Self-healing Langerhans cell histiocytosis (Hashimoto-Pritzker disease): two Tunisian cases

H. Belhadjali, M. Mohamed, H. Mahmoudi, M. Youssef, A. Moussa,
S. Achour Chouchane, C. Chouchane, A. Zakhama and J. Zili

ABSTRACT

"Self-healing" Langerhans cell histiocytosis (SHLCH) is a rare self-limited variant of Langerhans cell histiocytosis that presents at birth or during the neonatal period. It was first described by Hashimoto and Pritzker in 1973. Subsequently, more than 70 cases have been reported in the literature. Regarding age of onset, SHLCH should be divided into congenital SHLCH and rare late-onset type. We report here two additional cases of SHLCH in Tunisian infants. We emphasize the need for long-term follow-up in such patients.

KEY WORDS

histiocytosis, Langerhans cell self-healing, Hashimoto-Pritzker disease, childhood

Introduction

"Self-healing" Langerhans cell histiocytosis (SHLCH) is a rare self-limited variant of Langerhans cell histiocytosis (LCH) that presents at birth or during the neonatal period (1). It was first described by Hashimoto and Pritzker in 1973 (1). Subsequently, more than 70 cases have been reported in the literature (2). We report here two additional cases of SHLCH in Tunisian infants.

Case 1

A male infant, born at term after an uncomplicated pregnancy, presented at the age of 1 month with multiple skin lesions since birth, consisting of yellowish papules ranging in size from 5 to 15 mm in diameter, and sometimes with ulcerations and scabs. The lesions were distributed over the trunk, lower limbs, and soles (Fig. 1 and Fig. 2). The child was otherwise healthy with no involvement of the mucous membranes. A skin biopsy revealed a massive infiltration of mononuclear cells in the superficial and deep dermis surrounding the sweat glands. The cells had eccentric, pale, reniform nuclei, and abundant eosinophilic cytoplasm. Figure 3. Occasional eosinophils were also present. Infiltrating histiocytic cells made micro-abscess-like clusters within the epidermis, which was ulcerated. Figure 3.. Immunohistochemistry demonstrated that most infiltrating cells were positive for S-100 protein and CD 1a antigen. Based on histological and immunohistochemical findings, we concluded that the lesions should be categorized as LCH.

Systemic evaluation of the child, including complete blood counts, serum biochemistry, liver function tests, radiographic skeletal survey, ultrasound of the abdomen, and bone marrow aspiration, produced normal results. Due to the absence of involvement of the internal organs, we decided to observe the course without

aggressive treatment. The skin lesions regressed, and after a few weeks they completely disappeared. By 4 years of age the child was symptom-free with no signs of a relapse. Based on the clinical pictures, histopathologic and immunohistochemical features, and a self-healing course, the diagnosis of congenital SHLCH was established.

Case 2

A 4-month-old girl presented at our dermatology department with a history of multiple papulonodules on the face and trunk from 20 days of age. She was born at term after an uncomplicated pregnancy. The physical examination revealed multiple 5 to 20 mm brownish-red papulonodules with a smooth surface distributed over the face and trunk (Fig.4). The mucous membranes, palms, and soles were spared. The child was otherwise healthy and the physical examination was normal. Due to the nodular lesions, a diagnosis of juvenile xanthogranuloma was considered. A skin biopsy showed a dense infiltrate of histiocytic cells in the superficial and deep dermis, which were also invading the subcutaneous fat. The cells had vesicular, sometimes reniform nuclei, and foamy cytoplasm. Sparse eosinophils were also seen and there was no epidermotropism. On immunohistochemical analysis, most of the cells were positive for S-100 protein and CD 1a antigen (Fig. 5). Systemic evaluation of the tests (blood counts, serum biochemistry, liver function tests, a radiographic skeletal survey, ultrasound of the abdomen, and bone marrow aspiration) were normal. We decided to simply observe the child. Although the skin lesions completely disappeared by the age of 5 months, at the age of 8 months we observed a recurrence of a small number of them. A new systemic evaluation of the child produced normal results. All the skin lesions disappeared within a few weeks, leaving behind pigmented scars. After an 8-year follow-up, the child was symptom-free with no signs of further relapses. The diagnosis of late-onset SHLCH was confirmed.

Discussion

Langerhans cell histiocytosis (LCH) is a generic term that identifies several clinical diseases characterized by proliferation of distinctive cells that are S-100- and CD 1a-positive and contain Birbeck granules in their cytoplasm (3–4).

More than 70 cases of SHLCH have been reported in the literature (2). The real incidence of this disorder may be underreported due to its high rate of spontaneous resolution and failure of clinical recognition (5).

