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CASE REPORT

Ear Discharge and Destructive Postauricular Mass: An ENT Manifestation of Langerhans Cell Histiocytosis

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Abstract

Langerhans cell histiocytosis (LCH) is a rare, life-threatening condition that predominantly affects children. It is a diagnostically challenging condition due to several different clinical presentations. Presentations of LCH with otological involvement are considered rare. We report a case where LCH presented a six-month-old boy to our tertiary teaching hospital. The patient presented with a unilateral left postauricular soft tissue mass, with an associated left external ear canal lesion and middle ear effusion, which initially had the working diagnosis of mastoiditis. However, further imaging and molecular testing concluded the final diagnosis as LCH with multisystem involvement. When LCH does have otological involvement, it commonly involves the external and the middle ear, which can often be confused with otitis media and otitis externa. This case report highlights that misdiagnosis of LCH can occur due to its broad presentation. The case report also raises the importance that in cases of unilateral postauricular soft tissue masses with destructive findings on cross-sectional imaging and systemic symptoms and signs, LCH must be a differential diagnosis, and biopsy should be considered.

Key words: Langerhans cell histiocytosis; ear, nose and throat (ENT); case report

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Introduction

Langerhans cell histiocytosis (LCH) is a rare condition, predominantly affecting children. LCH is a heterogeneous disease, where dendritic cells accumulate in the body's organs and is an inflammatory myeloid neoplasia which can be classified into three categories: unifocal, multifocal uni-system and multisystem (Vashisht et al, 2015). Whilst the most affected systems are the skeletal system, skin and pituitary, all organs or body systems can be affected (Haupt et al, 2013). LCH should be suspected in patients who present with lytic bony lesions, a skin rash, arginine vasopressin deficiency, pituitary mass or respiratory symptoms. Whilst it predominantly affects children, it can affect patients of all ages. It is a diagnostically challenging condition due to its broad presentation. Diagnosis of LCH recommends biopsy of the lesion tissue using imaging features and establishing B-Raf proto-oncogene, serine/threonine kinase (*BRAF*) or another mitogen-activated protein kinase extracellular signal-regulated kinase (MAPK-ERK) pathway mutational status (Goyal et al, 2022). Treatment is dependent on both the severity of the disease and the extent of the disease. LCH is a rare disease, therefore, there is a limited previous randomised controlled trials and large surveys available.

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This case focuses on the LCH multisystem with organ involvement (Vashisht et al, 2015). Prognosis is determined by organ involvement in the initial presentation. Low-risk disease constitutes involvement of the skin, bones, lymph nodes and pituitary glands (Tillotson et al, 2024), whilst high-risk disease involves the bone marrow, liver, spleen and lungs (Jezierska et al, 2018). Involvement of the ear is uncommon, and in rare reported cases, diagnosis is often delayed because the presentation resembles mastoiditis (Hong et al, 2020). We report a case where LCH presented with a unilateral left postauricular soft tissue mass, with an associated left external ear canal lesion and middle ear effusion.

A review of the literature using PubMed (https://pubmed.ncbi.nlm.nih.gov/), Embase (https://www.embase.com) and Google Scholar (https://scholar.google.com/) was performed to ascertain the current understanding of LCH in researching this case.

Case Report

A six-month-old boy presented to our tertiary teaching hospital generally unwell, with several recent paediatric emergency department visits in the last month for Respiratory Syncytial Virus (RSV) and bronchiolitis. He had a reduced appetite, a non-blanching rash to the torso, and pancytopenia. He was previously well, with no significant past medical or perinatal history. He was admitted under the paediatric haematology and oncology team who organised a bone marrow biopsy, which excluded leukaemia. An ear, nose, and throat (ENT) review was sought when the patient's left ear started discharging, a left postauricular mass and a left external auditory canal lesion were also noted; instead of, a differential diagnosis of mastoiditis was proposed.

Cross-sectional imaging was performed. A temporal bone computed tomography (CT) (Fig. 1) and head magnetic resonance imaging (MRI) showed significant destruction of the adjacent petrous bone and mastoid process of the lesion. An open biopsy of the postauricular soft tissue mass proved highly consistent with LCH (Figs. 2,3,4,5,6,7). Further imaging, including a whole-body MRI (Figs. 8,9), a chest X-ray and an abdominal X-ray reported left lower zone patch consolidation, hepatomegaly, splenomegaly and multifocal bony lesions affecting the left mastoid, 11th thoracic vertebra and possible left tibial involvement. Vinblastine and prednisolone induction therapy were started, alongside blood product transfusions. The parents were kept informed throughout and counselled appropriately.

