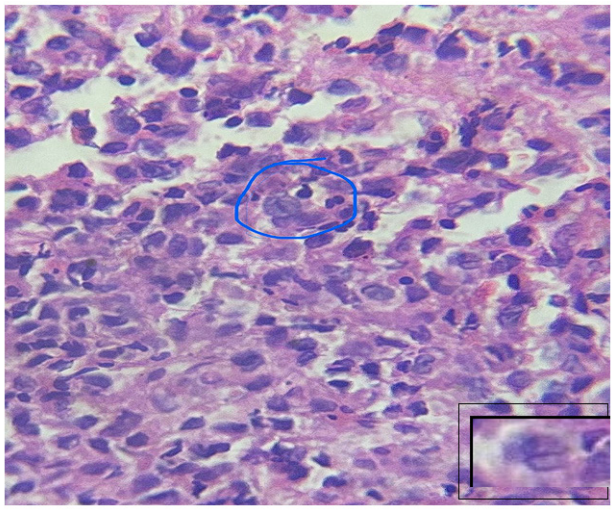

Figure 4c. **Cells have moderate eosinophilic cytoplasm, oval vesicular nuclei with fine chromatin land showing folded grooved nuclei ,400x (inset shows nuclear grooving)**

No significant intracranial abnormality and no evidence of any other lytic lesions in visualized bones were noted.

Differential diagnoses considered were

1. Langerhans Cell Histiocytosis,
2. Aggressive neoplasms like Rhabdomyosarcoma,
3. Lymphoma

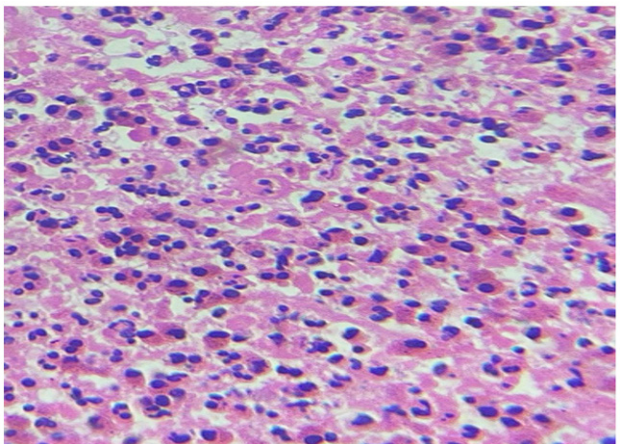

Figure 4d. **Inflammatory cells composed predominantly of eosinophils with areas of necrosis, 400x**

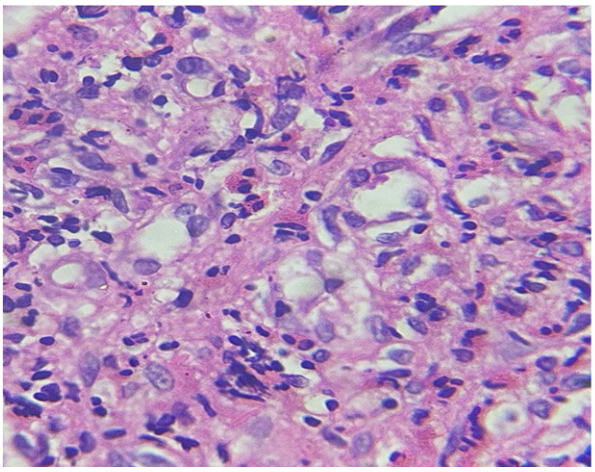

Figure 4e. **Proliferated blood vessels, 400x**

Examination Under the Microscope of the right ear with a biopsy of the polypoidal lesion seen only outside of the External auditory canal was done under local anesthesia in the ENT Department.

We received two grey-white tissue bits aggregate measuring 0.6x0.2x0.1cm. The Cut section was grey and white. Microscopy showed tissue fragments lined by stratified squamous epithelium and a neoplasm composed of cells arranged diffusely, interspersed among these are numerous inflammatory cells composed of predominantly eosinophils with neutrophils, plasma cells, and areas of hemorrhage. Individual tumor cells are oval with moderate eosinophilic cytoplasm, and oval vesicular nuclei with many having grooved, folded nuclei with fine chromatin and minimal nuclear atypia. Areas of dense inflammation and necrosis are present. Proliferated capillaries with plump endothelial cells were noted in between **(Figures 4 a-e).**