Regarding the age of onset, SHLCH should be divided into the common type, namely congenital SHLCH, as observed in our first case, and a rare late-onset type. To the best of our knowledge, only 8 cases of late-onset SHLCH have been reported in the literature (2, 6–10). Late-onset SHLCH cases are summarized in Table 1.

Table 1. Case reports of late-onset SHLCH in the literature.

Series	Number of cases	Age at onset
Jang et al. (6)	3	1, 2, 7 months
Hashimoto et al. (7)	1	17 days
Masouye et al. (8)	1	2 months
Campourcy et al. (9)	1	18 months
Weiss et al. (10)	1	7 months
Nakahighashi et al. (2)	1	8 years
Our report	1	20 days

SHLCH is clinically characterized by skin lesions consisting of multiple, disseminated, firm, red-brown, painless papulonodules affecting the entire body, but with a predilection for the cephalic area and the scalp (4, 11). Palms and soles (4, 11), as observed in our first case, were also reported. SHLCH does not involve the internal organs. A few cases of SHLCH also had bone marrow (7), bone (12), lung (13), and eye (14) involvement. Therefore, in all cases of SHLCH, a thorough systemic evaluation is warranted to exclude visceral disease (4). In both our cases, lesions were restricted to the skin.

Histologically, SHLCH demonstrates massive dermal infiltrates of pleomorphic histiocytes with abundant eosinophilic ground-glass cytoplasm (8) and reniform nuclei with irregular contours (15). As observed in our second case, xanthomatous features, eosinophils, lymphocytes, and neutrophils are also common (16). Multinucleated giant cells may also exist (16, 17). Infiltrating histiocytic cells can extend into the epidermis and consequently cause ulcerations, as observed in our first case (11, 17). Moreover, in our second case, subcutaneous fat showed the same infiltrate type as the dermis (mainly as nodular lesions).

The cells in the infiltrate were S-100- and CD 1a-positive to immunolabelling. They can also be positive for macrophage and/or monocyte lineage (11).

Electron microscopic evaluation was not performed, but it can reveal Birbeck granules or laminated dense bodies inside 10 to 30% of the histiocytes (17).

The most interesting feature of Hashimoto-Pritzker disease is its spontaneous involution, usually within 1 to 3 months (17). Spontaneous regression may end with hypopigmented, pigmented, or atrophic scars (11).

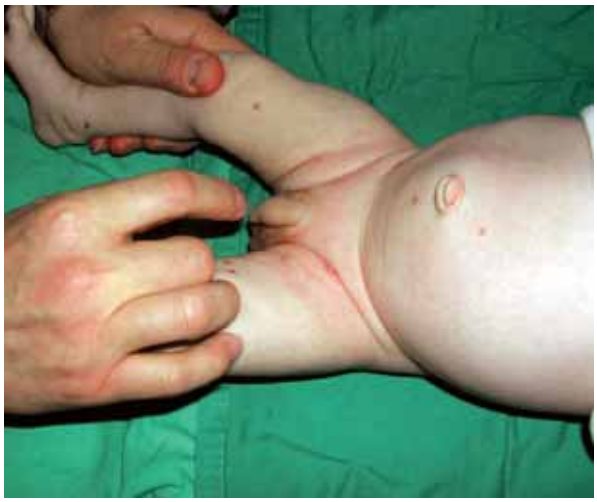

Figure 1. Papules distributed over the trunk and lower limbs. Case 1.

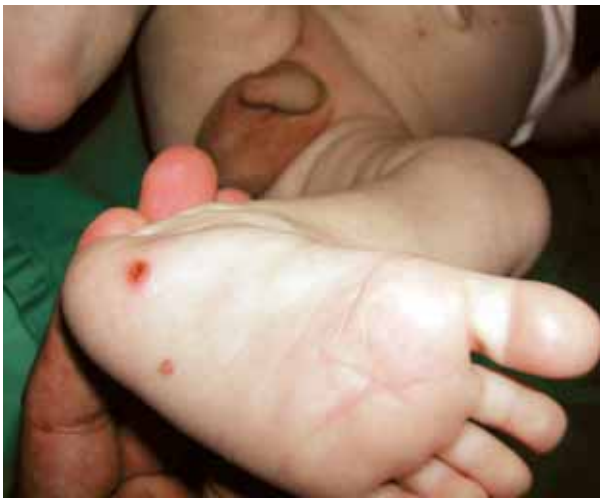

Figure 2. Two papules on the left sole. Case 1.

Possible relapses either in the skin (as observed in our second case) or at extracutaneous sites have been reported up to 4 years after the initial disappearance of the congenital lesions (3, 18, 19, 20, 21). A close follow-up is therefore necessary (11).

