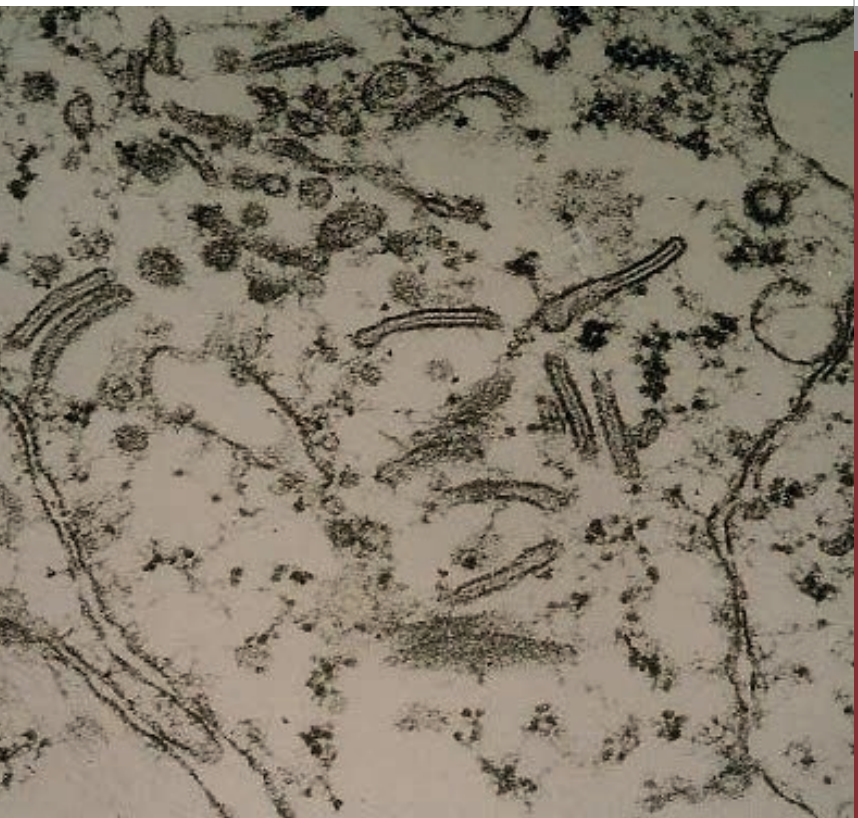
SWISS SOCIETY OF NEONATOLOGY

A newborn with a papulonodular rash at birth



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INTRODUCTION

Congenital skin lesions are rare disorders in the newborn period. Apart from primary skin disorders, the differential diagnosis includes infectious diseases, benign or malignant tumors and storage diseases. We present an infant born with numerous papules, nodules and initially vesicles.

CASE REPORT

A one day old boy, weighting 3380 g, was admitted to our NICU on September 1997. He was born at term after an uncomplicated pregnancy. He was the fifth child of healthy parents, his four sisters were also in good health. In addition, there was no known family history of atopy or skin disorders.

At birth, the boy was noted to have innumerable papulonodular and some vesicular skin lesions in a generalized distribution, predominantly on the scalp, face, trunk, and all four extremities including both hands and feet. One lesion could be found on the palate, but no more mucous membrane locations were obvious.

The multiple skin lesions were 1mm to 8mm in diameter and by DOL 2, the vesicles changed also to red-brown papules and nodules, partly honey-like crusted, partly hemorrhagic (Fig. 1-3).

