

‘Beneath the Surface’: When a Child’s Head Swelling Reveals More

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Abstract

Presentation

A 6.5-month-old male infant presented with a progressively enlarging, firm, non-mobile left parietotemporal swelling. Parents reported a minor head impact a week prior. He also had recurrent eczematous dermatitis resistant to treatment. Examination revealed a hemodynamically stable infant with normal neurological findings.

Diagnosis

Laboratory tests showed bicytopenia and elevated CRP. Neuroimaging detected multifocal lytic skull lesions, and abdominal ultrasound revealed hepatic nodules, suggesting systemic involvement. Histopathology confirmed Langerhans Cell Histiocytosis (LCH), a rare histiocytic disorder.

Treatment

Given multisystem involvement, chemotherapy was initiated with two drugs. The patient is under oncology follow-up for further management.

Discussion

LCH results from abnormal Langerhans cell proliferation and affects multiple organs. Diagnosis requires histopathology and immunophenotyping. Treatment varies based on severity, with systemic therapy for multisystem cases. Prognosis depends on age and organ involvement, with younger patients and high-risk organ disease having poorer outcomes.

Introduction

Langerhans cell histiocytosis (LCH) is a rare clonal disease affecting the monocyte-macrophage system. Langerhans cell histiocytosis (LCH) is characterised by the uncontrolled proliferation and accumulation of CD1a+/CD207+ dendritic cells (DCs) in response to persistent immunological activation¹. Clinical signs can range from isolated, self-healing bone and skin lesions to multi-system illness, which can be life-threatening. Peak prevalence occurs between the ages of 1-4 year. The incidence of LCH in children is 2-9/1000 000/year, with males slightly higher prevalence (M/F = 1.2-1.4)².

Case presentation

A 6.5-month-old male infant presented to the Emergency Department with a progressive left temporal swelling. It first appeared three days ago and progressively increased in size. Parents reported a head impact on the edge of the table 7 days prior but no loss of consciousness, vomiting, seizures, or otorrhagia was reported. In addition, the infant experienced recurrent eczematous dermatitis that was resistant to treatment for several weeks by GP. On assessment, he was alert, interactive, and hemodynamically stable, though he was pale with normal vital signs and no lymphadenopathy. The neurological exam was unremarkable with GCS of 15/15, an open, non-tense anterior fontanelle, and symmetrical reflexes. A firm, non mobile and non tender 4x5 cm mass was observed over the left parietotemporal area. Systematic evaluation was unremarkable. His developmental milestones were age-appropriate. Laboratory tests revealed bicytopenia (WBC 2.8, hemoglobin 8.6 g/dL) with microcytic hypochromic indices, while thrombocytes, coagulation, renal, and hepatic profiles were normal. CRP was modestly elevated at 59.5. Neuroimaging via CT revealed multifocal lytic skull lesions without intracranial extension, suggesting a neoplastic process. Ancillary abdominal ultrasound detected two well-circumscribed hepatic nodules (1cm & 3.5mm), raising suspicion for systemic involvement. A multidisciplinary team strongly suspected Langerhans Cell Histiocytosis (LCH), which was subsequently confirmed via histopathological analysis of a cutaneous biopsy taken from his back. Given the multisystemic nature of the disease, chemotherapy with vinblastine and corticosteroids was promptly initiated and the patient has ongoing follow up with the oncology team.