SHLCH should be differentiated from the malignant

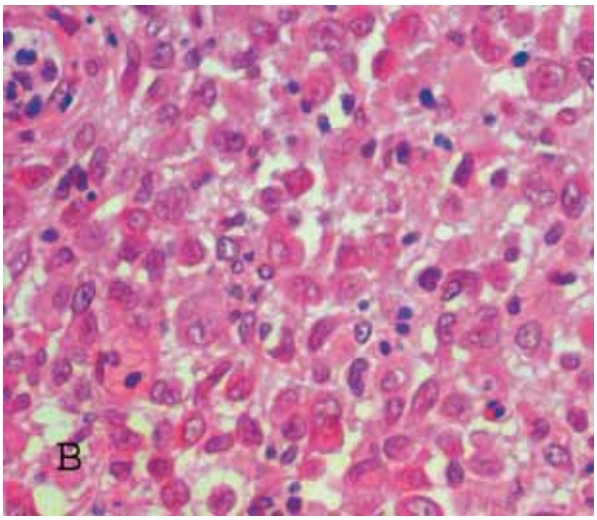

Figure 3. Skin biopsy specimen showing histiocytic cells admixed with rare eosinophils (magnification × 400)

form of other LCHs, such as Letterer-Siwe disease. However, the healthy general condition, the lack of multiorgan involvement, and the spontaneous regression of the lesions (1, 4) suggest the diagnosis of SHLCH. It should also be differentiated from other histiocytic disorders known to regress spontaneously, namely ju-

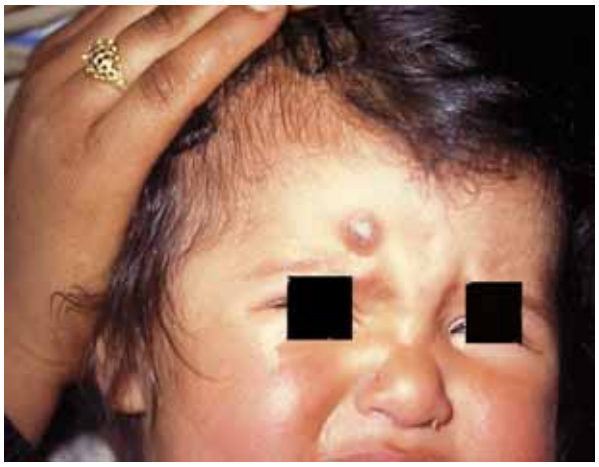

Figure 4. Brownish-red nodule on the face. Case 2.

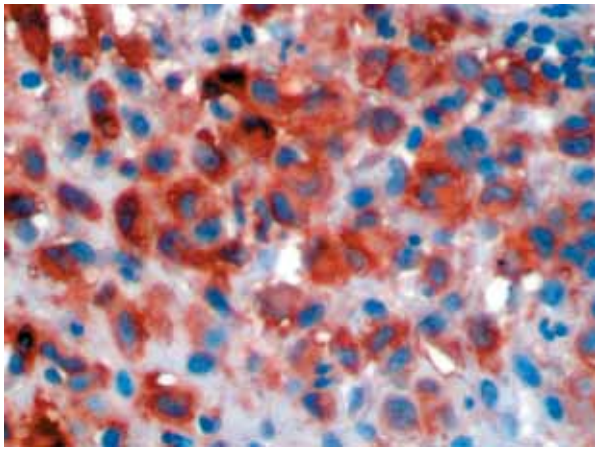

Figure 5. The proliferating histiocytic cells were positive for anti-CD 1a. Case 2.

venile xanthogranuloma (4).

The treatment protocol for single-system LCH involvement, as in SHLCH, is "wait and watch" for spontaneous regression. Even in patients with cutaneous relapses, most clinicians follow the wait-and-watch policy with good results (18, 20). SHLCH patients with multisystem involvement may also show spontaneous regression (13, 20).

REFERENCES

1. Hashimoto K, Pritzker MS. Electron microscopic study of reticulohistiocytoma: an unusual case of congenital, self-healing reticulohistiocytosis. Arch Dermatol. 1973;107:263–70.

2. Nakahigashi K, Ohta M, Sakai R, Sugimoto Y, Ikoma Y, Horiguchi Y. Late-onset self-healing reticulohistiocytosis: pediatric case of Hashimoto-Pritzker type Langerhans cell histiocytosis. J Dermatol. 2007;34:205–9.

3. Larralde M, Rositto A, Giardelli M, Gatti CF, Santos-Muñoz A. Congenital self-healing Langerhans cell histiocytosis: the need for a long term follow up. Int J Dermatol. 2003;42:245–6.