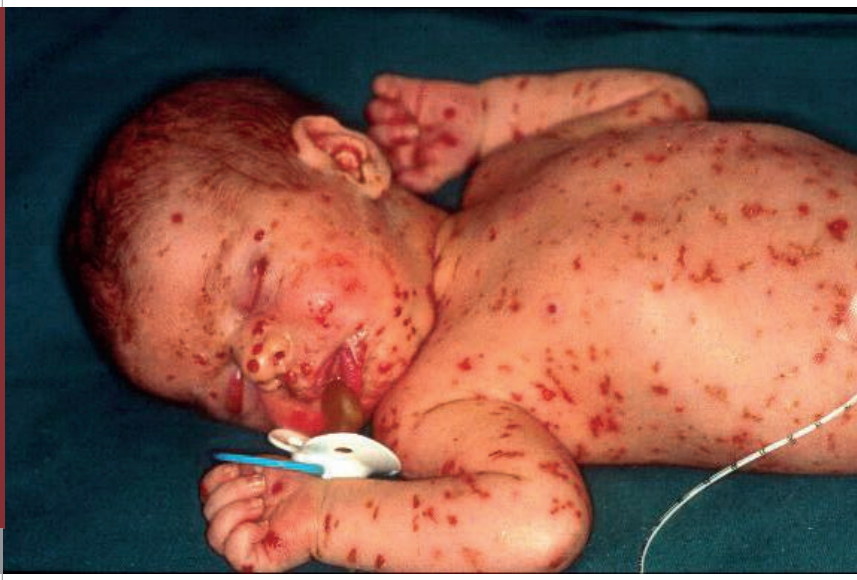

Fig. 1

Appearance of rash on day of life 3.

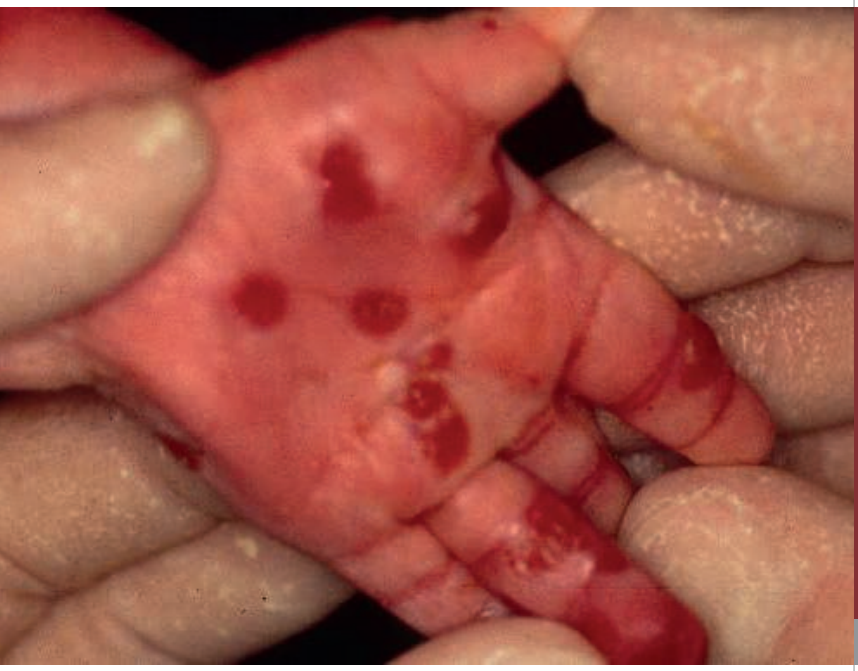

Fig. 2

Rash involving the palms of the hands.

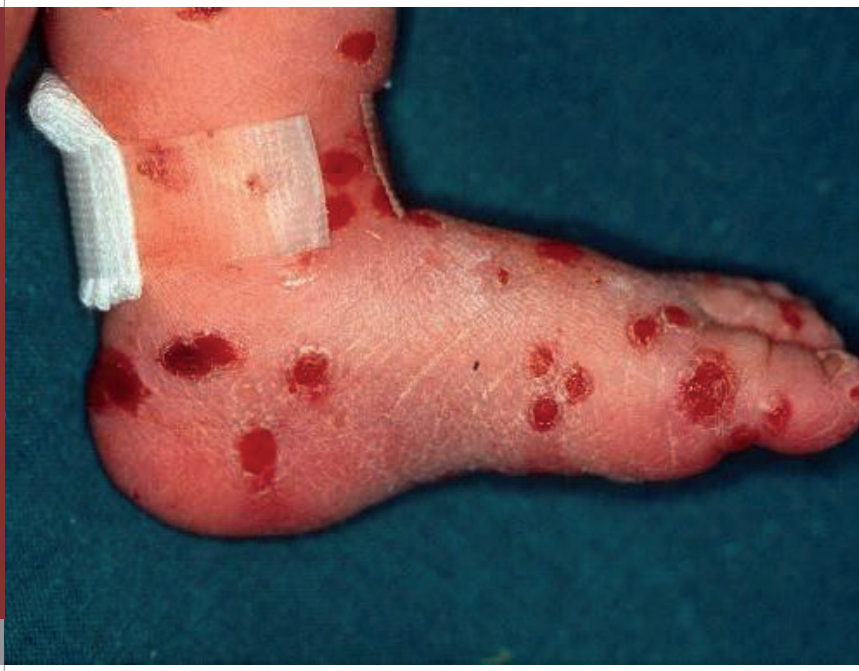

Fig. 3

Rash involving the left foot.

