Medical and Clinical Research: Open Access

Case report

Langerhans Cell Histiocytosis: A Case Report

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Received: July 14, 2021; **Accepted:** August 16, 2021; **Published:** August 20, 2021

Citation: Fonseca S, Moreira T, Simões D, et al. Langerhans Cell Histiocytosis: A Case Report. Med Clin Res Open Access. 2021; 2(4):1-3.

ABSTRACT

Langerhans cell histiocytosis is a rare disease characterized by clonal proliferation of dendritic cells. Diagnosis can be difficult due to heterogeneity of clinical manifestations, affecting several organs and/or systems. We report the case of a 9-month-year-old boy who is referenced to our center due to anemia and iron deficiency. The clinical presentation with exuberant skin manifestations and persistent/recurrent infections raised the suspicion of Langerhans cell histiocytosis, confirmed with positive immunoreactivity of bone marrow cells for CD1a and protein S100. We highlight the importance of detailed clinical history in the diagnosis of Langerhans cell histiocytosis and the importance of an early diagnosis.

Keywords

Langerhans cell histiocytosis, Children, Recurrent Otitis Media, Anemia, Dermatitis.

Introduction

Langerhans cells histiocytosis (LCH) is an uncommon and clinically heterogeneous disease whose etiology is not yet fully understood. It results from clonal proliferation of myeloid precursor cells which leads to recruitment of other inflammatory cells leading to a prolonged and extensive inflammation with destruction of the affected organ [1].

This is a rare disease whose incidence in pediatric age is approximately three to five cases per million children. It can occur at any age, but the incidence is higher in children between one and three years [2].

Clinical manifestations are multiple, according to the affected tissues, the extent of disease, and age at diagnosis, which makes diagnosis challenging. LCH can be divided into two major groups: single-system LCH (single organ or system involvement) and multisystem LCH (two or more organs or systems, with or without the involvement of risk organs) [3]. The most frequently affected is the bone, with the development of osteolytic lesions, more often the skull. Cutaneous involvement is also common, particularly in children. Spleen, liver, and hematopoietic system involvement is associated with a worse prognosis [3].

The diagnostic approach begins with a complete clinical history and physical examination, with particular attention to risk organ or central nervous system involvement. Although signs and symptoms along with imaging findings can help determine the extension and severity of the disease, the final diagnosis is established with affected tissue biopsy.

We report the case of an infant with exuberant dermatosis, persistent/recurrent otitis media, and severe anemia in whom, following an investigation, LCH was diagnosed.

Case Report

Infant, 9 months old. He was born by emergent cesarean delivery at 33 weeks, due to metrorrhagia. His weight and height were appropriate for gestational age, and he did not need resuscitation maneuvers. Neonatal period with jaundice requiring phototherapy, without other complications. At 4 months old, due to the suspicion of urinary tract infection and conjunctivitis, he was treated with oral cefixime and topical azithromycin. Since the age of 5 months, he developed exuberant dermatitis involving the axillary, inguinal, and perianal regions, refractory to multiple emollient creams, topical antibiotics, and antifungal therapy. At 6 months old, he presented acute otitis media (AOM), and he had been treated with oral antibiotic therapy, with persistence/recurrence of infection, having completed several courses of antibiotic therapy. At 9 months old, he was referred to our center due to anemia. On admission, he had been feverish for 4 days. On physical examination, he presented skin pallor and discolored mucous membranes; crusted lesions on the scalp, more prominent in the frontotemporal region, crusted papules on the face, chest, abdomen, and back; and exuberant erythematous scaling plaques in the axillary and inguinal folds and the perianal region (Figures 1 and 2); and an AOM was identified. No hepatosplenomegaly, nor other relevant findings. From the investigation, microcytic and hypochromic anemia (Hb 4,8 g/dl) with low transferrin saturation (12%). Peripheral blood smear showed anisocytosis and some ovalocytes. No analytical evidence of hemolysis; immunoglobulins assay and complement without changes; viral serologies without evidence of infection. Chest X-ray and abdominal ultrasound were irrelevant. Empirical intravenous antibiotic therapy was started, and red blood cell transfusion support was necessary twice. He presented rapid and marked clinical deterioration within less than a week, with the development of hepatosplenomegaly and bilateral cervical lymphadenopathies, associated with worsening of anemia, reduction in the reticulocyte production index, and a pronounced reduction in platelet count. A myelogram was performed showing massive infiltration by groups of spindle cells, low nucleus-to-cytoplasm ratio, and dendritic aspect. Bone marrow biopsy revealed an extensive bone marrow infiltration by "towels" of large cells with an irregularly lobed nucleus and abundant cytoplasm (Figure 3); the residual hematopoietic population was very scarce, and rare histiocytic cells with signs of erythrophagocytosis were present. Immunoreactivity of the cells described was positive for CD1a and protein S100 confirming the diagnosis of LCH. He also underwent a skin biopsy (Figure 4) that corroborated the diagnosis, being immediately transferred to an oncology center for further care.