Finally, molecular diagnosis showed the involvement of the *BRAF* codon 600 variant and V600E/V600E2/V6000D defects. *BRAF* is a human gene responsible for producing the protein B-Raf, which is involved in signalling direct cell growth (John Hopkins Medicine, 2023).

The final diagnosis was LCH with multisystem involvement. The patient continues to be managed by the paediatric haematology and oncology multidisciplinary team.

The CARE Checklist has been attached as **Supplementary material** associated with this article.

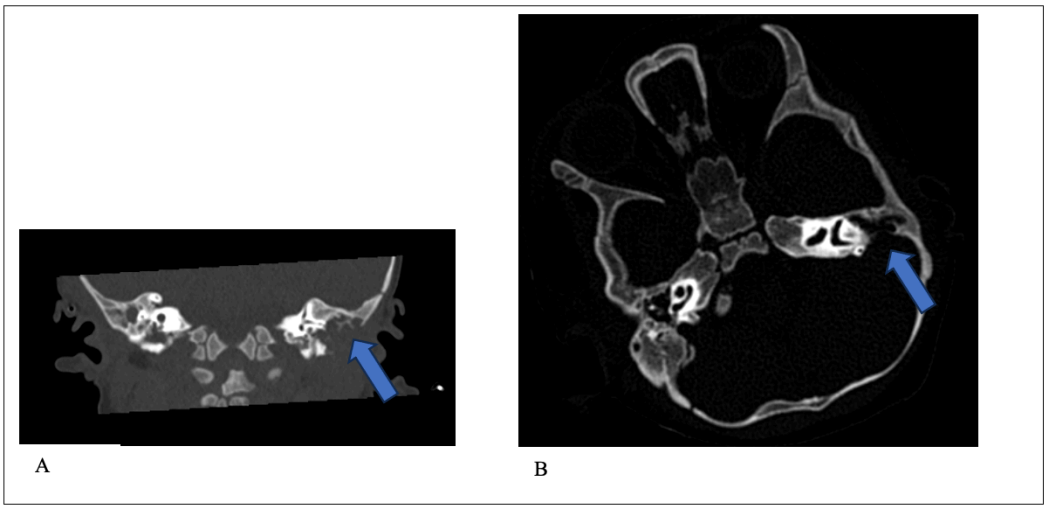

Fig. 1. Coronal (A) and Axial (B) Temporal bone computed tomography (CT), showing extensive destruction of the left mastoid (shown by arrows).