The infant was afebrile, without organomegaly or lymphadenopathy and in a stable condition. There was no additional information about maternal infections (like varicella or herpes simplex) or even maternal contact to any infected person.

Complete blood cell count and coagulation parameters were normal. Blood chemistry studies (electrolytes, BUN, creatinine, ASAT, ALAT, gamma-GT, bilirubin), blood gas analyses, blood glucose and CRP also revealed no abnormalities. Antibody titers of TORCH and syphilis were inconspicuous. Bacterial and viral (herpes simplex, varicella, cytomegalovirus) cultures of blood, eye secretions, urine, stool and vesicle fluid were negative. X-rays of the chest and abdomen and ultrasonography of the abdomen and brain were also normal. An eye examination was performed without signs of ocular pathology.

Our first differential diagnoses included some type of infectious disease (congenital herpes simplex, varicella zoster), tumors (histiocytosis X, disseminated mastocytosis or others) or skin pathologies (epidermolysis bullosa, pemphigus, neonatal lupus erythematosus). Therefore, parenteral therapy with ceftazidime, clindamycin and acyclovir was started. When all cultures returned negative, antimicrobials were stopped.

Histopathologic examination of a skin biopsy of the left foot revealed diffuse infiltration of the epidermis and dermis, extending into adnexal structures. The infiltration consisted of pleomorphic histiocyte-like cells with nuclei varying in form and size. Irregular vacuols and foamy cytoplasm could be observed. An associated infiltration with eosinophils and lymphocytes were also seen, but there was no erythrophagocytosis. Electron microscopic examination showed Birbeck granules in more than 10% of the cells (Fig 4). Immunohistochemistry showed the histiocytic cells to be positive for S-100 protein and CD 1a antigen (Fig. 5 and 6, respectively). A presumptive diagnosis of Langerhans cell histiocytosis was made.

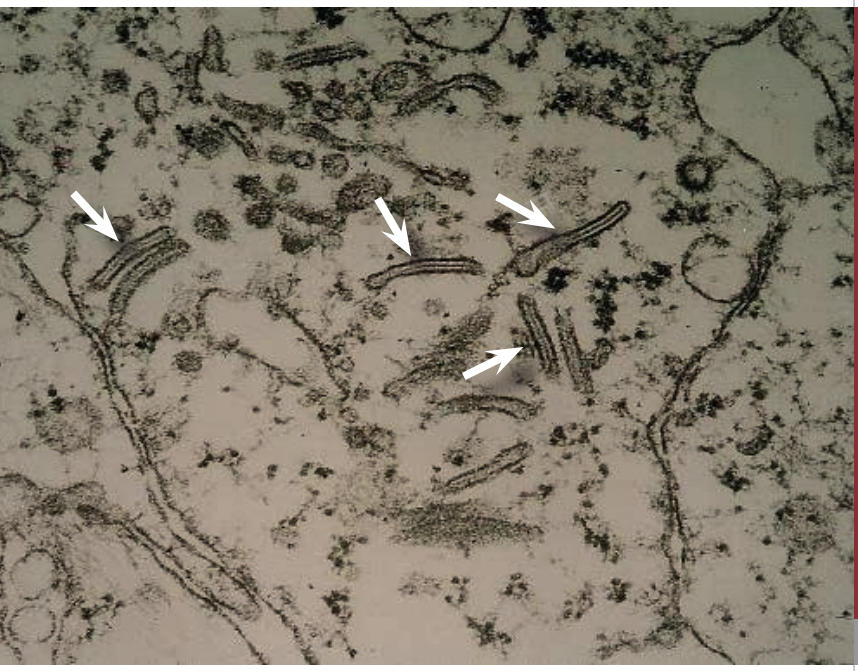

Fig. 4

TEM showing Birbeck granules (arrows).

