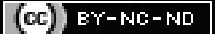


# Langerhans Cell Histiocytosis with Temporal Bone Involvement- A Case Report

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## ABSTRACT

Langerhans Cell Histiocytosis (LCH) is a rare disorder of the reticuloendothelial system associated with proliferation of Langerhans cells and mature eosinophils. The hallmark of LCH is the proliferation and accumulation of a specific histiocyte: the Langerhan's cell. Any organ or system can be affected. Here, a case of multisystem LCH with skeletal, lung and hepatobiliary involvement in a two-year child who presented with painless forehead swelling following trauma. The patient was systematically worked up with blood investigations, imaging and histopathological analysis which ultimately revealed the diagnosis of LCH. This case report is unique in that it presented with involvement of temporal bone wherein it can be confused with inflammatory pathologies like Cholesteatoma and tumours like Rhabdomyosarcoma. The child was started on vinblastine based chemotherapy and showed good response to therapy. This case report discusses the imaging differential diagnosis in temporal bone LCH along with utility of Positron Emission Tomography and Computed Tomography (PET-CT) in planning treatment of these cases.

**Keywords:** Histiocyte, Multisystem, Temporal bone

## CASE REPORT

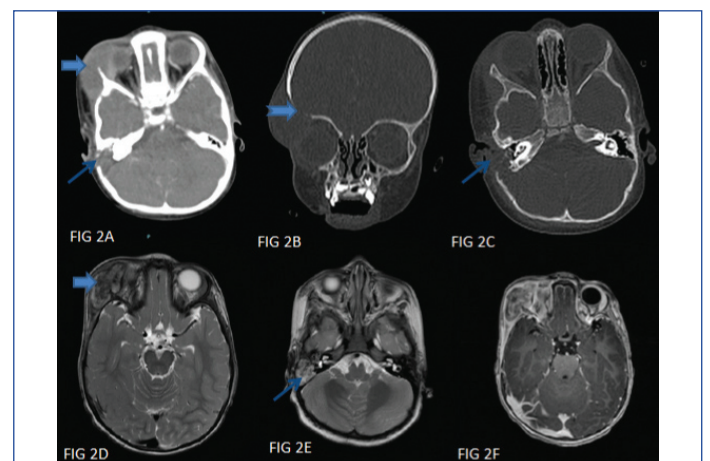
A two-year-old girl presented to Department of Paediatrics with history of right frontal swelling. The child had a history of fall six weeks back, followed by swelling over right forehead which resolved within two weeks. A recent gradual increase in the size of the swelling was seen. Family history was unremarkable. Past history of the child was remarkable for ear discharge on both sides since 6 months, scalp rash and nail changes since the age of four months and one year of age, respectively.

On examination, the right forehead swelling was soft, non fluctuant with no impulse on crying. Crusty, scaly, seborrheic dermatitis like rash was seen over the scalp. Granuloma/ polyp-like tissue were seen protruding through the external auditory canal. Longitudinal lines were seen on nails of both the hands [Table/Fig-1A-D]. Liver was palpable slightly below the costal margin in mid-clavicular line. Rest of the examination was within normal limits. The differential diagnosis at this stage was growing skull fracture or neoplastic lesion like metastasis.



