Langerhans cell histiocytosis presenting as a blueberry muffin rash

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Abstract

Langerhans cells, often referred to as the "macrophages of the skin", are dendritic cells that normally reside in the epidermis and papillary dermis. Just like macrophages, they function as antigen-presenting cells that activate naive T cells. Certain mutations such as those involving the *BRAF* gene can cause unopposed production of Langerhans cells, which is known as Langerhans cell histiocytosis (LCH). LCH triggers an inflammatory immune response that causes systemic manifestations such as fever and fatigue, as well as other manifestations depending on the affected organs. The pathogenesis behind LCH remains poorly understood. It is still unknown whether it is a neoplastic process or a reactive cancer-mimicking illness. Diagnosis of LCH is confirmed by biopsy, and treatment is largely dependent on the extent and severity of the disease. Common treatments include corticosteroids, excision, radiation, and chemotherapy. We present a case of a 1-year-old Saudi male with LCH.

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Introduction

Langerhans cell histiocytosis (LCH) is a rare disease that is derived from myeloid Langerhans cells. The clonal proliferation of these cells is not from the epidermis and exhibits aspects of both a neoplastic and a reactive process. The condition can be unifocal affecting one system such as the skin or the bony skeleton, or multifocal affecting two or more organs including lymph nodes, bone marrow, lungs, liver, spleen, pituitary gland, the nervous system, and the gastrointestinal tract. Presentation varies from one patient to another, however, the most common initial presentation is a rash.[1] In children, bone involvement and skin involvement are present in 77% and 39% of LCH patients, respectively. Cutaneous manifestations can be seen in unifocal or multisystem LCH. The most common cutaneous manifestation is an eczematous rash that resembles candidal diaper rash, as well as brown papules. The rash usually involves the groin, abdomen, back, or chest.[2] It is often hard to diagnose LCH clinically as the presentation differs based on the affected systems. Thus, clinical evaluation, imaging, and histopathology are usually required to establish a diagnosis. The gold standard for diagnosis is the presence of Birbeck granules on electron microscopy of a biopsy sample.[3] Specific markers of Langerhans cells include CD1a and CD207 (langerin). They may also express S100. Over half of LCH cases reported in the literature involve a mutated BRAF V600E gene. Treatment of LCH varies depending on the manifestations. The goal of treatment is to reduce morbidity and prevent complications.[4] For purely cutaneous LCH, topical corticosteroids such as triamcinolone and nitrogen mustard (mechlorethamine 20%) are commonly used agents. LCH is generally regarded as a disease of children. It is most commonly diagnosed in children aged one to three.[2] The incidence of LCH in children is estimated to be four to five cases per million per year, with males being affected twice as females.[1]

Case Report

A 1-year-old male was admitted electively at the age of 5 weeks under the care of the hematology department to investigate

a blueberry muffin rash that had been present since birth. The rash consisted of blue to purple plaques resembling purpuric lesions scattered over the face and body (Figures 1 and 2).

The patient's development was appropriate for his age, and he was up to date with his vaccinations. The patient's mother reported no history of perinatal infections or pregnancy complications.

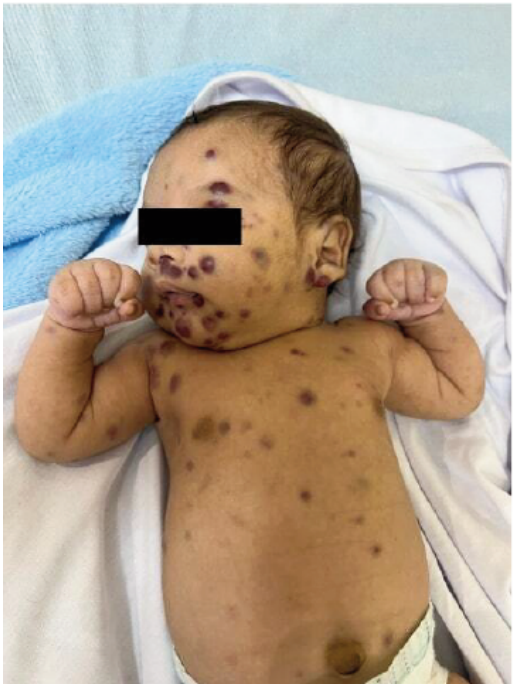

Figure 1. Rash on face and chest. Purple plaques of varying sizes overlying the face and chest.

