Solitary, Late-onset, Self-healing Langerhans' Cell Histiocytosis

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"Self-healing" Langerhans' cell histiocytosis (LCH), first reported by Hashimoto & Pritzker in 1973 (1), is a rare primary skin disorder that presents at birth or just after birth. It can be categorized based on the involvement of solitary or multiple sites and can be further classified as congenital or late-onset (2). Although more than 100 cases of self-healing LCH have been reported (3), solitary, late-onset, self-healing LCH is extremely rare (4–7). We herein report a case of solitary, late-onset, self-healing LCH and review previous reported cases.

CASE REPORT

A 5-month-old healthy female infant was referred to our clinic with a reddish-yellow nodule on the right side of her forehead. Her parents had first noticed the nodule about one month previously. In spite of treatment with topical steroid ointment its size increased to 14 × 10 mm. It was non-ulcerated and rubber-like in consistency (Fig. 1a). On dermoscopic examination, the nodule was found to be white in the centre with peripheral telangiectasia (Fig. 1b). Results of laboratory tests were mostly within normal limits. Histopathological examination revealed diffuse infiltration of mononucleated histiocytic cells from just below the epidermis to the base of the dermis. These cells had abundant acidophilic cytoplasm and some contained kidney-shaped nuclei (Fig. 1c). There were few mitoses and no apparent atypia in the infiltrates. Immunohistochemically, the histiocytic cells were positive for CD1a (Fig. 1d) and S100, but negative for CD68, indicating that they were Langerhans' cells. Further immunohistochemical analysis showed that they were also negative for langerin, a marker for Birbeck granules (data not shown). The patient was examined for systematic involvement of disease. Whole-body bone scintigraphy, cerebral magnetic resonance imaging, chest computed tomography, and cerebrospinal fluid examination revealed no abnormalities. The nodule had almost disappeared 2 months after consultation. No recurrence was observed up to the age of 16 months. Based on these findings, a diagnosis of solitary, late-onset, self-healing LCH was made.

DISCUSSION

Congenital, self-healing LCH usually involves only a cutaneous lesion and lacks the systemic involvement seen in more common forms of LCH (8). Solitary, congenital, self-healing LCH accounts for about 25% of cases reported so far (9). Both LCH and self-healing LCH display various cutaneous manifestations, including papules, nodules, macules and vesicles. Since it is difficult to differentiate LCH from self-healing LCH based only on the skin lesions present, systemic evaluation should be performed to exclude possible extracutaneous disease. Ulceration or necrosis on the surface of the solitary nodule has been proposed as an indicator of good prognosis (3).

Histological differentiation of self-healing LCH from other types of LCH seems to be difficult. Ultrastructural differences originally proposed by Hashimoto & Pritzker (1) still remain important tools for distinguishing

