
CASE REPORT

THERAPEUTIC AND DIAGNOSTIC CONSIDERATIONS IN CONGENITAL LANGERHANS CELL HISTIOCYTOSIS

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare histiocytic disorder that can affect nearly every organ (most notably the skin, lymph nodes, lungs, thymus, liver, spleen, bone marrow, or central nervous system with the exception of the heart and kidneys). Histiocytosis is a group of disorders characterized by proliferation of histiocytes. Histiocytes come from the system of mononuclear phagocytes and all cells that come from this system have phagocytic properties and have the ability to transform into epithelioid cells and giant cells. Within the same system Langerhans cell (3-5% of epidermal cells) is considered to be part. This type of cell presents lymphocyte antigen and ultrastructurally has Birbeck granules. Langerhans cells are dendritic and express CD1 antigen, which makes it possible to identify them with monoclonal antibodies. In this report, we present a rare case of Congenital histiocytosis in a newborn male baby with hemorrhagic vesicular lesions, with a rough and painless appearance disseminated in the upper and lower limbs, in the trunk, both anterior and posterior, scalp and cervical area.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare histiocytic disorder most commonly characterized by single or multiple osteolytic bone lesions demonstrating infiltration with histiocytes having bean-shaped nuclei on biopsy. These histiocytes, along with lymphocytes, macrophages, and eosinophils may infiltrate nearly every organ (most notably the skin, lymph nodes, lungs, thymus, liver, spleen, bone marrow, or central nervous system with the exception of the heart and kidneys).

LCH is so named because the morphology and immunophenotype of the pathologic cells resemble Langerhans cells, which are specialized dendritic cells found in the skin and mucosa. However, LCH is derived from myeloid progenitor cells from the bone marrow, and is not derived from the Langerhans cell of the skin.

Histiocytosis is a group of disorders characterized by proliferation of histiocytes. Histiocytes come from the system of mononuclear phagocytes, the current name of the old reticulo-endothelial system. All cells that come from this system have phagocytic properties and have the ability to transform into epithelioid cells and giant cells. Within the same system Langerhans cell (3-5% of epidermal cells) is considered to be part. This type of cell presents lymphocyte antigen and ultrastructurally has Birbeck granules. Langerhans cells are dendritic and express CD1 antigen, which makes it possible to identify them with monoclonal antibodies. Two types of Langerhans cells have been described in the epidermis: type I, cells located in the spinous state, with clear cytoplasm, numerous dendrites, multiple Birbeck granules; type II, cells located in the basal layer with denser cytoplasm, less lysosomal granules and few

prolongations [1].

For now, "Langerhans cell histiocytosis" remains the preferred nomenclature; the historical terms histiocytosis-X, Letterer-Siwe disease, Hand-Schüller-Christian disease, and diffuse reticuloendotheliosis have been abandoned. The archaic term "histiocyte" refers to large white blood cells resident in tissues, including Langerhans cells, monocytes/macrophages, and dermal/interstitial dendritic cells [2]. LCH is a rare histiocytic disorder and the true incidence is unknown. The genetics of LCH have not been well elucidated. There is no evidence that relatives of patients with LCH are at increased risk of developing LCH [3].

In this report, we present a rare case of Congenital histiocytosis in a newborn male baby with hemorrhagic blisters disseminated throughout the skin.

CASE REPORT

We present the case of a new born normoponderal male (3240 grams) with hemorrhagic blisters disseminated throughout the skin, extracted by caesarean section at 39 weeks for lack of labor progression. It was the mother's first pregnancy and had a 8/10 Apgar scores. The mother was 31-years-old with physiological pregnancy, negative TORCH tests and negative history of teratogen exposure. No abnormal family history was reported and both parents were apparently healthy and had no abnormalities of skin, skin appendages or mucous membrane.

The patient was referred to the newborn intensive care unit, which consulted with the Department of Dermatology because of the skin problems. On physical examination hemorrhagic vesicular lesions, with

a rough and painless appearance disseminated in the upper and lower limbs, in the trunk, both anterior and posterior, scalp and cervical area.

Initial paraclinical investigations revealed a hemogram in dynamics is normal, dynamics ionogram is normal, LDH in normal limits, blood glucose, transaminases, urea, creatinine in dynamics is normal, coagulation tests in normal limits, inflammatory biological syndrome positive: C reactive protein 25.6 mg / l at 24 hours, 3.7 mg / l at 5 days. Cranial ultrasound shows easy cerebral edema. Abdominal ultrasound shows moderate hepatomegaly.