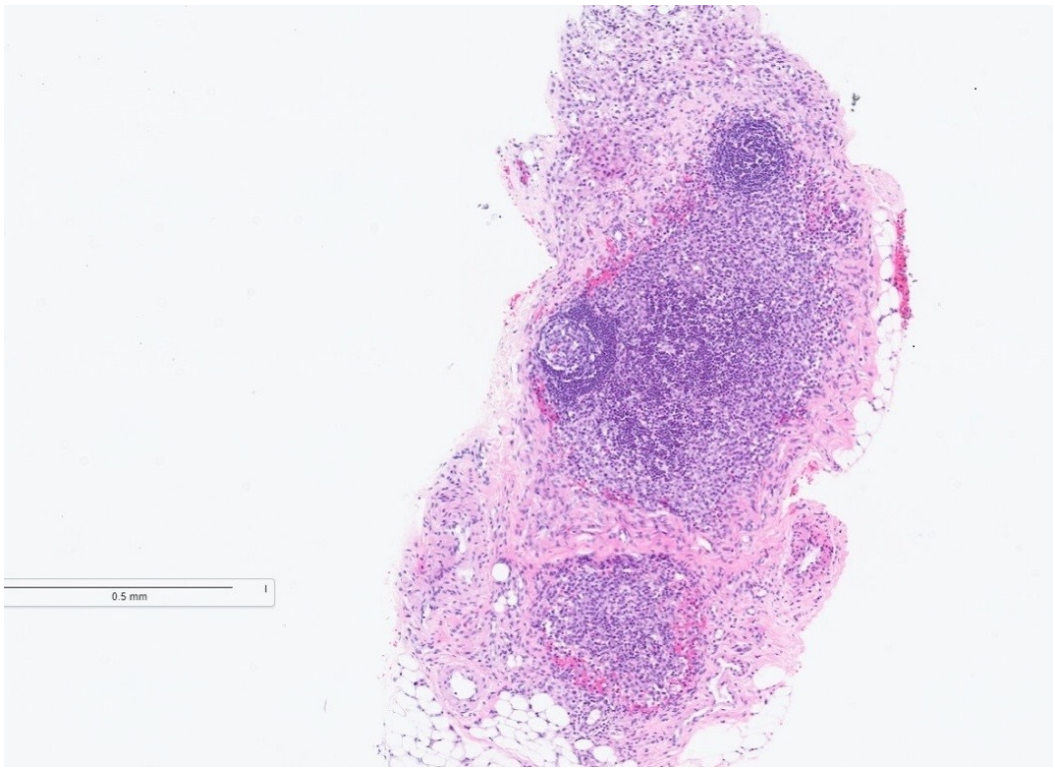

Fig. 2. Histology image: left postauricular nodule comprising Lymphoid infiltrate with reactive germinal centre surrounded by numerous medium-sized, pale histiocytic cells.

Discussion

LCH is a rare condition where there is abnormal proliferation or differentiation of cells from the myeloid lineage (Allen et al, 2018). Studies have shown that in over 80% of cases, there has been MAPK-ERK pathway activation, which includes *BRAF-V600E* and mitogen-activated protein kinase kinase 1 (*MAP2K1*) mutations (Badalian-Very et al, 2010). LCH usually affects children, but it can also affect

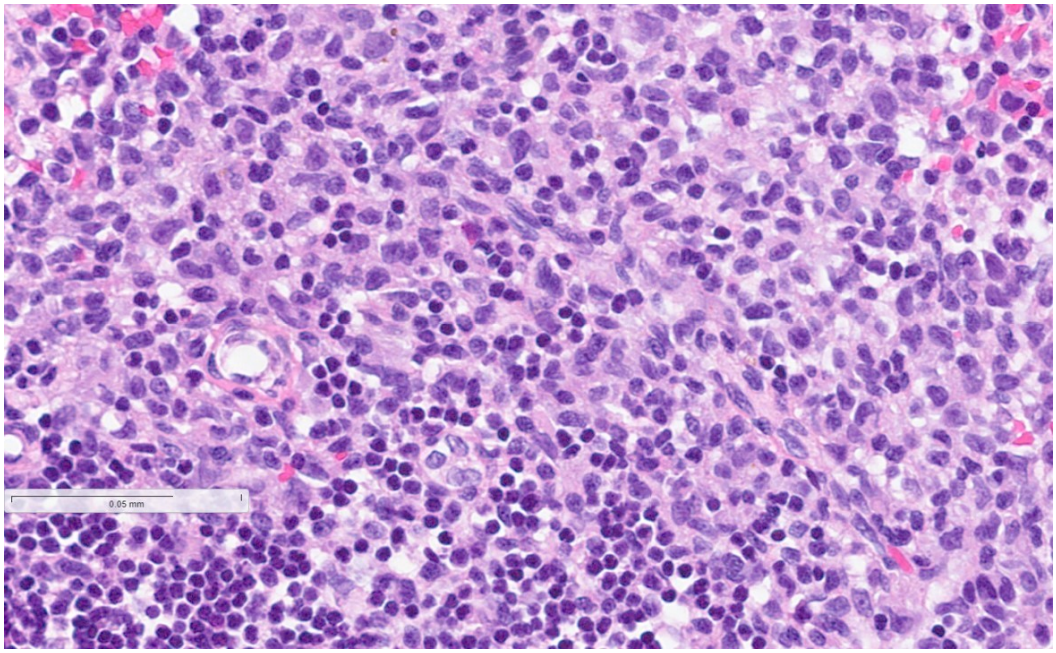

Fig. 3. Higher magnification showing a histiocytic population.