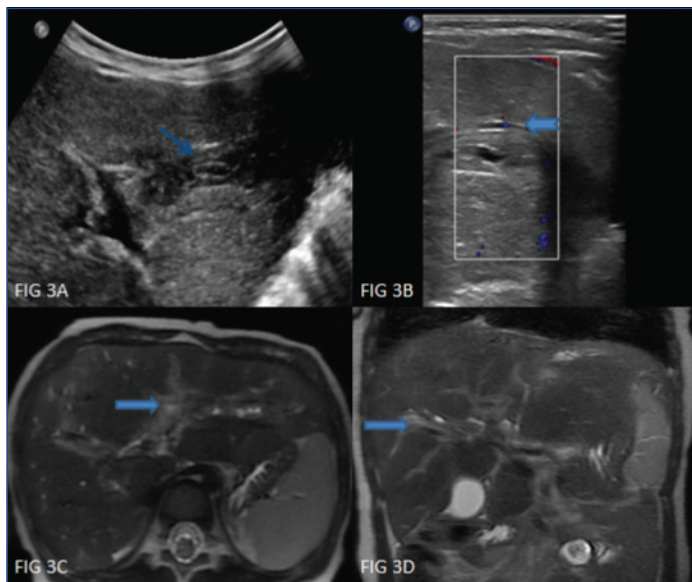
**[Table/Fig-1]:** (A) Showing frontal swelling in right supraorbital region (Thick arrow). Longitudinal nail lines were seen (B) With seborrheic dermatitis like rash all over the scalp (Arrow in C). (D) Showing right aural polyp like lesion (Notched arrow).

Pertinent blood investigations revealed anaemia (Hb=9 gm%) with mild leucocytosis. Other routine blood biochemistry tests including serum electrolytes and liver function tests were normal. The child was then referred to imaging for the assessment of scalp swelling. CT scans revealed an expansile lytic lesion involving right frontal bone and adjoining roof of right orbit. The lesion was causing destruction of inner and outer tables of skull with beveling of edges and associated soft tissue component. Intraorbital extension was seen into superior extraconal compartment causing mild proptosis of right eye. Similar lesion was also seen in right temporal bone with its epicenter in mastoid air cells and resultant loss of pneumatization. Erosion of posterior wall of external auditory canal was seen with extension to external ear as aural polyp. No obvious extension to middle ear cavity seen though the tympanic membrane is not visualised. Ear ossicles appear intact with no erosion. Lateral mastoid cortex and tegmen tympani also appear intact. On Magnetic Resonance Imaging (MRI), lesions appear predominantly T2 hyperintense with areas of diffusion restriction and heterogeneous post-contrast enhancement [Table/Fig-2A-F].



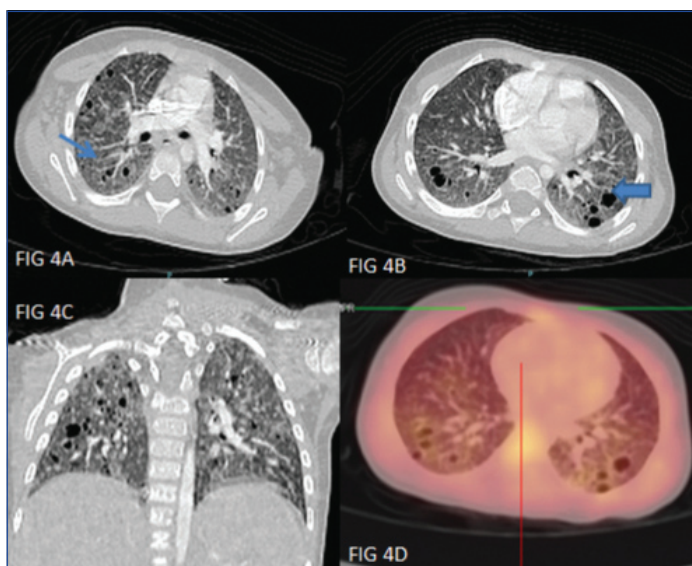
**[Table/Fig-2]:** (2A) Showing expansile lytic lesions involving right frontal bone (thick arrow) and within right mastoid air cells (thin arrow). On bony window settings (2B), Lytic lesion demonstrates beveled edge with no sclerotic rim (notched arrow). The right mastoid lesion is seen extending to external auditory canal with no ossicular erosion (thin arrow) (2C). MRI (2D and E) demonstrates gourd-shaped soft-tissue masses in right frontal and mastoid regions (thick arrow in 2D and thin arrow in 2E) with heterogeneous post contrast enhancement (2F).