There was also a consultation on infectious diseases, which recommended harvesting, in order to exclude the infectious etiology of: Ig M and Ig G antibodies against varicellosterone virus - within normal limits; Ig M and Ig G antibodies against cytomegalovirus - within normal limits; Ig M and anti Ig G antibodies against Epstein Barr virus - within normal limits; Ig M antibodies herpes antivirus 1 and 2 - within normal limits; IG M anti-parvovirus B 19 antibodies - within normal limits; RPR - within normal limits. Thus, an etiology of an infectious nature could not be confirmed.

Due to disseminated bleeding bullous lesions (Figure 1 and 2), neonatal pemphigus is initially suspected. Thus, it is recommended to harvest anti-desmoglein 1 and desmoglein 3 antibodies, which had a normal titer. In addition, HLA B 27 antigen, rheumatoid factor, complement C 3, C 4 are harvested, which were also normal. The titration of the epidermal basal anti-membrane antibodies (EBMA) was also recommended due to the suspicion in the differential diagnosis of the epidermolysis bullosa. Another suspected diagnosis was Porphyria drug because in the sixth week of pregnancy, the mother received Prednison treatment for one month.

To determine the diagnosis of certainty, we decided to perform a biopsy. Under local anesthesia with 1% Xiline, a punch biopsy was performed approximately 5 mm in diameter from the level of the external face of the left thigh. Macroscopic description of the skin fragment of 4/4/3 mm describes a slightly highlighted area, of 3/3 mm, light brown color and an irregular contour. and small areas of spongiosis. At the histopathological exam, in the superficial dermis are identified rich cellular, perivascular and perianexial infiltrates, arranged in the subepidermal band, composed of round / oval cells with the bulky nucleus, sometimes lobed, with rare mitosis; rare nuclei with central or reniform appearance, lymphocytes, eosinophilic polymorphonuclear cells, rare multinucleated giant cells and histiocytes (Figure 3). Thus, the histopathological appearance indicates congenital histiocytosis with Langerhans cells. The specialist anatomopathologist who performed the histopathological examination recommended performing immunohistochemical tests for confirmation and differential diagnosis.

Immunohistochemical examination revealed the presence of histiocyte cells that were positive for CD1 α and Langerina (Langerhans histiocyte markers). Also in Langerhans cells we have positive S100 protein. Triptase highlights the presence of isolated mast cells. Thus, histopathological appearance and immunohistochemical staining indicate Langerhans cell histiocytosis. In our case, it is necessary to correlate with the clinical-imaging data to establish the strict cutaneous vs. extensive (bone, visceralized) character of the histiocytic proliferation.

For continuation of the subsequent treatment plan, patient monitoring was performed in the neonatal intensive care unit. The diet should have breast milk, complete with milk powder from the bottle. Local treatment was prepared with 1% Mercurocrom solution, Castellani solution and Baneocin pulvis. The next step in therapeutic management has been decided if antibiotic therapy is started. For the prophylaxis of a bacterial over-infection of the skin lesions it could lead to the deterioration of the patient's condition or of some neonatal clarity, of maintaining a vascular approach - branches, if the parenteral antibiotic treatment with Meronem and Vancomycin is started. Reminds hemoculture before the initiation of antibiotic therapy.

At 48 hours after the initiation of treatment the evolution is favorable, the patient is balanced cardiorespiratory, good digestive tolerance to feeding at the bottle, normal tone and reactivity the skin lesions have a stationary appearance without appearing new lesions and some of the bleeding bubbles have acquired the appearance of crusts. Antibiotic treatment was maintained for 5 days until normalization inflammatory markers and obtaining the result from hemoculture (no germs developed). The patient was discharged 7 days after birth, with skin lesions covered by crusts, some partially remitted, but without new lesions. At one month, a screening was performed to detect the damage of other organs that may occur in congenital Langerhans cell histiocytosis. An ultrasound of the general abdomen (upper and lower) was performed, which revealed a liver of normal size, without other changes; cranial ultrasound, with normal appearance, without cerebral edema; and a long bone scan that looked normal.

The clinical evolution was for remission of the skin lesions during the next 5 months, without clinical or paraclinical signs of multisystemic impairment. Also subsequent imaging investigations have fosed within normal limits. All of these are arguments that support the diagnosis of self-limiting Haschimoto-Pritzker disease.

DISCUSSIONS

Langerhans histiocytosis is a rare disease that manifests through the clonal proliferation of Langerhans cells. It is a disorder of the reticulohistiocytic system characterized by the proliferation of large, monoclonal cells, with an eccentric nucleus, with a granulating

cytoplasm, vacuolated with Birbeck granules and showing on their surface CD1 antigenic markers and S 100 protein. at birth to adolescence with an incidence peak between 1 and 3 years, male being twice as frequently affected.