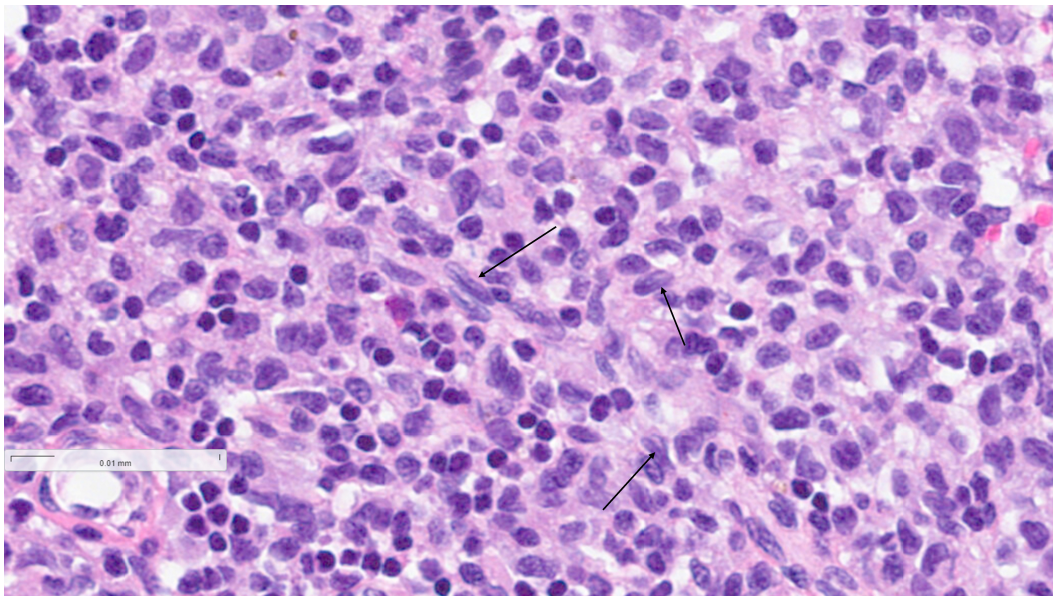

Fig. 4. Convoluted nuclei with nuclear grooves (shown by arrows).

adults. Children are usually affected between the ages of 1 and 15, with the highest incidence shown between 2 and 4 years old (Rao et al, 2017). LCH is twice as likely to affect males as females (Yashoda-Devi et al, 2012).

LCH was previously called "histiocytosis X" and was further split into three subtypes. These current subtypes are now called Single-System Single Site (SS-s), Single-System Multi-Site (SS-m), and Multisystem type (MS). LCH Multisystem type can present with different organ involvement. Different organs involved can be considered either low risk or high risk, with the skin, bones, lymph nodes and pituitary glands considered low risk and bone marrow, liver, spleen, and lungs con-

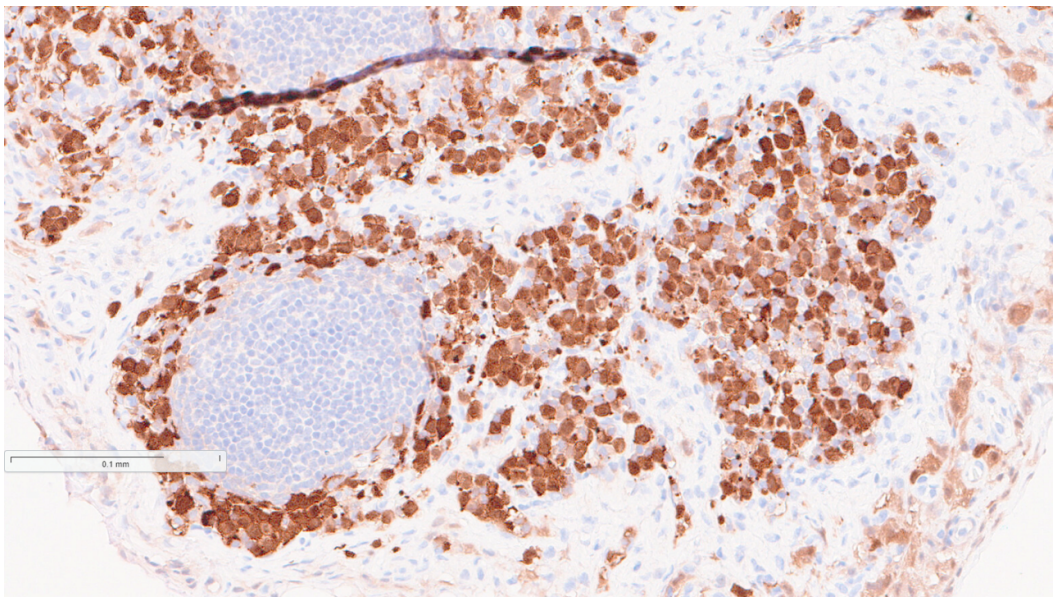

Fig. 5. S100+ cells.