The child was then evaluated for hepatomegaly using Ultrasonography (USG) and MR imaging. On sonography, hepatomegaly was seen with evidence of mild intrahepatic biliary dilatation in both lobes of liver. Furthermore there was evidence of linear hypoechoogenicity along the dilated biliary radicles. On MRI, these appeared as diffuse T2 hyperintensities in periportal location of both lobes of liver. On Magnetic Resonance Cholangiopancreatography (MRCP), evidence of alternate focal dilatations and narrowing of intrahepatic biliary tree mimicking picture of that seen in sclerosing cholangitis [Table/Fig-3A-D].

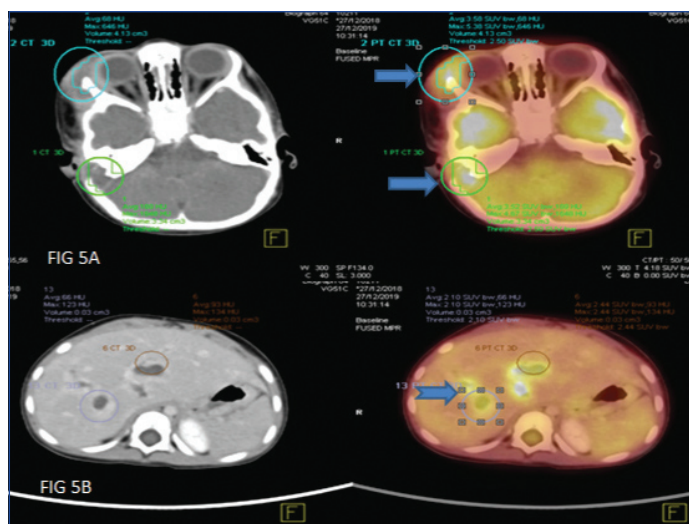


**[Table/Fig-3]:** High resolution ultrasonography showing diffuse periportal hypoechoogenicity in both lobes of liver (arrow in 3A), mild prominence of intrahepatic biliary radicles (notched arrow in 3B) with MRI (3C and D) demonstrates hepatomegaly with diffuse T2 hyperintense periportal cuffing in both lobes of liver (thick arrows).

In view of multisystem involvement, PET-CT was done to assess the accurate extent of the disease. The lytic lesions in calvarium were Fluorodeoxyglucose (FDG) avid with right frontal lesion exhibiting SUV max of 5.4 and right temporal lesion showing Standardized Uptake Values (SUV) max of 4.7. No other metabolically active focal bony lesions were seen. On chest CT, there was evidence of multiple cysts of size 0.5 to 1.5 cm scattered in both lungs with predominant affliction of lower lobes. Associated thickening of interlobar interstitium seen with low uptake (SUV max of 2.5 to 3) on PET scans. The periportal hypo-attenuating lesions identified on USG and MRI showed FDG avidity with SUV max of 2.4 [Table/Fig-4,5].

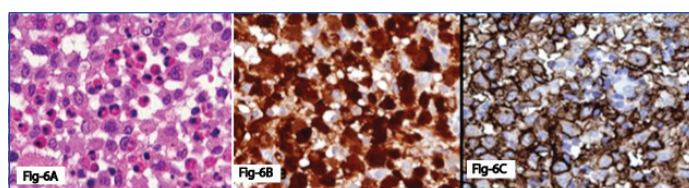


**[Table/Fig-4]:** Axial (FIG 4A and 4B) and coronal (FIG 4C) CT scans in lung window multiple cysts of variable sizes with associated thickening of interlobar interstitium and lower lobe preponderance.



**[Table/Fig-5]:** On PET-CT, A and B shows metabolically active lytic lesions in right frontal (blue circle) and mastoid bone (green circle) demonstrating SUV Max of 5.4 and 4.7, respectively (arrows). Periportal cuffing in liver shows SUV Max of 2.4 (circles in both) with associated mild dilatation of intrahepatic biliary radicles (notched arrows).