The classification of Histiocytosis comprises 3 classes: Class I Histiocytosis (Langerhans cell histiocytosis) - eosinophilic granuloma, Hand-Schuller-Christian disease, Letterer-Siwe disease, Haschimoto-Pritzken autoimmune disease; Histiocytosis class II (histiocytosis with mononuclear phagocytes, other than Langerhans cells), reactive proliferation in infections with - herpes virus, Epstein Barr virus, cytomegalovirus, other viruses, bacteria; Histiocytosis class III - malignant histiocytosis [1]. From the clinical point of view, there may be various manifestations - unifocal resolute forms spontaneously to severe forms with multivisceral touches that play the prognosis of life.

Within the newborn autoimmune histiocytosis, we find the following disorders: Isolated autoinvolutive histiocytoma, Hashimoto-Pritzker congenital reticulo-histiocytosis and Self-involuntary histiocytosis gained with predominantly cutaneous expression (occurring in the first hours / days after birth). Congenital reticulo-histiocytosis Hashimoto-Pritzker is a papulo-nodular histiocytosis with a tendency to ulceration. The lesions are yellow, by fat storage. Spontaneous regression occurs within a few months [1].

Infants may present with brown to purplish papules over any part of their body (congenital self-healing reticulohistiocytosis, Hashimoto-Pritzker disease) [4,5]. If solitary, this manifestation is benign and the lesions disappear during the first year of life with no therapy. However, neonates with apparently isolated skin involvement need thorough evaluation to confirm that no other sites are involved, as well as close follow-up for later risk organ involvement.

The importance of a thorough evaluation was demonstrated in a series of 19 neonatal LCH cases with skin involvement in which 12 of the 19 also had multisystem disease that affected other organs [6]. In another report of 61 neonatal cases from 1069 patients in the Histiocyte Society database, 36 of 61 (59 percent) had multisystem disease and 25 of 61 (42 percent) had risk organ involvement [7]. Lesions range in size from 1 to 10 mm in diameter. Seborrhic involvement of the scalp may be mistaken for prolonged "cradle cap" in. Ulcerative lesions behind the ears, in the scalp, genitalia, or perianal region are especially troublesome, as they often are misdiagnosed as bacterial or fungal lesions [8].

Patients with skin-only involvement must have a thorough evaluation to determine if other sites of disease are present. A subset of patients will have spontaneous regression of cutaneous LCH ("self-healing cutaneous LCH"), but this can only be identified retrospectively. Thus, close observation is an option for patients with skin-only disease. However, a significant percentage (up

to 40 percent of infants) have been reported to progress to multisystem involvement [9,10,11].

Small retrospective studies and case reports have described responses to topical corticosteroids, topical nitrogen mustard, oral methotrexate, and oral thalidomide [12,12,14,15]. As an example, a retrospective study of 14 patients with cutaneous LCH treated with topical nitrogen mustard reported responses in 13 patients. Although eight patients achieved a complete response after a median of 12.3 months, six ultimately relapsed [15].

CONCLUSIONS

Congenital histiocytosis is a rare disease but it is important to consider it in a newborn with bleeding, bleeding skin. The diagnosis of certainty is based on the examination histopathological supplemented with immunohistochemical examination (CD1a). The treatment is varied and depends on the severity of the disease. The key to proper therapeutic conduct is the efficient multidisciplinary-physician collaboration - neonatologist, dermatologist, infection doctor, medical imaging specialist, anatomopathologist.

The particularities of the case include the difficulty of establishing the positive diagnosis in the first days after birth in the absence of the results of the histopathological examination completed by the immunohistochemical examination until the newborn's discharge on the 7th day of life, the initial ultrasound aspect of moderate hepatomegaly and the clinical edema in this case. And, the therapeutic dilemma of our case: if antibiotic therapy was justified.

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Figure 1.

Hemorrhagic blisters disseminated throughout the skin upon first examinations after birth:
 a) anterior face of the trunk; b) exterior face of the left thigh; c) right shoulder



Figure 2.

Hemorrhagic blisters disseminated throughout the skin upon first examinations after birth: a) postero-lateral face of the trunk; b) scalp.