Immunohistochemically, the cells showed diffuse strong positivity for CD1a, S100 and CD68 **(Figures 5,6,7).**

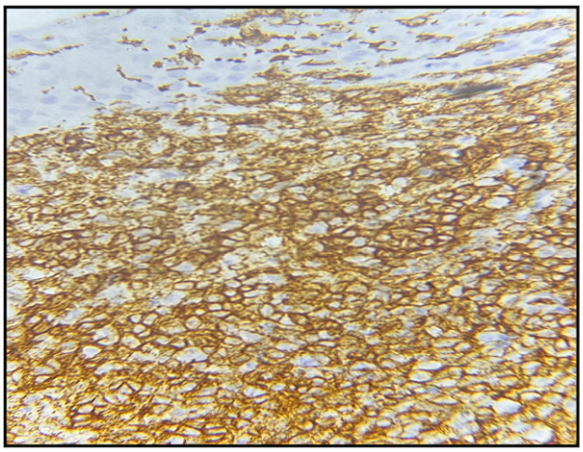

Figure 5. **Immunohistochemistry - CD1a**

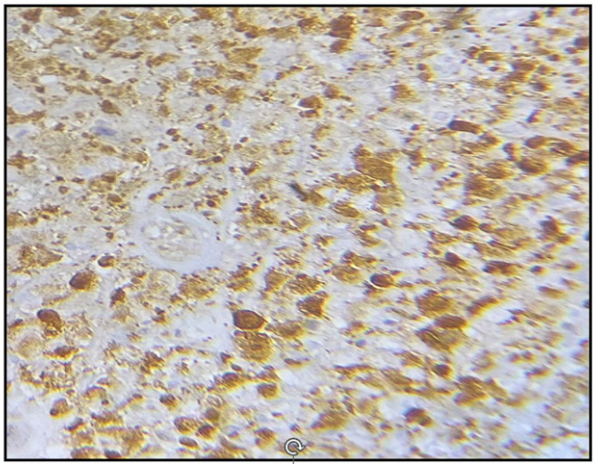

Figure 6. **Immunohistochemistry - S100**

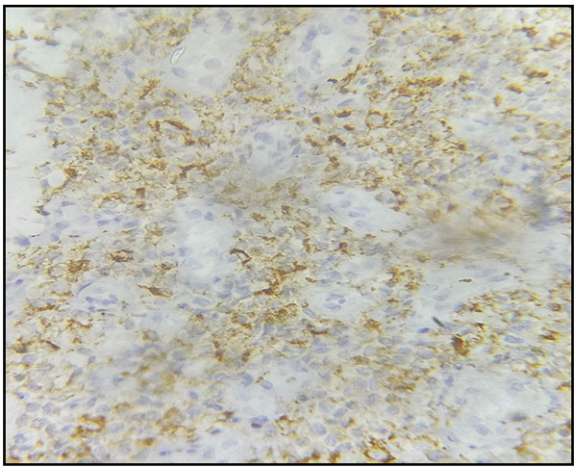

Figure 7. **Immunohistochemistry - CD68**

CD34 highlights the vasculature **(Figure 8).** Desmin was negative **(Figure 9).**

Hence, the diagnosis of Langerhans Cell Histiocytosis was made.