Biopsy was done from right external auditory canal polypoidal lesion which revealed sheets of mixed inflammatory cells intermixed with large polygonal cells with round to oval nuclei and indistinct cytoplasm. Surrounding inflammatory infiltrate predominantly composed of many eosinophils and few lymphocytes, multinucleated giant cells were seen. On Immunohistochemistry (IHC), CD1a and S-100 were positive in many of the large cells. The above morphological and IHC findings were suggestive of LCH [Table/Fig-6A-C].



**[Table/Fig-6]:** Light microscopy of biopsy specimen (Hematoxylin and Eosin, x 400) showing large polygonal cells with round to oval nuclei and indistinct cytoplasm with surrounding inflammatory infiltrate composed of predominantly eosinophils (6A). Immunohistochemistry (IHC) showed CD1a (6B) and S-100 (6C) positivity in many of the large cells (magnification x400).

Risk stratification was done based on the organ involved in which involvement of liver, spleen, hematopoietic system and lungs are considered as those with high risk or target organ involvement. Based on the International collaborative treatment protocol for children and adolescents with LCH, the child was placed in stratum I category and started on Vinblastine 6 mg/m<sup>2</sup> i.v. weekly bolus for six weeks, with prednisone 40 mg/m<sup>2</sup>/day given orally in three divided doses for four weeks and then tapered over the following four weeks [1]. Follow-up PET-CT showed good metabolic response to therapy with virtual total resolution of right mastoid soft tissue with decrease in right frontal lesion [Table/Fig-7] and also reduction in extent of lung and peribiliary involvement in liver. Based on PET-CT findings and according to the protocol, 6-Mercaptopurine was added to Prednisolone and Vinblastine and currently the child is on follow-up.

## DISCUSSION

Langerhan's cell histiocytosis (LCH) is an uncommon hematological disorder affecting infants and young children [1]. It represents a clonal proliferation of Langerhans cells with dendritic cell features. LCH can affect patients of any age, although most present less than 15 years, with males being slightly more commonly affected than females [2]. It was formerly known as Histiocytosis X, encompassing three classic clinical syndromes that are considered to be clinical variations of the same disease: 1) Eosinophilic granuloma (benign localised form, restricted to bone and often monostotic); 2) Hand-Schuller-Christian disease (classic triad of skull lesions, exophthalmos, and diabetes insipidus); and 3) Letterer-Siwe disease (disseminated





**[Table/Fig-7]:** Follow up PET-CT showing near complete resolution of right mastoid lesion with right frontal bone lesion showing decrease in volume of right frontal region from previous of 17.4 cm<sup>3</sup> to present of 3.4 cm<sup>3</sup> (green circle). However, its SUV MAX remains more or less same at 5.5 suggestive of partial response to therapy.

lesions involving multiple visceral organs). Current classification is based on the number of lesions and the involved systems, wherein it can be divided into three stages: Single system (Stage 1), Low-risk multisystem (Stage 2), and Multisystem with risk-organ involvement (Stage 3) [3].

Flat bones of the skull are the most frequently involved. Other organs like skin, pituitary, liver, spleen, lung and lymph nodes can also be involved [4]. Disease involvement of risk organs such as the liver and spleen is a sign of poor prognosis [5]. About 50 to 80% of paediatric LCH is found in the head and neck regions. The temporal bone is involved approximately 15 to 60% of cases in skull base region [6]. The present case depicts multisystem manifestations involving bones, lung and hepatobiliary system.