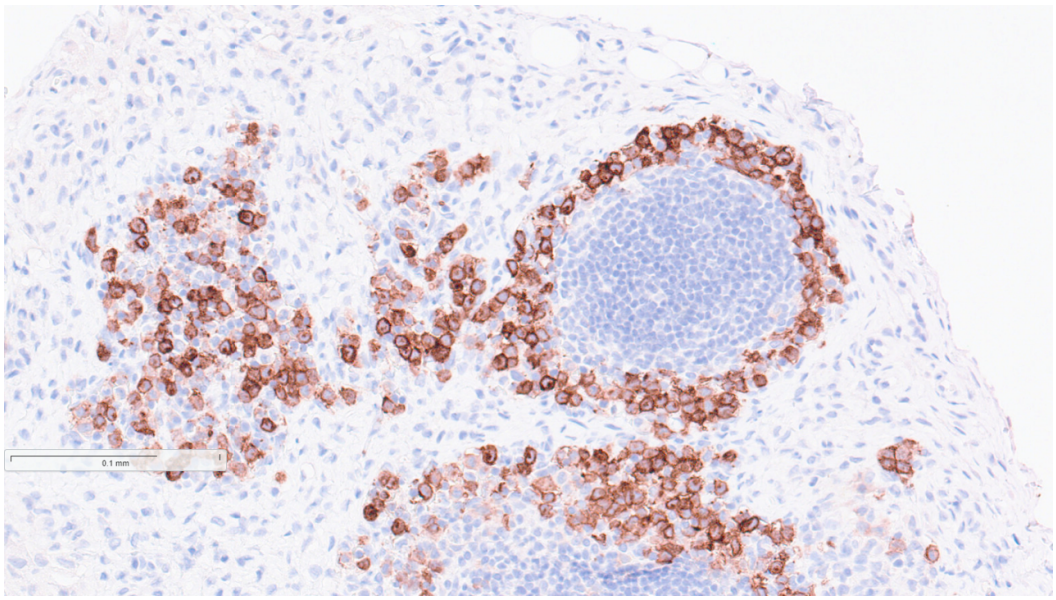

Fig. 6. CD1a+.

sidered high risk. Involvement of high-risk organs impacts treatment and prognosis (Jezierska et al, 2018). High-risk LCH can be diagnosed when LCH cells are present in the spleen, liver, lungs or bones. The presence of pathological LCH cells in these organs is associated with high mortality and worsening prognosis (Allen et al, 2018). One study showed that of the children with LCH, two-thirds were classed as single-system, which had a five-year survival rate of effectively 100%. Whereas, those patients with multisystem LCH proved to have more uncertain outcomes by comparison (Feng et al, 2021).

LCH has several different clinical presentations; presentations with otological involvement are considered rare. When LCH does have otological involvement, it

