

CLINICAL REPORT

Purely Cutaneous Langerhans' Cell Histiocytosis in an Adult Woman

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Langerhans' cell histiocytosis (LCH) is a clonal, histiocytic, proliferative disorder of unknown aetiology originating from Langerhans' cells. Although the clinical presentation and therapeutic approach to the disease in children have been well established, few data are available concerning the disease in adults. Moreover, unique cutaneous involvement by LCH in a woman older than 70 years has been described very rarely. We report here a case of a 75-year-old woman with cutaneous LCH confined to the inframammary fold, and highlight some medical problems regarding the management of a purely cutaneous form of LCH in adults. Key words: Langerhans' cell histiocytosis; skin; elderly.

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Adult Langerhans' cell histiocytosis (LCH) is a group of histiocytic disorders characterized by proliferation of Langerhans' cells (LC) with several grades of tissue infiltration and systemic compromise (1). Several tissues may be involved simultaneously: bones, lungs, skin, oral-genital mucosa and endocrine glands (2). Although the skin is a common target, purely cutaneous forms of LCH with adult onset have been described very rarely in the literature (3).

We report here a new case of cutaneous LCH in a 75-year-old woman with no other signs of systemic involvement.

CASE REPORT

In December 2006, a 75-year-old woman was referred to our clinic with a dermatosis of one-year duration. Dermatological examination revealed the presence of a diffuse erythematous, infiltrative plaque of the inframammary fold, associated with severe crusting, scaling and erosions of the involved skin (Fig. 1). The clinical features of the skin lesions were not specific, and had similarities to those of inverted psoriasis, impetiginized



Fig. 1. Erythematous, erosive plaques in the inframammary fold in a 75-year-old woman with Langerhans' cell histiocytosis confined to the skin.

eczema, or intertrigo. Physical examination revealed no lymphadenopathy of the axillary nodes or abdominal organomegaly.

The patient reported great discomfort related to a persistent pruritus, and pain confined to the involved area, and denied systemic symptoms including fever, fatigue, vomiting, diarrhoea, polyuria, dyspnoea and bone pain.

Histological examination of the affected skin revealed a diffuse, superficial and deep dermal lymphohistiocytic infiltrate, with a predominance of dendrite LC showing pale cytoplasm and kidney-shaped nuclei (Fig. 2). Clusters of proliferating cells demonstrated epidermotropism, with focal crossing of dermoepidermal junction and invasion of the epidermis (Fig. 2).

Immunohistochemistry confirmed the dendritic nature of the infiltrating cells, which showed a diffuse expression of CD1a and S-100 (Fig. 2) and a mild immunostaining for CD68.

Routine urine analysis, biochemical investigations, haemoglobin, haematocrit, white blood cell count and platelet levels were within normal limits. Abdominal ultrasonography, X-rays of the chest and of the entire skeleton including the skull showed minimal changes consistent with the age of the patient. No pathological findings were detected in a bone marrow biopsy. Overall, the clinical, laboratory, instrumental and histological findings fulfilled the criteria for diagnosis of cutaneous LCH with adult onset, according to the Writing Group of the Histiocyte Society (4).

