LANGERHANS CELL HISTIOCYTOSIS IN TWO INFANTS

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Abbreviation **LCH** = Langerhans cell histiocytosis.

Case 1. An 18-month-old male infant was referred to the Dermatology outpatient clinic for multiple erythematous or skin-colored papules and plaques involving the scalp, face, neck, trunk, and inguinal folds that had been present for 10 months. Additional findings included yellowish greasy scales on the scalp, subungual hyperkeratosis with elevation of the nail plate (Fig. 1), tooth mobility, and gingival swelling (Fig. 2). Over the previous five months, the infant had experienced intermittent episodes of fever and otorrhea, treated symptomatically. He had previously been treated for seborrheic dermatitis with low-potency topical corticosteroids and antifungals, with minimal improvement.

Complete blood count revealed microcytic hypochromic anemia on peripheral smear, with a hemoglobin level of 6.6 g/dL (normal range 11-14).

Skin biopsy showed numerous Langerhans-type histiocytes with abundant pale eosinophilic cytoplasm and elongated nuclei with prominent grooves and folds, surrounded by an eosinophilic and neutrophilic infiltrate with multinucleated foreign-body-type giant cells. The infiltrating cells were positive for S100, CD1a, and langerin. Whole-body positron emission tomography (PET) and computed tomography (CT) demonstrated multiple 18F-fluorodeoxyglucose–avid soft-tissue lesions, with skull bone erosions, several enlarged lymph nodes at bilateral levels 1b and 2, and multiple hypodense lesions in both hepatic lobes.

A definitive diagnosis of multisystem Langerhans cell histiocytosis (LCH) was established. A packed red blood cell transfusion was performed, and the infant was referred to Pediatric Oncology for further management. Treatment with oral prednisolone 3 mg three times daily and weekly intravenous vinblastine 1.6 mg in 20 mL was initiated, in association with topical corticosteroids and emollients. The child is currently under regular follow-up and has shown a favorable response with improvement of both cutaneous and systemic manifestations.

Case 2. A 10-month-old male infant was admitted to the pediatric intensive care unit for recurrent diarrhea, intermittent fever, failure to thrive, and a skin eruption that had been present for six months. General physical examination revealed marked abdominal distention. Cutaneous examination showed multiple well-defined erythematous papules and plaques, bilaterally symmetrical, with maceration in the axillae and inguinal folds and purpuric patches in the groin folds (Fig. 3). Multiple erythematous scaly papules were also present on the chest, abdomen, and back, along with petechiae on the palms (Fig. 4). Multiple petechiae were also noted on the scalp. The oral cavity showed multiple swellings on the hard palate.

Laboratory investigations revealed hemoglobin 3.9 g/dL (normal range 11-14), C-reactive protein 17.7 µg/mL (normal ≤10), D-dimer 3167 ng/mL (normal ≤500), prothrombin time 18 sec (normal 11-13), INR 1.2 (normal 0.9-1.3), activated partial thromboplastin time 27.6 sec (normal 28-40), total bilirubin 2.5 mg/dL (normal 0.3-1.2), direct bilirubin 1.6 mg/dL (normal <0.3), indirect bilirubin 0.9