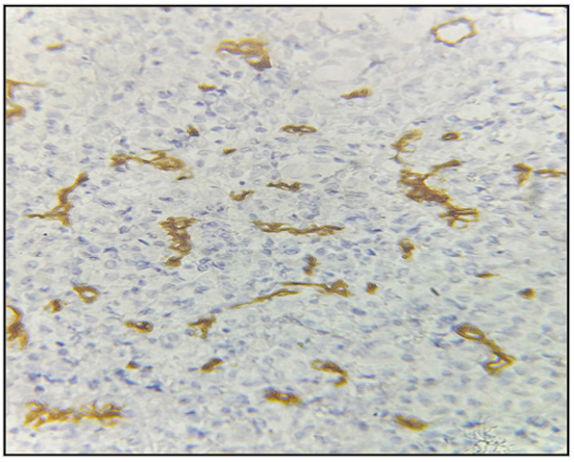

Figure 8. **Immunohistochemistry - CD34**

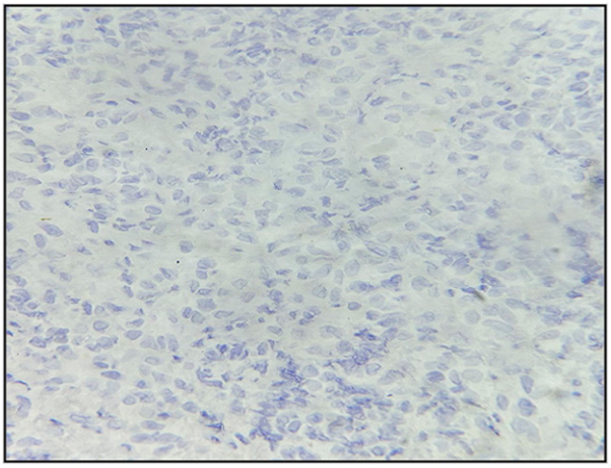

Figure 9. **Immunohistochemistry - Desmin**

DISCUSSION

The incidence of Langerhans cell histiocytosis (LCH) is similar to that of pediatric Hodgkin's lymphoma, raising the question of whether LCH is an "orphan disease" or one of the most common pediatric cancers. This identity crisis not only has limited the development of rational therapeutic strategies for patients with LCH but also has hindered access to funding and organisational resources that have catalysed advances in other pediatric neoplastic disorders.[4]

The benign histologic appearance of the CD207 + cell, the accompanying inflammatory infiltrate and the characteristic local and systemic cytokine storm support an inflammatory origin of LCH whereas clonality, somatic activating gene mutations in the Mitogen Activated Protein Kinase (MAPK) pathway, and shared mutations with hematopoietic precursors favour reclassification of LCH as a myeloid neoplastic disorder.

BRAF V600E mutation is associated with 57% of the cases. The BRAF V600E mutation renders the MAPK pathway constitutively active.

The state of differentiation of the hematopoietic stem cell precursor cell in which somatic MAPK activating mutations arise defines the clinical extent and severity of disease. In the proposed misguided myeloid differentiation model. Activating MAPK mutations in pluripotent hematopoietic stem cell precursors may give rise to high risk LCH, whereas the same mutations in more committed or tissue restricted precursors can give rise to multifocal low risk LCH and mutations in a local precursor can give rise to a single lesion.[1,4]

According to the Histiocyte Society's 2009 evaluation and treatment guidelines, single-system LCH is defined by the involvement of one organ system (unifocal or multifocal), and multisystem

LCH is defined by the involvement of two or more organs/systems (with or without risk organ involvement, the risk organs being - hematological system, spleen and the liver). Multiple bone lesions can be associated with proptosis, diabetes insipidus, chronic otitis media or a combination of these historically referred to as Hand–Schüller–Christian disease. It has a prolonged clinical course with a favorable outcome.[1,3]

Letter-Siwe disease, the development of Langerhans cell histiocytosis in multiple organ systems follows a more aggressive course.

Diagnosis of LCH is clinicopathologic and along with clinical and radiological features, should always be based on histological and immunophenotypic examination of lesional tissue that should be taken from the most easily accessible, yet representative lesion.

There is a well-defined histologically characteristic appearance of the LCH lesions on H&E sections, but positive CD1a and/or CD207 (Langerin) staining of the lesional cells is required for a definitive diagnosis. Electron microscopy is no longer needed since it has been shown that expression of Langerin correlates with the ultrastructural presence of Birbeck granules.[5]

Upon receiving the diagnosis of LCH, the child was referred to RCC, Thiruvananthapuram where he underwent 14 cycles of chemotherapy without surgery consisting of iv injections of vinblastine every week along with prednisolone syrup.

FDG PET CT revealed a hypermetabolic lesion in the right temporal bone and mastoid process. No evidence of new hypermetabolic lesions in the rest of the scan. The child has to undergo further more cycles. There is no visible mass in the right ear at present and the child is currently doing well.

CONCLUSION

Our patient was an infant male with single system LCH with unifocal bone involvement. Unifocal lesions are the predominant clinical form of LCH. The decision on the most appropriate treatment approach should be based on clinical symptoms, the size and location of the disease and on any evidence of healing on imaging. Often, simple curettage during diagnostic biopsy will result in spontaneous regression or healing and further intervention may not be necessary.

Because of the potential for development of sequelae, systemic therapy is indicated in patients with lesions involving the skull base, temporal bone, orbits, and vertebral column, where there is also involvement of soft tissues.[5]

END NOTE

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Conflict of interest : None declared

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