

Skin-limited Langerhans cell histiocytosis in an adult

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Abstract

Langerhans cell histiocytosis (LCH) is an idiopathic group of disorders characterized histologically by proliferation and infiltration of tissue by Langerhans cell-type histiocytes. This disease can affect various organs. Patients with single system lesion should be followed carefully. Detection of somatic *BRAF*-V600E mutation in circulating blood cells or in lesional biopsies has been associated with high-risk clinical characteristics. A 38-year-old male presented to our Dermatology Centre with a 3-month history of a small nodule on his right leg skin. Surgery to remove the lesion was performed. The diagnosis of skin-limited LCH was established. Due to possible systemic spread, the patient was referred to a hematologist for further evaluation. A full-body computed tomography (CT) scan did not show any infiltrates in other organs. Bone marrow aspirate and biopsy were performed; no Langerhans cells were detected. Sometimes skin lesions may represent the most clinically evident manifestation of potentially life-threatening multisystem disease.

Key words: skin-limited; Langerhans cell histiocytosis; CD1a; S100; Adult.

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Introduction

Langerhans cell histiocytosis (LCH) is a rare, idiopathic group of disorders of unknown etiology characterized histologically by infiltration and proliferation of various organs by Langerhans cell-type histiocytes, which are S100 and CD1a⁺.^{1,2} LCH is diagnosed in all age groups, most commonly in young children with a peak incidence during the first 4 years of life, and is rarely seen in the adult population.³ We present a rare case of skin-limited LCH in an adult male patient.

Case Report

A 38-year-old male presented to our Dermatovenereology Centre with a 3-month history of a nodule on his right lower leg. No pain, itching, or other complaints were reported. A dermatological examination revealed a 1.2×0.6 cm solitary, firm, cyanotic, ulcerating nodule on the posterior side of his right shin (Figure 1). General physical examination was unremarkable. No lymphadenopathy nor any systemic symptoms were observed. Routine laboratory blood and urine tests, blood chemistry tests, and chest X-ray were normal. The lesion was excised. Histological examination of the skin lesion showed infiltration in the papillary and reticular dermis consisting of medium-sized and large mononuclear cells with eosinophilic cytoplasm and kidney-shaped nuclei (Figure 2a). The immunohistochemical examination revealed pos-

itive staining for S100 protein, CD1a, and langerin (Figure 2 b-d). Due to a possible systemic spread of the disease, the patient was referred to a hematologist for further evaluation. Abdominal ultrasound showed no specific changes. A full-body computed tomography (CT) scan did not show any suspicious infiltrates in other organs. Bone marrow aspirate and biopsy were performed, and no Langerhans cells were detected. The diagnosis of skin-limited LCH was established based on the histopathological and immunohistochemical results. No additional treatment was prescribed as no new skin or systemic symptoms developed. Further follow-up of the patient is ongoing.

Discussion

LCH is a rare disorder of abnormal proliferation of bone marrow-derived histiocytes, with the incidence of one to two cases per million in adults. The true incidence might be underestimated due to the high rate of misdiagnosis and cases of spontaneous resolution of the lesions. Usually, LCH patients are males.^{3,4} According to the Writing Group of the Histiocyte Society, three stages of LCH are described: single-system disease, multisystem disease, and multisystem disease with evidence of organ dysfunction.⁵ Etiology of LCH is not clear. The occurrence and development of this disease are related to chromosomal instability and gene mutation. Tissue cells have the feature of clonal proliferation, which means that the initial lesion of the disease is a tumor.⁶ Some authors describe association with neoplasia, immunostimulation, dendritic

cell disorders, and viral infection.^{7,8} Detection of somatic *BRAF*-V600E mutation in circulating blood cells or in lesional biopsies has been associated with high-risk clinical characteristics.⁹ The disease can affect various organs: skin, lymph nodes, bone marrow, lungs, thymus, liver, and spleen. In approximately half of patients, the disease is limited to one organ, while the others present with multisystem disease that predicts increased mortality. The clinical manifestation depends on the age of onset, the proliferation rate of Langerhans cells, and the affected tissues and organs. Skin-limited lesions may be present in about 4.4-7.1% of all LCH cases. Generally, it appears as a single or generalized pinkish or reddish-brown papule, plaque, or nodules that may become crusted and infected. In some cases, patients have seborrheic dermatitis-like rashes. Most predominant lesion sites are scalp, torso, flexural and intertriginous area, external genitalia, perianal area, and glabrous skin. Also, it may manifest as ulcers, scabby plaque, and granuloma at the groin, armpit, or other frictional area as well.¹⁰ The differential diagnosis includes eczema, seborrheic dermatitis, psoriasis, *Candida* infection, lichen planus, vasculitis, cutaneous lymphoma, malignant histiocytosis, sarcoidosis, and cutaneous involvement of Erdheim-Chester disease.^{11,12} The diagnosis of LCH is based on clinical manifestation, histopathology, and immunohistochemistry. The main histological finding is the presence of the characteristic Langerhans-like cells with “coffee bean” or “kidney” shaped nuclei. On immunohistochemistry, a proliferation of CD1a and S100 protein-positive cells is seen. Langerin (CD207) – a new monoclonal antibody – shows higher specificity in Langerhans cells than CD1a, which is also a marker for T cells and dendritic cells. These markers together confirm the diagnosis of LCH; they were all detected in our case. In comparison with non-LCH cases, LCH may be immunohistochemically positive for CD68, and sometimes is found. However, this marker is an additional, but not specific, finding in LCH.^{13,14} Patients with single-