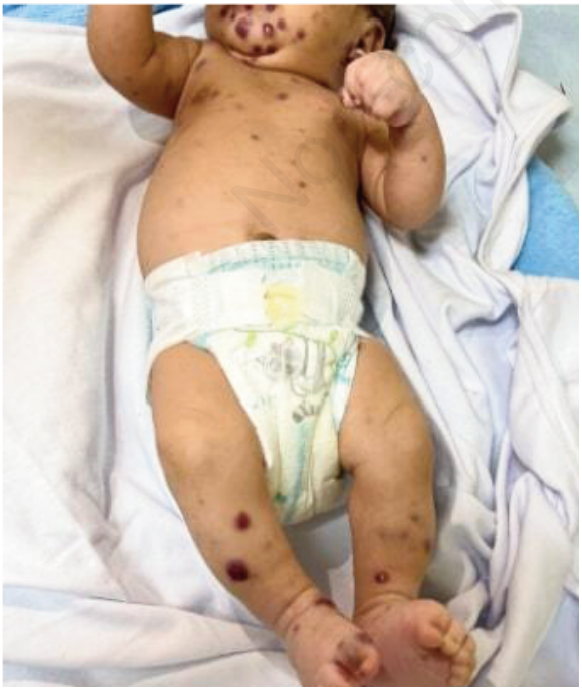

Figure 2. Rash on legs. Purple plaques on lower limbs.

She also denied a family history of similar symptoms. On admission, he was active and asymptomatic. Initial workup at the time of admission revealed anemia (hemoglobin of 8.2) and neutropenia (absolute neutrophil count of 710). A skin biopsy was obtained, and the patient was transfused with packed red blood cells. Pathological examination of the biopsy sample showed that the lesion was infiltrating into the subcutis with an area of focal necrosis and abundant mitosis (up to 20 mitoses/ 10 high-power field). There was no evidence of high-grade nuclear features or lymphovascular invasion. A diagnosis of LCH was confirmed by immunohistochemical staining which came back positive for S100, CD68, and CD1a. Other markers such as CD34, BCL2, MPO, and HMB45 came back negative. Further investigation to rule out possible complications included a bone marrow biopsy, an ultrasound of the abdomen and the pelvis, a skeletal survey, and a brain magnetic resonance imaging scan, all of which were normal. The patient was discharged home and prescribed topical hydrocortisone 1% cream every 12 hours. A follow-up appointment was scheduled.

Discussion

Langerhans cells are dendritic cells that are named after Paul Langerhans who initially described them as epidermal cells with extracutaneous nerves (dendrites).[5] Years later, it was discovered that they are dendritic cells rather than nerves. Langerhans cells classically stain positive for CD207 (Langerin) and CD1a.[5] The presence of Birbeck granules also exhibits high specificity to Langerhans cells. LCH is a rare condition that involves clonal proliferation of Langerhans cells resulting in different manifestations depending on the affected system. It is still debatable whether the disease is a neoplastic or a reactive condition. However, a BRAFV600E mutation has been identified in over half of LCH cases.[5] LCH can be classified into two subtypes: unifocal and multifocal. Unifocal LCH affects a single system while the multifocal subtype affects two or more organ systems. The most commonly affected systems are the skin and bones. The incidence of LCH in adults is estimated to be 1 to 2 cases per million, as compared to 4.6 cases per million in children.[5-7] In infants, LCH that is confined to the skin often resolves spontaneously within a few months. However, if other systems are involved, the disease is usually progressive and more severe. The rash often presents as erythematous papules resembling an eczematous rash and is often misdiagnosed as atopic dermatitis, but it does not respond to topical treatment. In our case, the rash is very different from the classical rash of LCH. Our patient presented with purple plaques that resemble purpuric lesions, which is why he was initially admitted to the hematology department. A biopsy and immunohistochemical staining guided the diagnosis of LCH; clinical diagnosis could not be established on the spot as the presentation was unusual. A skeletal survey and a bone marrow biopsy ruled out bone involvement. Different imaging modalities were used to rule out systemic disease. Vinblastine and prednisone remain the mainstay of treatment for low-risk LCH, such as this case.[5]

Conclusions

LCH is a rare condition that most commonly affects children during the first decade of life. The severity of the disease depends on the extent of disease spread; localized disease is associated with a better prognosis. The skin rash is usually an erythematous

eczematous rash; however, atypical rash presentation should not rule out LCH. Biopsy and immunohistochemical staining should be relied on more than clinical appearance.

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