Discussion

Histiocytic disorders are rare diseases caused by abnormal histiocyte accumulation. "Histiocyte" refers to large tissue-resident white blood cells, including Langerhans cells, monocytes/macrophages, and dendritic cells³. The Histiocytic Society classifies histiocytic

disorders into five groups based on clinical, histological, immunophenotypic, and molecular features (Table 1)⁴. LCH pathogenesis is unclear, but research shows MAPK pathway mutations in most cases, with 60% linked to BRAF-V600E⁵. Diagnosis requires histopathology and immunophenotyping, confirmed by markers like CD1a or CD207 (Langerin)⁶. In pediatric cases, around 55% of LCH patients have single-organ involvement, while the rest present with multisystem disease⁷. Acute, disseminated multisystem disease is more frequently observed in children under the age of three, whereas single-organ involvement is more common in older children and adults. A study analyzed 1,741 children with LCH and reported the organ involvement at diagnosis as Bone – 77%, Skin – 39%, Lymph nodes – 19%, Liver – 16%, Spleen – 13%, Oral mucosa – 13%, Lungs – 10%, Central nervous system (CNS) – 6% (7). LCH, whether single or multisystem, can cause fever, fatigue, and weight loss⁸. Bone lesions are usually unifocal, presenting as a soft tissue mass with or without pain. In our case the patient had painless swelling on his head with multiple lytic lesions in the skull which were evident on the CT brain (figure 1). Skin is the second most involved organ. These lesions may be well-defined or more diffuse, appearing as single or multiple lesions which are usually resistant to regular eczema treatments as in our case (figure 2). High-risk organs include the hematologic system, spleen, and liver⁸. LCH treatment varies by type. The standard regimen uses vinblastine and prednisone (same as our patient), with 6–12 weeks of induction followed by at least 12 months of maintenance⁶. Non-responders, especially with high-risk organ involvement, may receive salvage therapy with cladribine, cytarabine, or clofarabine, alone or combined, and possibly undergo bone marrow or organ transplantation⁶. Patients diagnosed at age two or older have a 97% 10-year survival rate, while those under two have a 77% rate⁹. Multisystem disease lowers survival to 71%, and involvement of high-risk organs further reduces it to 50%⁹.

This case highlights the importance of considering Langerhans Cell Histiocytosis in infants presenting with atypical skull lesions and systemic symptoms. Early diagnosis through imaging and histopathology is crucial for timely initiation of appropriate systemic therapy, which can improve outcomes in multisystem disease. Additionally, resistant eczema or diaper rash should prompt early review by a dermatologist or pediatrician to rule out underlying systemic conditions like LCH. Ongoing monitoring is essential due to the variable prognosis depending on organ involvement and patient age.

Declarations of Conflicts of Interest:

None declared.

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References:

1. Emile JF, Ablu O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood*. 2016;127(22):2672–81. doi: 10.1182/blood-2016-01-690636.
2. Jezierska M, Stefanowicz J, Romanowicz G, Kosiak W, Lange M. Langerhans cell histiocytosis in children - a disease with many faces. Recent advances in pathogenesis, diagnostic examinations and treatment. *Postepy Dermatol Alergol*. 2018;35(1):6–17. doi: 10.5114/pdia.2017.67095.
3. McClain KL, Bigenwald C, Collin M, Haroche J, Marsh RA, Merad M, Picarsic J, Ribeiro KB, Allen CE. Histiocytic disorders. *Nat Rev Dis Primers*. 2021 Oct 7;7(1):73. doi: 10.1038/s41572-021-00307-9. PMID: 34620874; PMCID: PMC10031765.
4. Emile JF, Ablu O, Fraitag S, Horne A, Haroche J, Donadieu J, Requena-Caballero L, Jordan MB, Abdel-Wahab O, Allen CE, Charlotte F, Diamond EL, Egeler RM, Fischer A, Herrera JG, Henter JI, Janku F, Merad M, Picarsic J, Rodriguez-Galindo C, Rollins BJ, Tazi A, Vassallo R, Weiss LM; Histiocyte Society. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood*. 2016 Jun 2;127(22):2672–81. doi: 10.1182/blood-2016-01-690636. Epub 2016 Mar 10. PMID: 26966089; PMCID: PMC5161007.
5. Eckstein OS, Visser J, Rodriguez-Galindo C, Allen CE, Group N-LS. Clinical responses and persistent BRAF V600E(+) blood cells in children with LCH treated with MAPK pathway inhibition. *Blood*. 2019;133(15):1691–4. doi: 10.1182/blood-2018-10-878363.
6. Jezierska M, Stefanowicz J, Romanowicz G, Kosiak W, Lange M. Langerhans cell histiocytosis in children - a disease with many faces. Recent advances in pathogenesis, diagnostic examinations and treatment. *Postepy Dermatol Alergol*. 2018 Feb;35(1):6–17. doi: 10.5114/pdia.2017.67095. Epub 2018 Feb 20. PMID: 29599667; PMCID: PMC5872238.