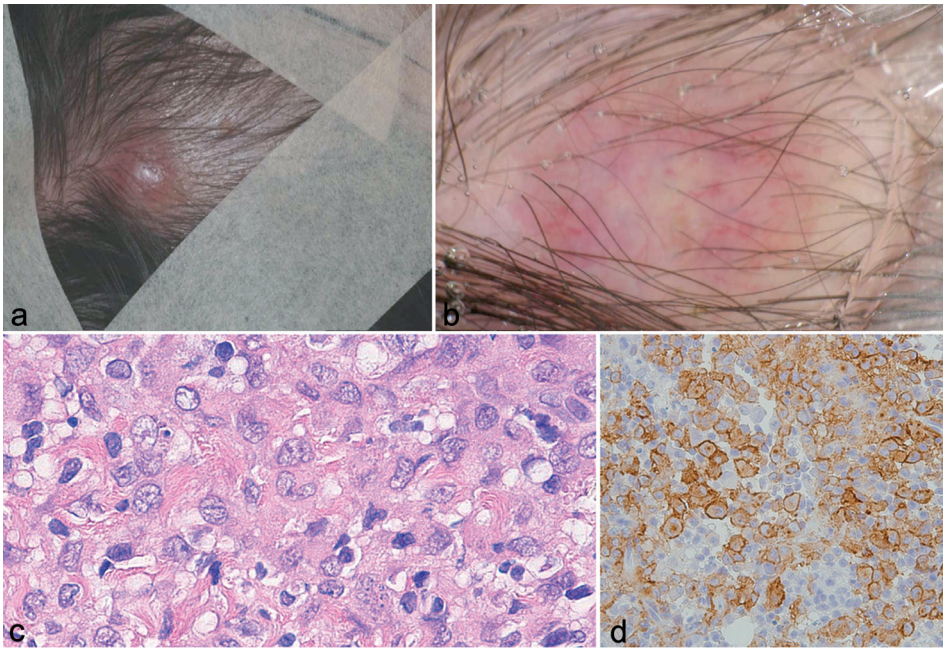

Fig. 1. (a) Solitary reddish-yellow nodule on the right side of the patient's forehead. (b) Dermoscopy showing a central white area with peripheral telangiectasia. (c) Lesion cells containing abundant acidophilic cytoplasm and kidney-shaped nuclei characteristic of Langerhans' cells (H&E; ×400). (d) Immunohistochemical staining for CD1a.

Table I. *Case reports of solitary, late-onset, self-healing Langerhans' cell histiocytosis*

Author	Age at onset	Site	Treatment	BG	Langerin	CD1a	S100	CD68
Taieb et al. (4)	3 weeks	L buttock	SE	+	NR	+	+	NR
Masouye et al. (5)	2 months	L thigh	SE	+	NR	NR	+	NR
Ikeda et al. (6)	1 month	C forehead	EBI	+	NR	+	+	NR
Weiss et al.(7)	7 months	R faces	SE	NR	–	+	+	–
This report	4 months	R forehead	None	NR	–	+	+	–

BG: Birbeck granules; L: left; C: centre; R: right; SE: surgical excision; EBI: electron beam irradiation; +: positive; –: negative; NR: not reported.

self-healing LCH from other types of LCH. Notably, coexistence of Birbeck granules and laminated dense bodies in the same cells is an important marker of self-healing LCH (8). Moreover, the use of anti-langerin (CD207) antibodies has been proposed as an alternative to electron microscopy for the detection of Birbeck granules (7).

Our case was different from classical cases of congenital, self-healing LCH in two key ways: (*i*) the onset of cutaneous symptoms occurred at 4 months of age, not at birth; and (*ii*) only a single site was involved. Only five cases of solitary, late-onset, self-healing LCH (including ours) have as yet been reported and, as far as we know, this is the first case in which dermoscopic examination was employed. Dermoscopy showed white colouration in the centre of the nodule, which may be linked to the proliferation of Langerhans' cells in the dermis. We do not know whether this feature is unique to self-healing LCH. While further investigation is certainly necessary, the identification of central white areas with peripheral telangiectasia through dermoscopic analysis may contribute to the diagnosis of self-healing LCH.

Previously reported cases of solitary, late-onset, self-healing LCH are summarised in Table I. Onset period varied from 3 weeks to 7 months. Interestingly, all cases involved female infants. Lesions were completely removed through surgery in 3 cases. Besides our case, only one other was biopsied (6): resolution occurred after electron beam irradiation following one month's observation. In our case, the nodule was present for 3 months and almost completely disappeared without treatment. All five reported cases were positive for both S100 and CD1a, except for one case in which CD1a staining was not performed. CD68 was investigated in 2 cases and was negative in both of them. Although conflicting reports describe the expression of langerin in self-healing LCH (10, 11), langerin was negative in two of the five previously reported cases of solitary, late-onset, self-healing LCH, and not determined in the remaining three. In contrast, langerin expression is a feature of non-self-healing LCH (12). This difference might be useful for predicting self-healing in LCH.

It should also be noted that relapse within 6 months of spontaneous resolution has been reported in congenital, self-healing LCH (13). Follow-up for at least one year is therefore recommended in patients with this disorder.

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