Skin-limited Langerhans cell histiocytosis in an adult: a case report

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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 months history of small nodule on his right leg skin. Surgery to remove the lesion was performed. The diagnosis of skin-limited Langerhans cell histiocytosis was established. Due to possible systemic spread the patient was referred to a haematologist for further evaluation. Full body CT scan did not show any infiltrates in other organs. Bone marrow aspirate and biopsy was performed, no Langerhans cells were detected. Sometimes skin lesions may represent the most clinically evident manifestation of potentially life-threatening multisystem disease.

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 positive (1,2). LCH is diagnosed in all age groups, most commonly in young children with a peak incidence during first 4 years of life and is rarely seen in the adult population (3).

We present a rare case of skin-limited Langerhans cell histiocytosis in an adult male patient.

Case report

A 38-year old male presented to our Dermatovenereology Centre with a 3 months history of nodule on his right lower leg. No pain, itching or other complaints were reported. A dermatological examination revealed 1.2 x 0.6 cm solitary, firm, cyanotic, ulcerating nodule on the posterior side of his right shin (Fig. 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 (Fig. 2. a). The immunohistochemical examination revealed positive staining for S100 protein, CD1a and langerin. (Fig. 2. b, c, d).
Due to a possible systemic spread of the disease the patient was referred to a haematologist for a further evaluation. Abdominal ultrasound showed no specific changes. Full body CT scan did not show any suspicious infiltrates in other organs. Bone marrow aspirate and biopsy was performed - no Langerhans cells were detected. The diagnosis of skin-limited Langerhans cell histiocytosis was established based on the histopathological and immunohistochemistry results. No additional treatment was prescribed as no new skin or systemic symptoms developed. Further follow-up of the patient is ongoing.

**Discussion**

Langerhans cell histiocytosis 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 since its 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, 3 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 is related to
chromosomal instability and gene mutation. Tissue cells have the feature of clonal proliferation, which aims that the initial lesion of the disease is tumor (6). Some authors describe association with neoplasia, immunostimulation and dendritic cell disorders, 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, 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 papules, plaques, 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 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, 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) - 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 diagnosis of LCH, they were all detected in our case. In comparison with non-Langerhans cell histiocytosis cases, LCH might be immunohistochemically positive for CD68 and sometimes is found. However, this marker is 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 systematic 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 number of the 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 lesion was performed.

The prognosis of LCH depends on the age of onset and the number of affected organs. The prognosis is good when 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 high mortality rate, ranging up to 66% (17).
Conclusion

Langerhans cell histiocytosis 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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