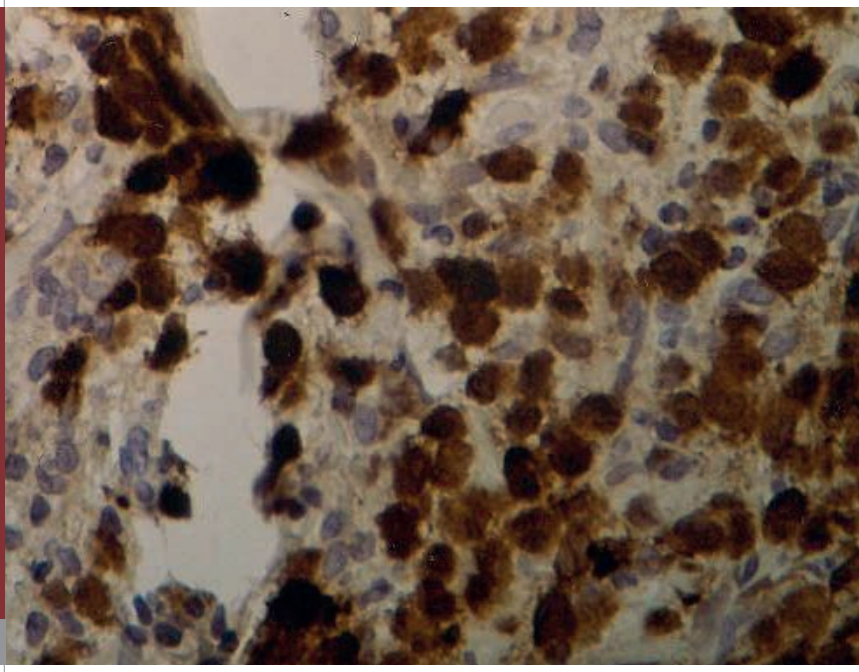

Fig. 5

Cells positive for S-100 protein.

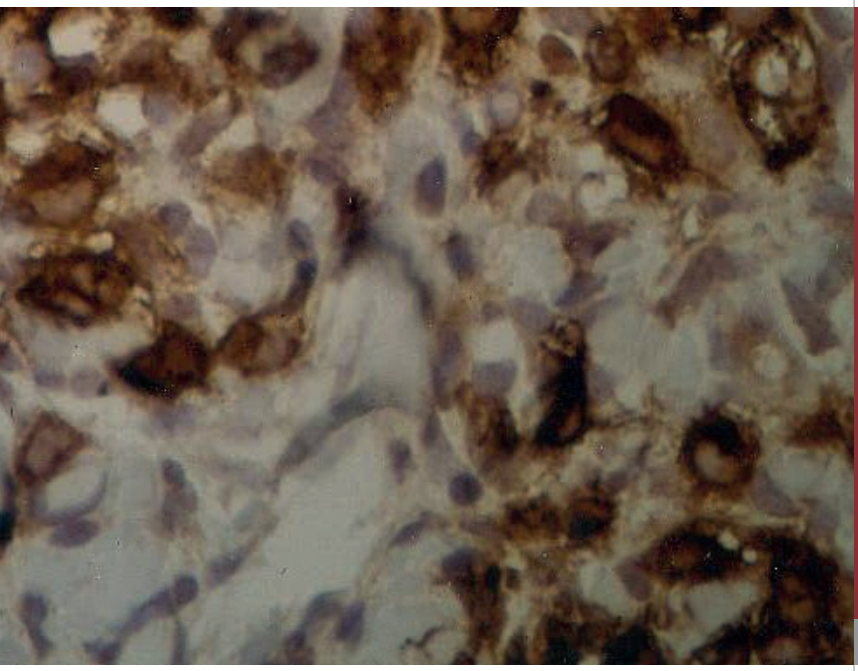

Fig. 6

Cells positive for CD 1a antigen.

The clinical course showed slow involution of the skin lesions, and the infant remained in excellent health and had no signs of systemic involvement. The papulonodular skin changes healed slowly or converted into a miliar fatty infiltration in the epidermis (Fig. 7, 8 and 9, at the age of 3 months).