Any bone can be involved in LCH. There is a predilection for flat bones, with the skull being most frequently involved, followed by the pelvis, spine, mandible, and ribs [7]. In patients with calvarial LCH involvement, the parietal and frontal bones are the most commonly affected. The typical imaging appearance of calvarial LCH on CT images is characterised by punched-out destructive lesions with non-sclerotic margins and a beveled edge [8]. MRI aids in the depiction of bone marrow or soft tissue involvement, but the signal intensity of these lesions is non-specific. Most frequently, LCH has low to intermediate signal on T1-weighted images and high signal on T2-weighted images, except in the healing phase when the signal is low on T2 imaging [8].

LCH in temporal bone is usually confused for inflammatory lesions like cholesteatoma and malignant tumours like Rhabdomyosarcoma. In LCH of the temporal bone, there is no characteristic clinical presentation and it varies a lot depending on the site of involvement. In the study done by Zheng H et al., they concluded that the paediatric cases with LCH of the temporal bone have no characteristic clinical features. Bilateral ear involvement can be seen in about half of cases, so the evaluation of both ears is necessary. The ossicular chain usually remains intact and the erosion of otic capsule occurs in about 18.4% of the cases. They also provided clues to differentiate LCH from cholesteatoma. Intact ossicular chain with breach in outer table of mastoid favor LCH as was present in this case. Lack of enhancement and diffusion restriction are features of cholesteatoma which were not there in the present case [9].

Another entity which can be confused in temporal bone region is Rhabdomyosarcoma. In study done by Chevallier KM et al.,

they concluded lesions involving only the anterior portion of the temporal bone (petrous apex and middle ear) are more likely to be rhabdomyosarcoma and lesions involving the mastoid are more likely to be LCH [10]. In infants and children, pulmonary LCH occurs as a part of disseminated LCH (multifocal and systemic forms). In review of Pulmonary LCH done by Bano S et al., they concluded that High-Resolution Computed Tomography (HRCT) allows a confident prospective diagnosis of Pulmonary Langerhans cell histiocytosis (PLCH) in the appropriate clinical setting. They also emphasised on use of Minimum Intensity Projection (MinIP) in all cases of pulmonary LCH for demonstration of occult cystic lesions. The clinical course and prognosis is variable with frequent regression or stability of the abnormalities [11].

Children with LCH often present with hepatomegaly along with multi-organ involvement. Histopathologically, liver shows periportal infiltration of langerhan's cells, resembling sclerosing cholangitis, bile ductular distortion with variable amount of fibrosis, nodules or even cirrhosis in end stages [12]. Imaging findings depends on the histologic phase of the disease. In early proliferative phase, lesions appear hypoechoic on USG which can be band like or nodular with some having target like appearance. These appear hypo-attenuating on CT with post-contrast enhancement. In advanced xanthomatous stage, lesions appear hyperechoic on USG; have low attenuation on CT with characteristics of fat on MR imaging [13].

Accurate risk stratification is important for determining the treatment plans and prognosis in patients with LCH. PET-CT is ideal for determining the extent of LCH in the initial evaluation and follow-up, because it can assess the physiological activity of the LCH lesion [14]. However, the exposure to ionising radiation limits the use of PET-CT, as patients with LCH require multiple imaging studies to monitor treatment response and detect possible recurrence during the course of their disease. PET-CT also has intrinsic limitations in the evaluation of LCH lesions in the Central Nervous System (CNS) and lungs. Whole Body MRI (WB-MRI) has been applied to a wide range of oncologic indications, including LCH, as it has a great capacity for the characterisation of soft tissue lesions with the absence of exposure to ionising radiation [15].

The present case report is similar to that of Ni M and Yang X wherein they reported a case of temporal bone LCH with multiorgan involvement and concluded that lesions in target organ have higher incidence of complications and mortality [16].

## CONCLUSION(S)

Although the diagnosis of LCH mainly depends on pathology and IHC, imaging findings have a major role in assisting an accurate diagnosis. Cross-sectional imaging with CT and MRI along with PET-CT help not only in planning treatment and accurate initial risk stratification based on target organ involvement, but also in monitoring treatment follow-up of these patients.

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