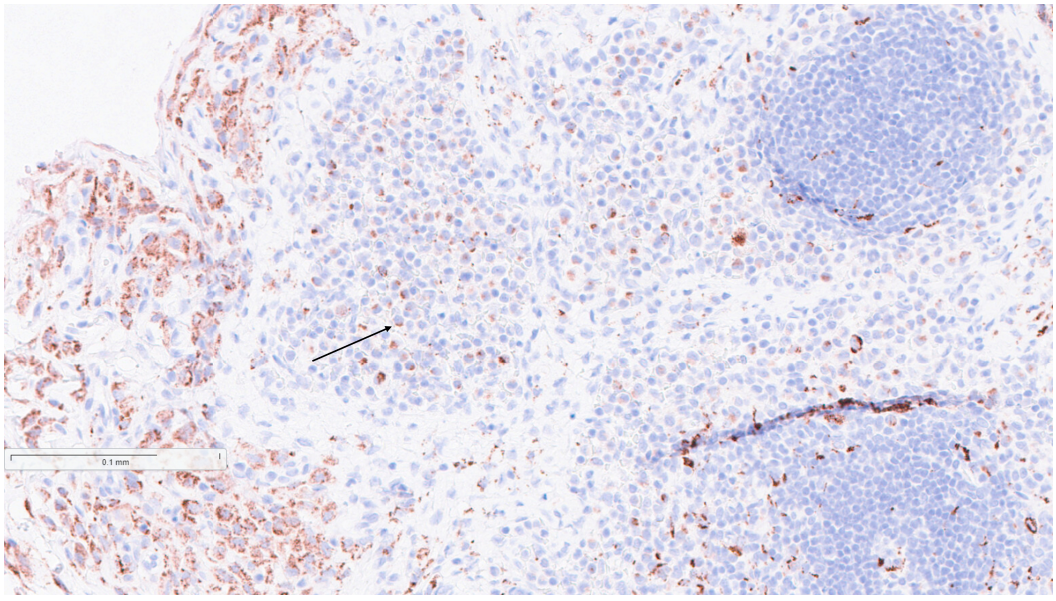

Fig. 7. CD68 showing dot-like Golgi staining in Langerhans cells (shown by arrow).

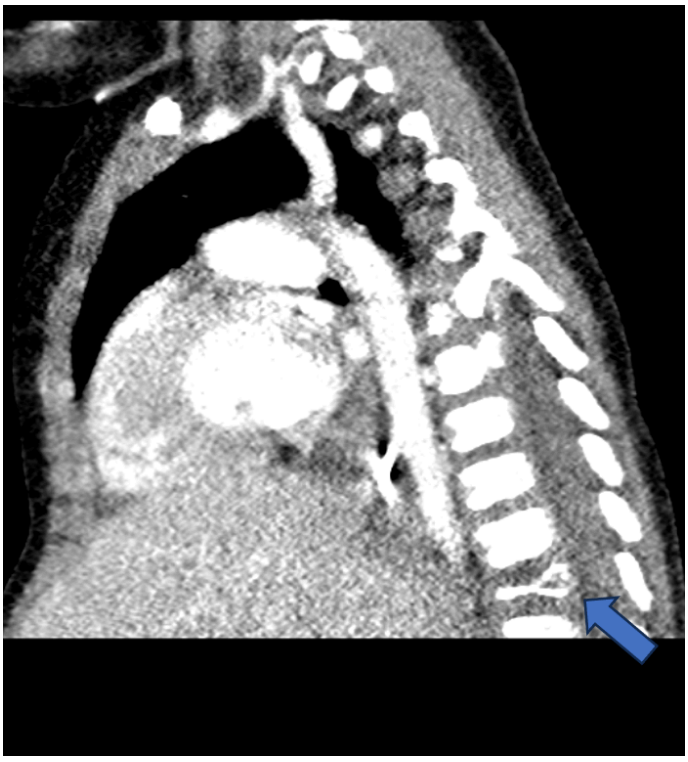

Fig. 8. Magnetic resonance imaging (MRI) demonstrating thoracic vertebra involvement (shown by arrow).

commonly involves the external and the middle ear, which can often be confused with otitis media and otitis externa. Studies have shown that the misdiagnosis rate for LCH is approximately 72.7% due to clinical presentations being very similar to common conditions such as otitis externa and otitis media (Ni and Yang, 2017).

LCH is diagnosed through immunohistochemistry or electron microscopy. *BRAF-V600E* mutations are seen in 40%–70% of LCH patients (Alayed et al, 2016).

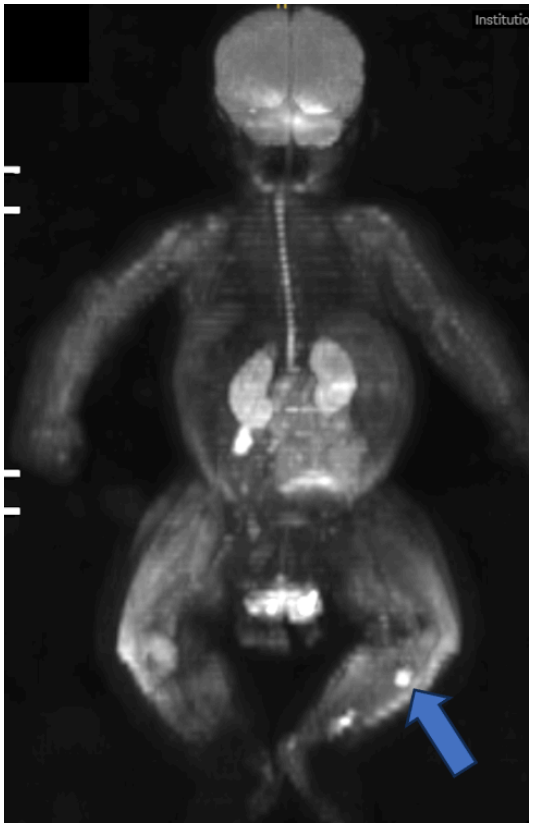

Fig. 9. Whole-body MRI demonstrating possible left tibial involvement (shown by arrow).