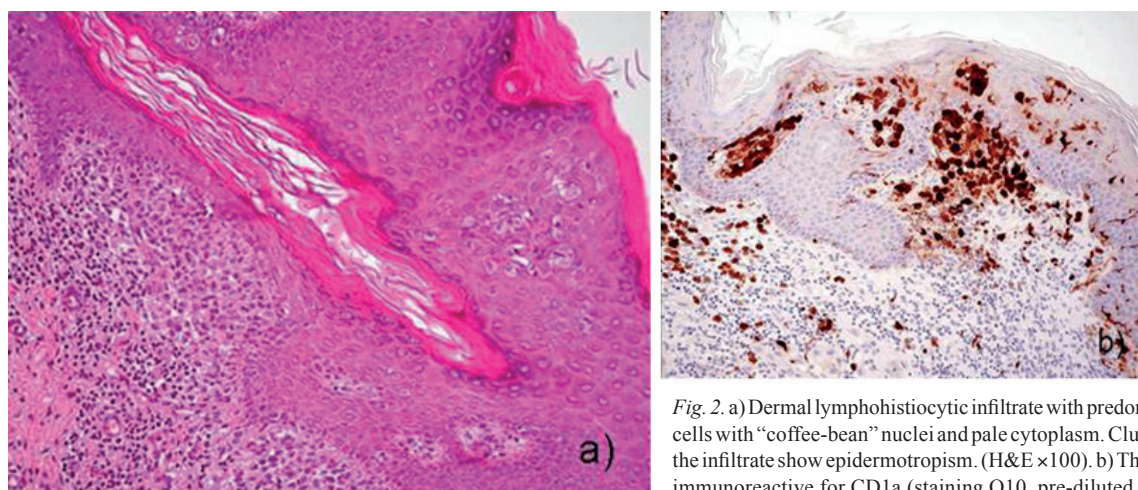


Fig. 2. a) Dermal lymphohistiocytic infiltrate with predominance of Langerhans' cells with "coffee-bean" nuclei and pale cytoplasm. Cluster of cells comprising the infiltrate show epidermotropism. (H&E $\times 100$). b) The infiltrate was strongly immunoreactive for CD1a (staining O10, pre-diluted, Immunotech $\times 100$).

The patient did not respond to topical application of betamethasone dipropionate twice a day for 8 weeks, or to topical administration of imiquimod for 5 consecutive days every week for 12 weeks. A poor response to oral administration of prednisolone 60 mg/day for 6 weeks was also shown. The patient refused psoralen plus ultraviolet A treatment (PUVA) because she suffered from claustrophobia, and started treatment with interferon (INF) α -2b (6 million units 3 times/week), which was discontinued 5 months later due to lack of efficacy. Therapy with vinblastine (6 mg/m², given intravenously every week) was about to start, but the patient died of massive, cerebral ischaemia, apparently unrelated to the LCH.

DISCUSSION

The interesting aspect of this case is its clinical presentation, since a purely cutaneous form of LCH is very rare in women older than 70 years (5, 6). The incidence of LCH in adults is 1–2 cases per million (7) and although skin represents the second most commonly involved organ in single system disease after bone (2), the prevalence of LCH confined to the skin ranged from 4.4% to 7.01% of cases (8); moreover, only 2% of patients with LCH, either multisystem or localized, are older than 70 years (8).

LCH is a group of idiopathic histiocytic disorders including a wide spectrum of diseases with different clinical features and prognosis, whose classification into separate entities named Letter-Siwe disease, Hand-Schuller-Christian disease, Hashimoto-Pritzker disease and eosinophilic granuloma is of historical interest only (9).

The classification of LCH actually follows the guidelines of the Histiocyte Society (1): according to the organ involvement LCH may be classified into a localized ("single-system disease") or a disseminated disease ("multisystem disease"), which may be further

Table I. Classification of Langerhans' cell histiocytosis according to the guidelines of the Histiocyte Society

"Single system disease"	
Single site	Monostotic bone involvement
	Isolated skin involvement
	Solitary lymph node involvement
Multiple site	Polyostotic bone involvement
	Multifocal bone disease (two or more different bones)
	Multiple lymph node involvement
"Multisystem disease"	
"Low risk group"	Disseminated disease without involvement of risk organs ^a
"Risk group"	Disseminated disease with involvement of one or more of the risk organs ^a

^aHaematopoietic system, lung, liver, spleen.

distinguished into two clinical variants with different course and prognosis ("low risk" and "high risk" groups) (1) (Table I).

Treatment of cutaneous LCH is controversial. Several therapeutic approaches have been reported in the literature, according to the extent of disease: topical and systemic corticosteroids, topical imiquimod, PUVA, thalidomide, INF α -2b, vinblastine and surgery have been used for treating the disease (3).

The reported prognosis in elderly patients with single-system disease involving the skin is controversial (10): despite its benign nature, cutaneous LCH is generally associated with a poor therapeutic response (11) and it tends to recur (12); thus patients may progress towards multisystem disease (13).

Overall, this case report re-frames the question regarding the wide spectrum of clinical presentations of histiocytic disorders, and highlights the need for the identification of prognostic markers and treatments for purely cutaneous LCH, in order to control cutaneous manifestations, to prevent disease progression and to increase awareness of this condition.

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