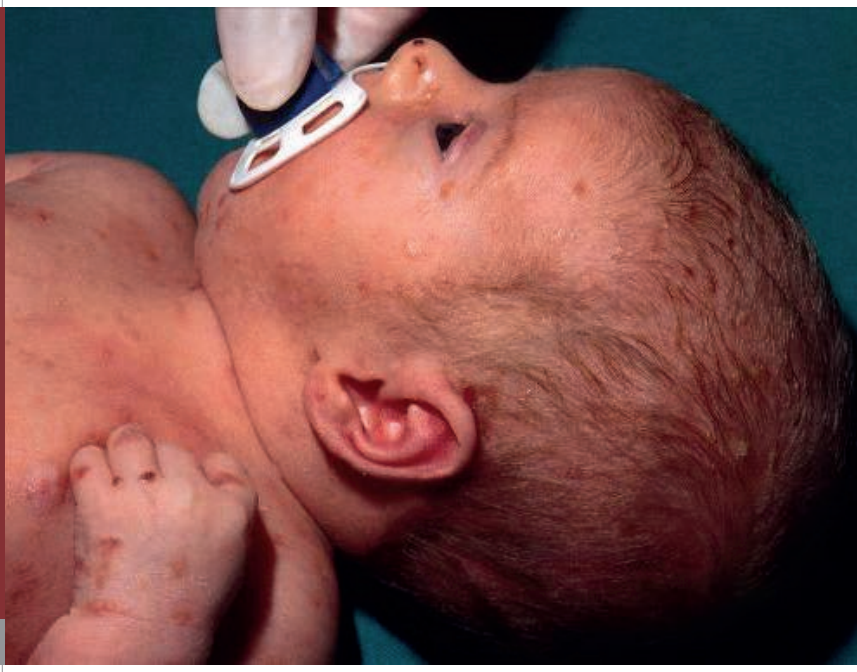

Fig. 7

Healing skin lesions at the age of 3 months.

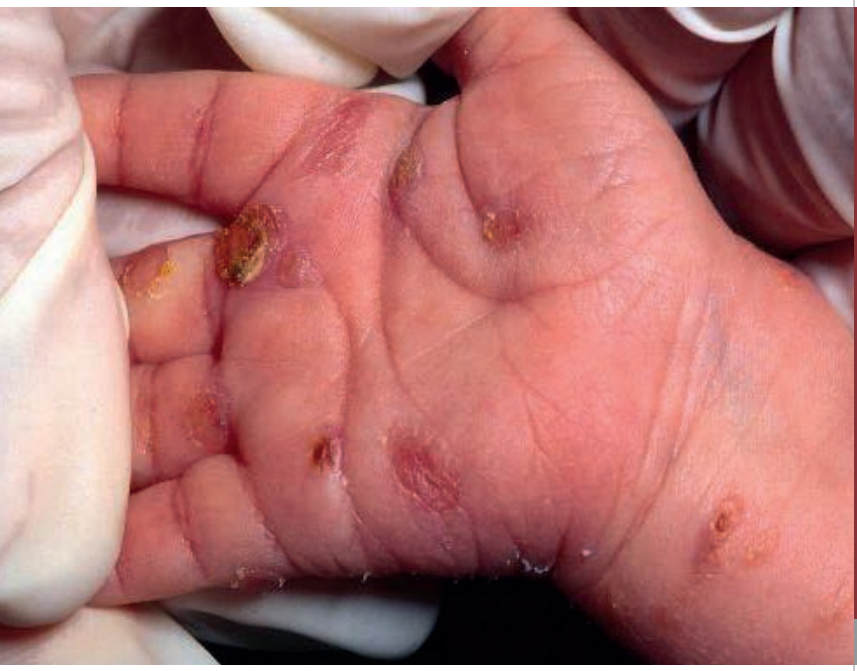

Fig. 8

Healing skin lesions at the age of 3 months.