For the diagnosis of LCH in paediatric patients, the current gold standard is a positive result of CD1a or Langerin CD207. Gene mutations in MAPK pathways are also becoming recognised to aid diagnosis, specifically or more difficult-to-diagnose cases (García Díaz et al, 2022).

There is currently no standard treatment for LCH, and the treatment plan is devised according to the clinical presentation. Steroids, chemotherapy, and kinase inhibitors can be used as part of targeted therapy. Reoccurrences of LCH have been observed, whilst not quantified, and the highest rates of reoccurrences have been seen in unifocal disease where bony lesions mainly occur in the femur, orbit, intracranial bones, maxilla and mandible (Al Abdulsalam et al, 2022).

Patients who are long-term survivors potentially encounter long-term consequences of LCH. These consequences may include endocrine deficiencies, such as diabetes insipidus and growth hormone deficiency (Jezierska et al, 2018). Those with LCH that affect the cranial bones, with intracranial soft tissue extension, are specifically at risk of diabetes insipidus (Grois et al, 2006). Other long-term consequences include orthopaedic problems, hearing loss or reduction, visual impairment, central nervous system (CNS) issues, reduced lung function and impaired liver function. Patients who have LCH are also at significant risk of developing secondary cancers such as leukaemia and non-Hodgkin lymphoma. One of the most severe consequences is LCH-associated neurodegenerative CNS-LCH. This can occur after treatment and recovery of LCH, presenting as slow, progressive cognitive and motor dysfunction (Grois et al, 2010). As LCH can cause manifestations

either at diagnosis or many years later, the literature suggests that it is important to continue to monitor these paediatric patients, sometimes up to adulthood. Recommendations depend on the LCH presentation in each patient. However, all patients should have routine assessments at clinically appropriate intervals to assess their history of thirst, polyuria, height, weight, pubertal status and neurological status. These patients should also have blood tests to include full blood count, erythrocyte sedimentation rate, liver enzymes and albumin (Haupt et al, 2013).

For patients with bone involvement, it is recommended that X-rays should be taken at 6 weeks, 3 months, and 6 months. If a patient has vertebral involvement, then these patients should be monitored for scoliosis, specifically during periods of rapid growth. If there is ear or temporal bone involvement, as in the case report presented, then patients should have an audiogram at the end of treatment and then again when they start school or should the patient develop any new symptoms (Haupt et al, 2013).

The unique features of this case are that it highlights how LCH, when there is otological involvement, which commonly involves the external and middle ear can be confused for otitis media and otitis externa. Therefore, it is important to raise awareness of this unique feature to ensure LCH is a differential diagnosis when considering external and middle ear symptoms where there is soft tissue swelling present. The limitations of this case report are that it is one case in isolation, and further analysis of similar cases will provide more insight as to how LCH with otological involvement can be mistaken for otitis media or otitis externa. Another limitation is that in countries where resources are limited, this diagnostic and follow-up pathway may be more difficult to implement.

Conclusion

LCH is a rare condition and, in many cases, is life-threatening. The presentations are broad. In cases of unliteral postauricular soft tissue masses with destructive findings on cross-sectional imaging and systemic symptoms and signs, LCH must be a differential and biopsy should be considered.

Learning Points

- When LCH does have otological involvement, it commonly involves the external and the middle ear, which can often be confused with otitis media and otitis externa.
- Presentations of LCH are broad and should be considered in the case of an unilateral postauricular soft tissue mass.
- When LCH is a differential, biopsy should be considered. LCH is diagnosed through immunohistochemistry or electron microscopy with BRAF V600E mutations seen in 40%–70% of LCH patients.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

FC and QB designed the work and drafted the manuscript. Both authors contributed to the important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Written consent was kindly provided by the patients' legal guardians. The research was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0498.

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