Fig. 1

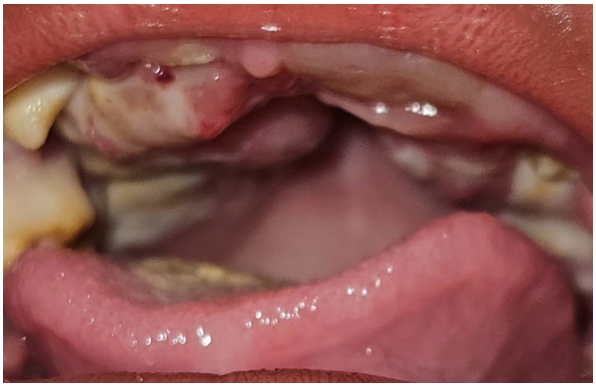

Fig. 2

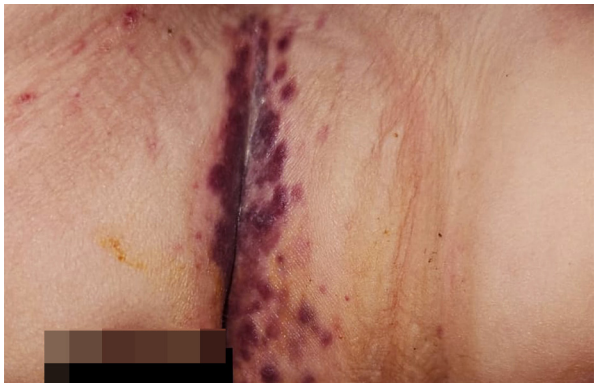

Fig. 3

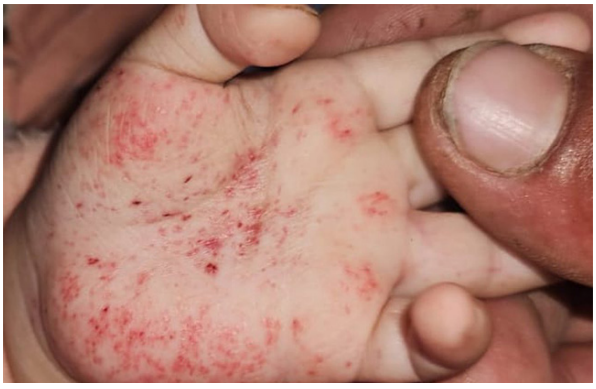

Fig. 4

Fig. 1, 2, 3, 4: Langerhans cell histiocytosis: subungual hyperkeratosis (Fig. 1) and gingival swelling (Fig. 2) in case 1. Purpuric lesions of the inguinal (Fig. 3) and palmar (Fig. 4) regions in case 2.

mg/dL (normal 0.2-0.9), alkaline phosphatase 902 U/L (normal 50-220), albumin 2.1 g/dL (normal 3.5-5.5), and negative blood cultures.

Abdominal and pelvic ultrasound revealed hepatosplenomegaly and an umbilical hernia with herniation of bowel loops. The infant was treated with intravenous fluids, broad-spectrum antibiotics, and supplemental oxygen. Two packed red blood cell transfusions were administered to correct the severe anemia.

Skin biopsy from one of the lesions showed extravasated erythrocytes together with a dense periappendageal lymphohistiocytic infiltrate composed of mononuclear histiocytes with a "ground-glass" appearance, some elongated spindle-shaped histiocytes, eosinophils, and lymphocytes in the papillary and mid dermis, consistent with Langerhans cell histiocytosis.

A follow-up telephone call with the parents revealed that the infant died one month after discharge.

Discussion. Langerhans cell histiocytosis (LCH) is a neoplasm arising from the expansion of early myeloid cells in the bone marrow, frequently due to a clonal mutation in the RAS/MAPK signaling pathway (1). This results in the dissemination of progenitor cells expressing CD1a and CD207 (langerin), which differentiate into monocytes and subsequently circulate as Langerhans cells (2).

LCH is a rare disease that generally affects children younger than 15 years; an incidence of approximately 3-4 cases per million per year has been reported, with a peak in infants younger than 2 years and a male predominance (3). However, it can occur at any age. It is the most common histiocytic

disorder, in which langerin-positive cells aggregate to form granulomatous lesions and deposit within tissues, causing damage to organs such as the skin, liver, lungs, gastrointestinal tract, bones, and the central nervous system (including the skull and pituitary gland). The acute disseminated multisystem form is more common in children younger than three years, whereas the single-organ form is more frequently observed in older children and adults (4).

Cutaneous involvement occurs in approximately 40% of patients; the most common manifestations are eczema-like lesions as well as papules that are often purpuric. Other cutaneous manifestations may include pustular, petechial, vesicular, and papulonodular lesions (5).

Several dermatologic conditions may resemble the cutaneous lesions of LCH, making the diagnosis challenging. These include seborrheic dermatitis, psoriasis, atopic dermatitis, and viral exanthems, which may mimic the eczematous or papular nature of LCH lesions (6). Because it is a rare disease with highly heterogeneous clinical presentation and a broad spectrum of symptoms, early diagnosis is often difficult. Diagnosis is confirmed by skin biopsy and immunohistochemistry, followed by fluorodeoxyglucose positron emission tomography (FDG-PET) to evaluate systemic involvement.

Prognosis is closely related to the age at onset and the extent of systemic involvement. Early age of onset and multisystem disease represent unfavorable prognostic factors (7).

Localized cutaneous lesions may be treated with topical corticosteroids or surgical excision. Systemic involvement requires chemotherapeutic agents, including vinblastine and corticosteroids (3, 8).

Conclusion. These two clinical cases highlight the importance of a multidisciplinary approach in this rare condition characterized by highly variable clinical manifestations.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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