Discussion

LCH is a rare disease. Nevertheless, most cases of multisystem LCH have been reported in younger children, carrying a worse prognosis [3,4].

Figure 1: Facial skin lesions, with crusted papules.

Figure 2: Erythematous scaling plaques in the perianal region.

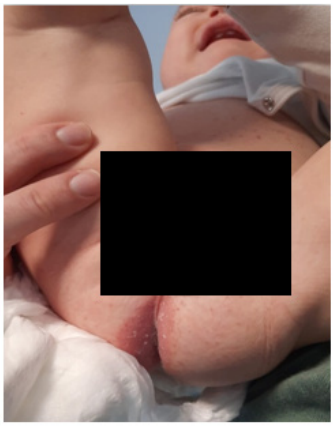
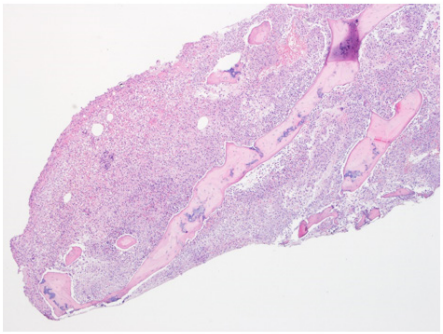


Figure 3: Inflammatory infiltrate with pathological Langerhans cells (bone marrow).



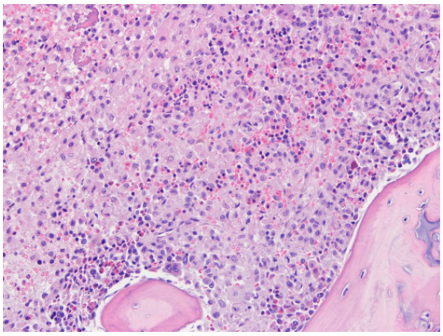
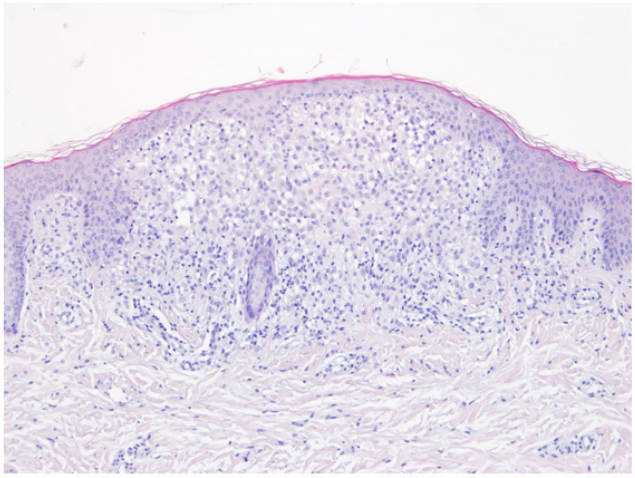


Figure 4: Inflammatory infiltrate with pathological Langerhans cells (skin).



The clinical presentation can include lytic bone lesions, recurrent otitis media, refractory dermatitis, particularly in children, with the development of erythematous papular rash and ulcerative lesions mostly in the cutaneous folders. It is worth noting that cutaneous lesions are frequently misdiagnosed as seborrheic dermatitis or bacterial/fungal infections. Hepatosplenomegaly, lymphadenopathies, cytopenias, ascites, and jaundice can also occur, related to the involvement of the hematopoietic system, liver, and spleen. In our case, the presence of severe anemia in an infant with exuberant and refractory skin lesions, and recurrent/persistent otitis media, raise the suspicion of LCH.

It should be noted that bone marrow involvement usually occurs in younger children and manifests with cytopenias, as in our case. He presented severe anemia requiring transfusion support, a reduction in the reticulocyte production index, and the evolution to a pronounced reduction in platelet count.

Our diagnostic approach included extensive analytical investigation and prompt myelogram and bone marrow biopsy. The LCH diagnosis is made by biopsy of the affected tissue or organ with histological analysis showing an inflammatory infiltrate with pathological Langerhans cells (big and oval cells, with coffee-bean nuclear grove, eosinophilic and abundant cytoplasm) [5] and identification of Birbeck granules by electron microscopy [6]. The confirmation is made by positive immunohistochemical staining of the tissue for CD1a, CD207, and/or S100 [3,6], as seen in our case. In this case, the rapid clinical and analytical deterioration presented is related to the marked bone marrow infiltration, which is notable.

The prognosis of LCH is related to the involvement of "risk organ" (spleen, liver, and hematopoietic systems) and age at diagnosis. In our case, the multisystemic disease and age < 2 years, are associated with lower response to treatment and poorer prognosis [3,7-9].

Conclusion

Finally, the authors underline that LCH may present with a wide spectrum of manifestations and emphasize the need for a high degree of suspicion for this diagnosis. This case illustrates the importance of considering the constellation of symptoms and signs presented in the differential diagnosis and diagnostic approach.

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