7. McClain KL, Bigenwald C, Collin M, Haroche J, Marsh RA, Merad M, Picarsic J, Ribeiro KB, Allen CE. Histiocytic disorders. Nat Rev Dis Primers. 2021 Oct 7;7(1):73. doi: 10.1038/s41572-021-00307-9. PMID: 34620874; PMCID: PMC10031765.
8. Krooks J, Minkov M, Weatherall AG. Langerhans cell histiocytosis in children: Diagnosis, differential diagnosis, treatment, sequelae, and standardized follow-up. J Am Acad Dermatol. 2018 Jun;78(6):1047–56. doi: 10.1016/j.jaad.2017.05.060. PMID: 29754886.
9. Ouali ZE, Khoubila N, Cherkaoui S, Rachid M, Lamchahab M, Qachouh M, Madani A, Quessar A. Langerhans cell histiocytosis in children: a case report and brief review of the literature. PAMJ Clin Med. 2019;1:10. doi: 10.11604/pamj-cm.2019.1.10.20810.

Figure 1:



Figure 2:

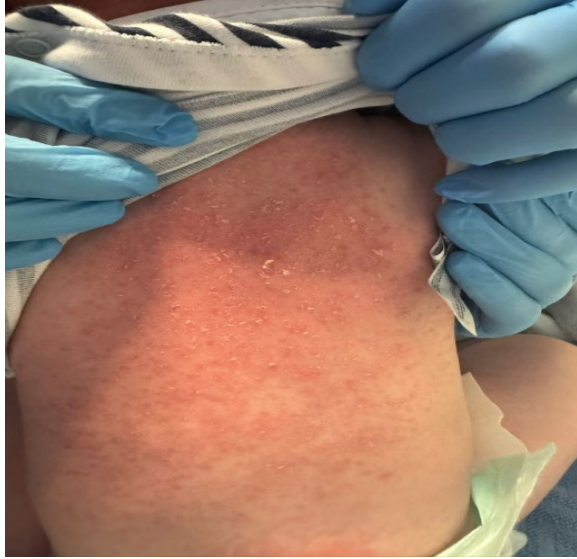


Table No. 1:

Group	Diseases
Langerhans (L)	Langerhans cell histiocytosis, Erdheim-Chester disease/extracutaneous juvenile xanthogranuloma, Indeterminate cell histiocytosis
Cutaneous and Mucocutaneous (C)	Juvenile xanthogranuloma, Adult xanthogranuloma, Solitary reticulohistiocytoma, Benign cephalic histiocytosis, Generalized eruptive histiocytosis, Progressive nodular histiocytosis, Xanthoma disseminatum, Cutaneous Rosai-Dorfman disease, Necrobiotic xanthogranuloma, Multicentric reticulohistiocytosis, Cutaneous histiocytoses not otherwise specified
Malignant (M)	Histiocytic sarcoma, Indeterminate cell sarcoma, Langerhans cell sarcoma, Follicular dendritic cell sarcoma
Rosai-Dorfman Disease (R)	Rosai-Dorfman disease, Noncutaneous, non-LCH not otherwise specified
Hemophagocytic Lymphohistiocytosis and Macrophage Activation Syndrome (H)	Hemophagocytic lymphohistiocytosis/macrophage activation syndrome