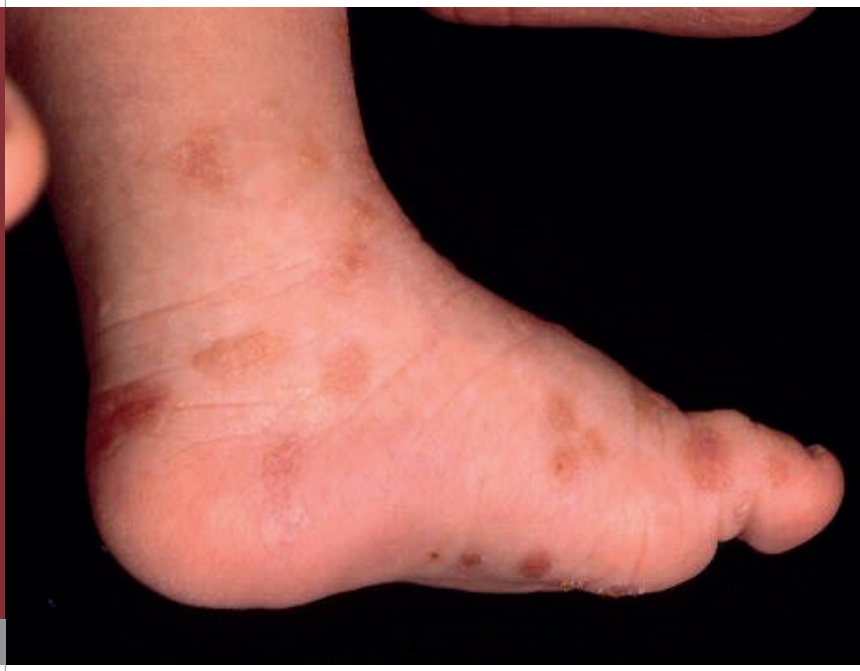

Fig. 9

Healing skin lesions at the age of 3 months.

The history, clinical presentation and course were consistent with a diagnosis of congenital self-healing reticulohistiocytosis (Hashimoto-Pritzker).

The child was seen regularly for follow-up. Hematology, blood chemistry, skull X-rays and ultrasonography of the abdomen remained normal. Clinically, no recurrence of skin lesions was detected, and the patient grew and developed normally. A second skin biopsy at the age of 6 months showed signs of histiocytosis in regression (Fig. 10).

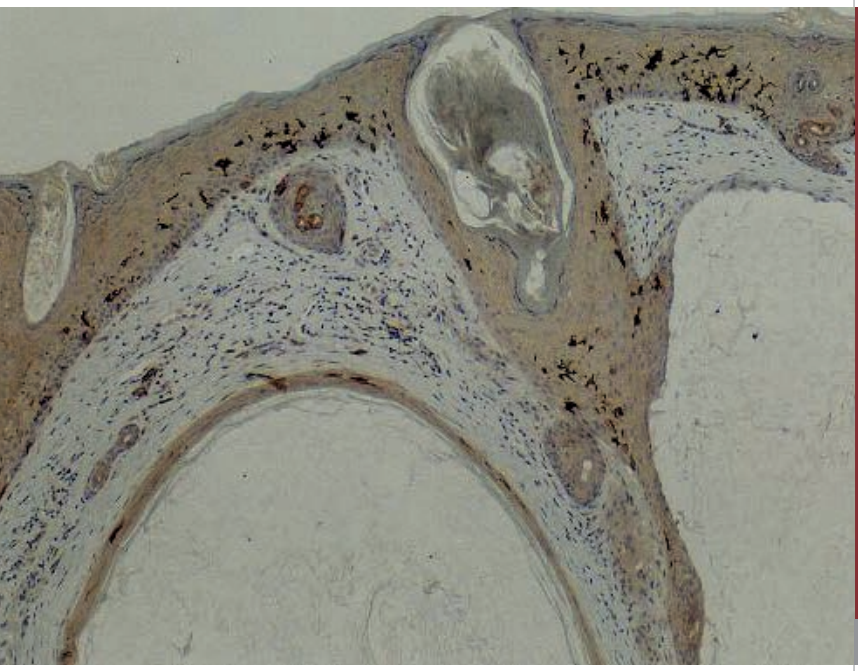

Fig. 10

Skin biopsy at 6 month of age: histiocytosis in regression.

Figures 10 to 12 shows the healthy boy at the age of 20 months. At 40 months, the skin lesions had involuted totally, partly leaving anetoderma-like lesions.