4. Walia M, Paul P, Mishra S, Mehta R. Congenital Langerhans cell histiocytosis: the self-healing variety. J Pediatr Hematol Oncol. 2004;26:398–402.

5. Kapur P, Erickson C, Rakheja D, Carder KR, Hoang MP. Congenital self-healing reticulohistiocytosis (Hashimoto-Pritzker disease): ten-year experience at Dallas Children's Medical Center. J Am Acad Dermatol. 2007;56:290–4.

6. Jang KA, Ahn SJ, Choi JH, Sung KJ, Moon KC, Koh JK. Histiocytic disorders with spontaneous regression in infancy. Pediatr Dermatol. 2000;17:364–8.

7. Hashimoto K, Griffin D, Kohsbaki M. Self-healing reticulohistiocytosis: a clinical, histologic, and ultrastructural study of the fourth case in the literature. Cancer 1982;49:331–7.

8. Masouye I, Chavaz P, Salomon D, Balderer J, Carraux P, Saurat JH. Solitary Langerhans cell histiocytoma: an unusual form of Hashimoto-Pritzker histiocytosis? Pediatr Dermatol. 1990;7:299–302.

9. Campourcy M, Moreau-Cabarrot A, Gorguet B, Samalens G, Daste B, Eclache F, Bazex J. Acquired regressive cutaneous non-Langerhans-cell histiocytosis in an infant. Ann Dermatol Venereol. 1997;124:167–70.

10. Weiss T, Weber L, Scharffetter-Kochanek K, Weiss JM. Solitary cutaneous dendritic cell tumor in a child: role of dendritic cell markers for the diagnosis of skin Langerhans cell histiocytosis. J Am Acad Dermatol. 2005;53:838–44.

11. Chevrel J, Barba G, Legrain-Lifermann V, Lecluse-Mendes I, Bourgade C, Bioulac-Sage P, Barbier R. Self-healing Hashimoto-Pritzker histiocytosis. Arch Pediatr. 2000;7:629–32.

12. García Muret MP, Fernández-Figueras MT, González MJ, De Moragas JM. Congenital spontaneously regressive cutaneous Langerhans cell histiocytosis with bone involvement (eosinophilic granuloma). Ann Dermatol Venereol. 1995;122:612–4.

13. Chunharas A, Pabunruang W, Hongeng S. Congenital self-healing Langerhans cell histiocytosis with pulmonary involvement: spontaneous regression. J Med Assoc Thai. 2002;85:S;1309–13.

14. Zaenglein AL, Steele MA, Kamino H, Chang MW. Congenital self-healing reticulohistiocytosis with eye involvement. Pediatr Dermatol. 2001;18:135–7.

15. Gianotti F, Caputto R. Histiocytic syndromes: a review. J Am Acad Dermatol. 1985;13:383–404.

16. Ricart J, Jimenez A, Marquina A, Villanueva A. Congenital self-healing reticulohistiocytosis: report of a case and review of the literature. Acta Paediatr. 2004;93:426–9.

17. Larralde M, Rositto A, Giardelli M, Gatti CF, Santos Muñoz A. Congenital self-healing histiocytosis (Hashimoto-Pritzker). Int J Dermatol. 1999;38:693–6.

18. Longaker MA, Frieden IJ, Leboit PE, Sherertz EF. Congenital self-healing Langerhans cell histiocytosis: the need for long-term follow-up. J Am Acad Dermatol. 1994;31:910–6.

19. Esterly NB, Maurer HS, Gonzalez-Crussi F. Histiocytosis X: a seven-year experience at a children's hospital. J Am Acad Dermatol. 1985;13:481–96.

20. Whitehead B, Michaels M, Sahni R, Strobel S, Harper JI. Congenital self-healing Langerhans cell histiocytosis with persistent cellular immunological abnormalities. Br J Dermatol. 1990;122:563–8.

21. Pujol RM, Moreno A, López D, Alomar A, de Moragas JM. Childhood self-healing histiocytosis X. Pediatr Dermatol. 1988;5:97–102.

A U T H O R S ' A D D R E S S E S *Hichem Belhadjali, MD, Department of Dermatology, Fattouma Bourguiba Hospital, Monastir 5000, Tunisia, corresponding author, E-mail: belhadjalihichem@yahoo.fr*
Mariem Mohamed, MD, same address
Houda Mahmoudi, MD, same address
Monia Youssef, MD, same address
Adnene Moussa, MD, same address
Sonia Chouchane, MD, same address
Achour Chouchane, MD, same address
Abdelfatah Zakhama, MD, same address
Jammeleddine Zili, MD, same address