system lesions or skin-limited LCH should be followed carefully. A detailed examination should be performed since there is a significant risk of disease spread to other organs. Specific treatment should be administered according to the form of the systemic disease, dysfunction of the affected organs, and the age of the patient. For patients with single-system LCH, the choice of therapy is generally based upon the site of involvement and the number of lesions. No standard of care exists for the therapy of skin-limited LCH. Various treatment options are described, including surgery, radiotherapy, topical corticosteroids, thalidomide, isotretinoin, PUVA and combination therapy.^{15,16} As treatment with topical corticosteroids was ineffective in our case, surgery to remove the



Figure 1. Solitary, firm, cyanotic, nodule with central ulceration on the posterior side of patient's right shin.

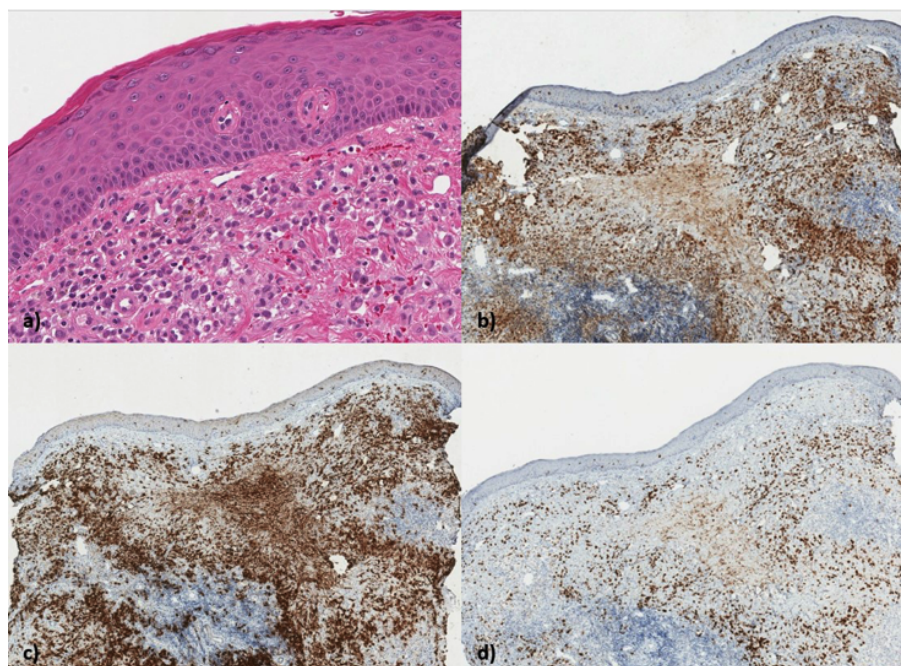


Figure 2. Histological and immunohistochemical examination. **a)** medium-sized and large mononuclear cells with eosinophilic cytoplasm and kidney-shaped nuclei infiltration in dermis; **b)** positive staining for S100 protein; **c)** positive staining for CD1a; **d)** positive staining for langerin.

lesion was performed. The prognosis of LCH depends on the age of onset and the number of affected organs. The prognosis is good when the disease is only skin or bone limited; however, it gets worse when more organs are affected, and there is bad response to primary early treatment. Although adult LCH normally has a good prognosis, further follow-up of the patient is recommended. Nevertheless, patients younger than 2 years old or with multiple system involvement have a high mortality rate, ranging up to 66%.¹⁷

Conclusions

LCH is a rare histiocytic disorder that may be seen in all age groups, but is most common in children. Although skin-limited disease can resolve spontaneously, sometimes skin lesions may represent the most clinically evident manifestation of potentially life-threatening multisystem disease. Close observation is an option for patients with skin-only LCH.

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Received: 13 February 2021; Accepted: 29 July 2021.

Contributions: Milda Krivickaitė: conceptualization; Neringa Guobytė, Emilija Šerpytienė: data collection; Neringa Guobytė, Emilija Šerpytienė, Monika Macejevskaja, Milda Krivickaitė: data analysis and interpretation, writing – original draft; Jūratė Grigaitienė, revision. All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: no ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Consent for publication: the patient gave his written consent to use his personal data for the publication of this case report and any accompanying images.

Availability of data and materials: data and materials are available from the authors upon reasonable request.

Conference presentation: this case was presented at the 28th EADV Congress in Madrid, Spain, in 2019.

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