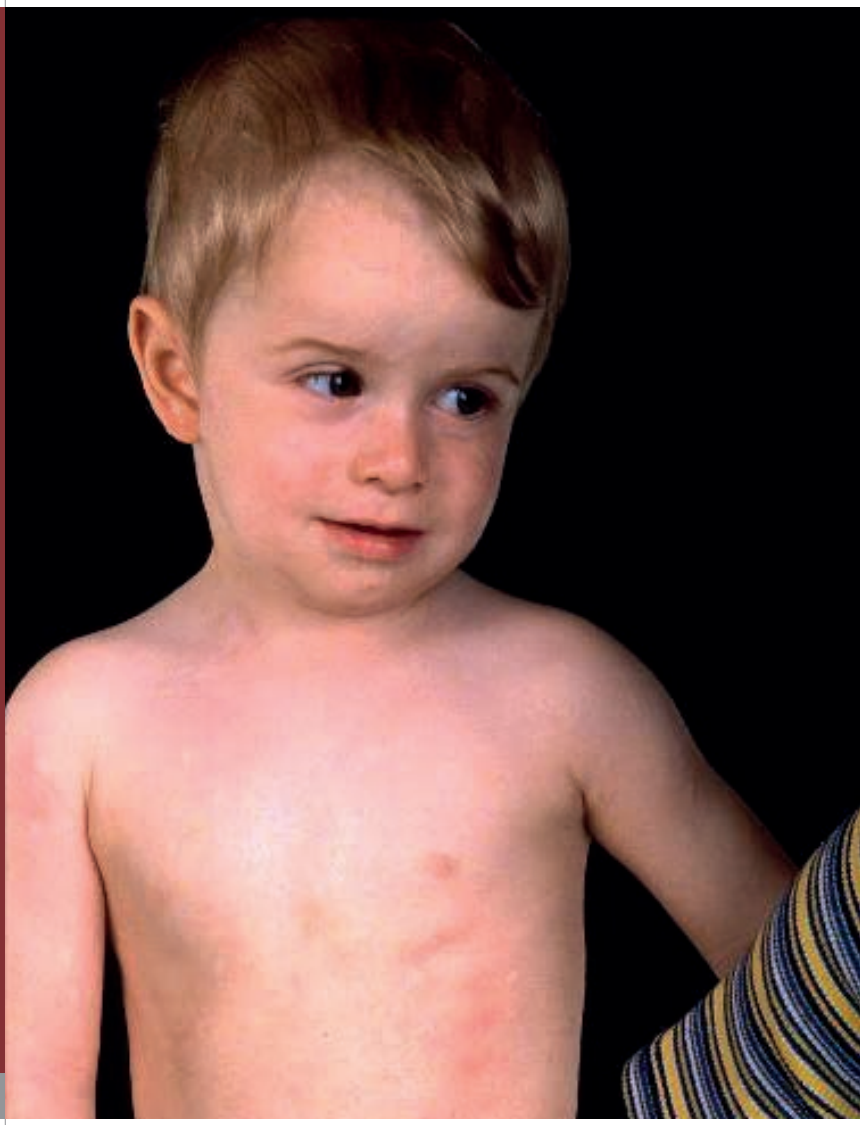

Fig. 11

Residual skin changes at the age of 20 month.

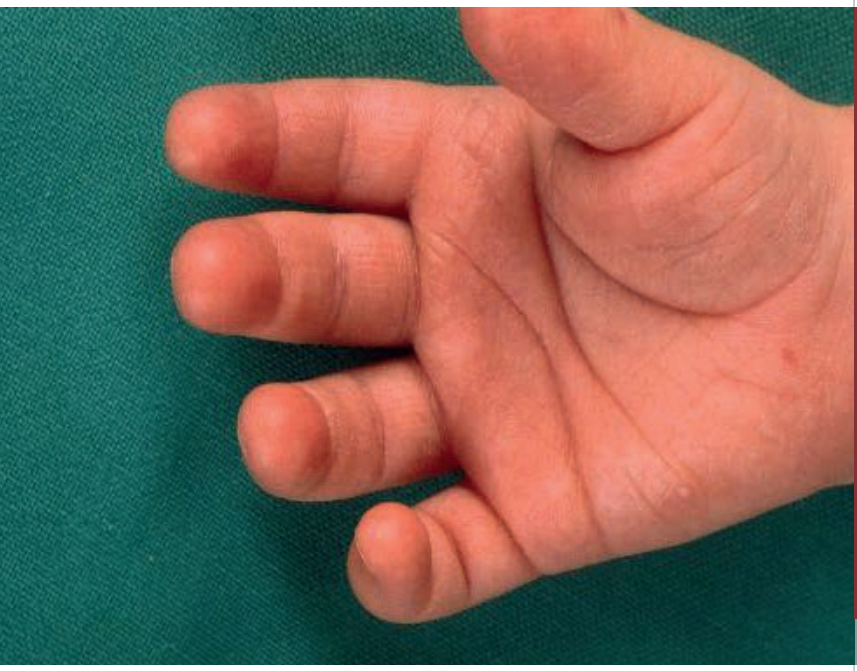

Fig. 12

Residual skin changes at the age of 20 month.