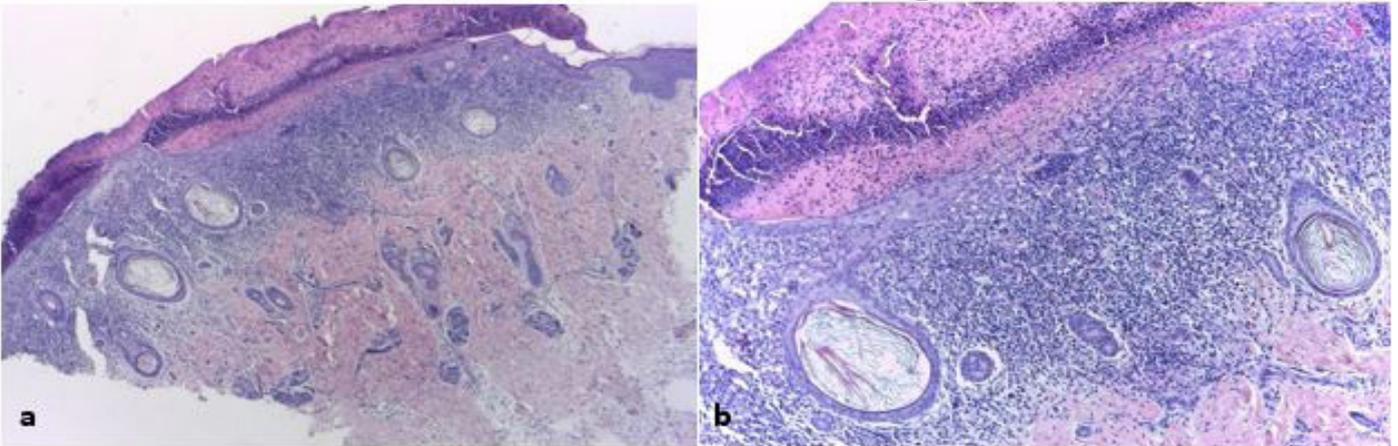
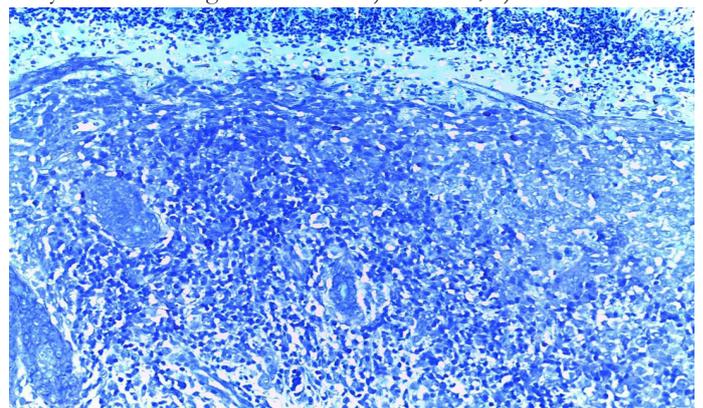


Figure 3.

Hematoxylin and Eosin staining indicating congenital histiocytosis with Langerhans cells: a) ob. X 40; b) ob. X 100.

Figure 4.

Toluidine Blue staining for mast cell highlighting, ob. X 200.



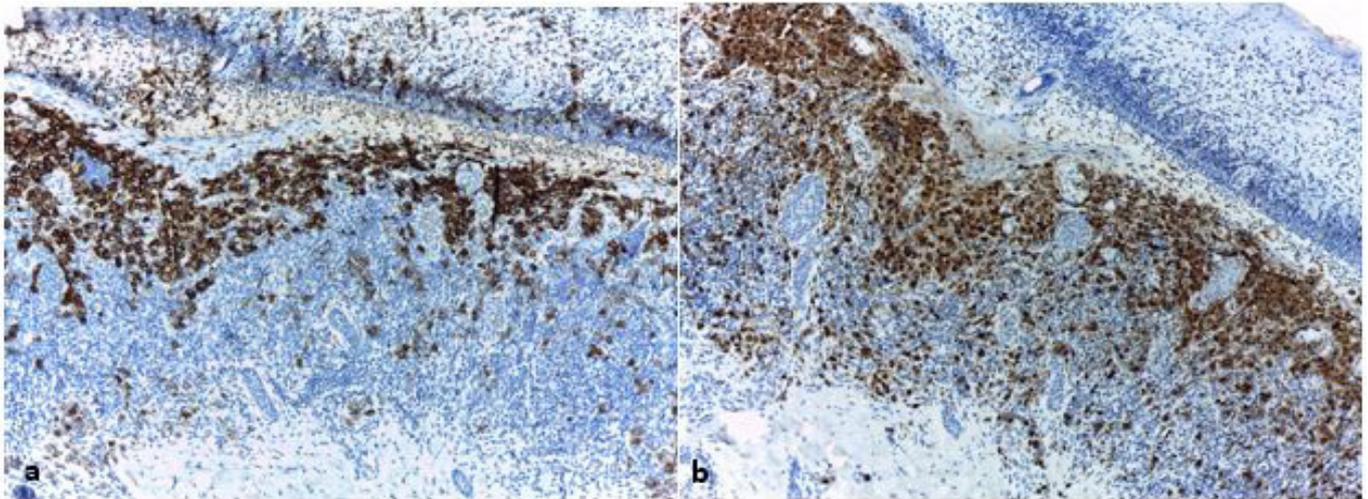


Figure 5.

Immunohistochemical examination: a) CD1a positive in the Langerhans cell; b) S 100 protein positive in the Langerhans cell.



Figure 6.

The skin lesions at 5 months: a) exterior face of the left thigh; b) the right leg.

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