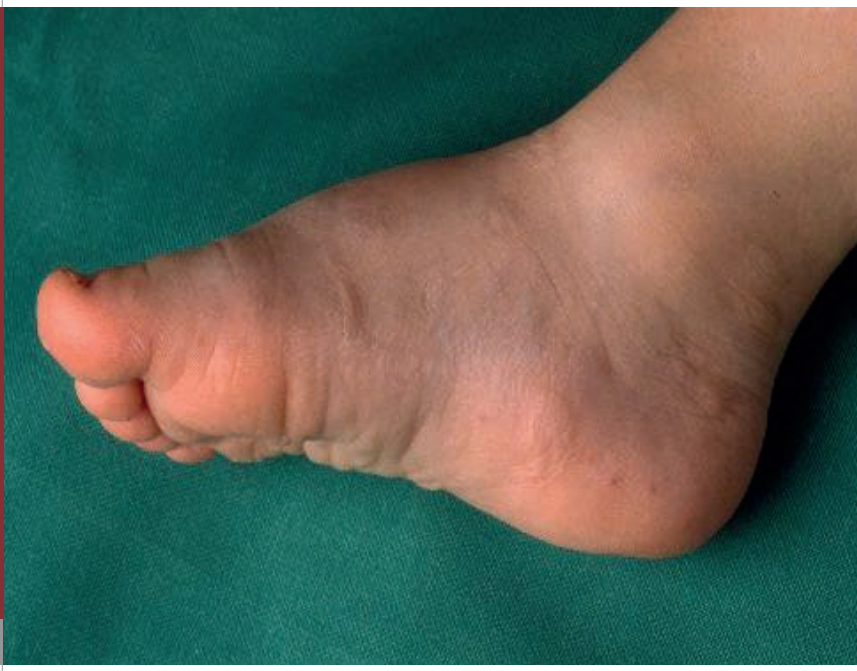

Fig. 13

Residual skin changes at the age of 20 month.

Congenital self-healing reticulohistiocytosis was first described in a female newborn in 1973 by Hashimoto and Pritzker (1). At birth, the girl presented with about 35 cutaneous nodules 2 mm to 4 mm in diameter, spread out over her scalp and face. No oral lesions were observed and she was otherwise in excellent health. All skin lesions disappeared within 3 1/2 months without any recurrence. On electron microscopic examination, the authors found typical histiocytic proliferation-like dense bodies, myelin-like laminations and Langerhans cell granules (called Birbeck granules). These features, which were little different from histiocytosis X and the benign course of the disease (self-healing) lead them to define this disease as a new entity. To date, more than 50 cases have been published in the literature; in most cases, the skin lesions were disseminated and only a minority had solitary lesions (5-7).

Reticulohistiocytosis Hashimoto-Pritzker is characterized by:

1. Generalized (most cases) or solitary papules, nodules and/or rarely vesicles apparent at birth or in the neonatal period.
2. The affected newborns are well without systemic signs of illness.
3. The skin lesions involute spontaneously within weeks to several months and relapse is uncommon, but has been described (2).

4. Typical histopathologic findings are dense nodular infiltration of mono- and multinucleated cells in the dermis with foamy eosinophilic cytoplasm.
5. Electron microscopic examination shows dense bodies and Birbeck granules in only 5%-20% of the infiltrated cells (in classical Langerhans cell histiocytosis more Birbeck granules are seen).
6. On immunohistochemistry, the „infiltrating cells" are positive for S-100 protein and CD 1a antigen.

The diagnosis of this rare neonatal disease is based on the clinical feature, on its benign course and on the demonstration of Langerhans cells with Birbeck granules. Etiology and pathogenesis of self-healing reticulohistiocytosis are still unknown, but its relationship to Langerhans cell histiocytosis is obvious. It is now suggested that self-healing reticulohisticytosis is a benign form of dendritic cell disorders resulting from abnormal dysregulated immune stimulation.

For a long time, self healing reticulohistiocytosis was classified by the Histiocyte Society in class II of the histiocytic disorders (3). Since 1997 the Working Group of the Histocyte Society proposed a new classification of this disease: it now belongs to class I, containing the whole entity of Langerhans cell histiocytosis as a subclass of dendritic cell related disorders (4).

As long as many questions remain unanswered and because of the apparent close relationship to malignant Langerhans cell histiocytosis, caution is indicated and longterm follow-up of these patients is recommended.

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