Langerhans' Cell Histiocytosis in an Adult

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A woman with typical skin lesions of histiocytosis X is reported. Electron microscopic and immunohistochemical investigations revealed a large number of markedly long Birbeck Langerhans' cell granulae. During treatment with Interferon α -2b, the patient developed infarctus cerebri and died. ***Key words: Histiocytosis X; Electron microscopy; Immunohistochemistry.***

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Histiocytosis X (1) is a proliferative disorder of specialized cells containing distinctive cytoplasmic structures characteristic of Langerhans' cells (2). Cutaneous lesions often occur. We present a fatal case of histiocytosis X with adult onset.

CASE REPORT

A 33-year-old woman had had diffuse redness, scaling and crusting of the skin of the scalp, axillae, and inguinal region since the age of fifteen (Fig. 1). Since the age of twenty, she had also had inflammation, swelling and necrosis of gingival tissue in the mouth and had been followed up by several dermatologists. When she was 24 years old, a gingival biopsy specimen showed typical changes resulting from histiocytosis X. No systemic involvement has occurred and roentgenographic examinations of the chest and osseous system as well as scintintillation scanning of the liver have not given any clear evidence of extension of the disease to these sites. Neither have there been any signs of lymph node enlargement, hepatosplenomegaly or manifest diabetes insipidus.

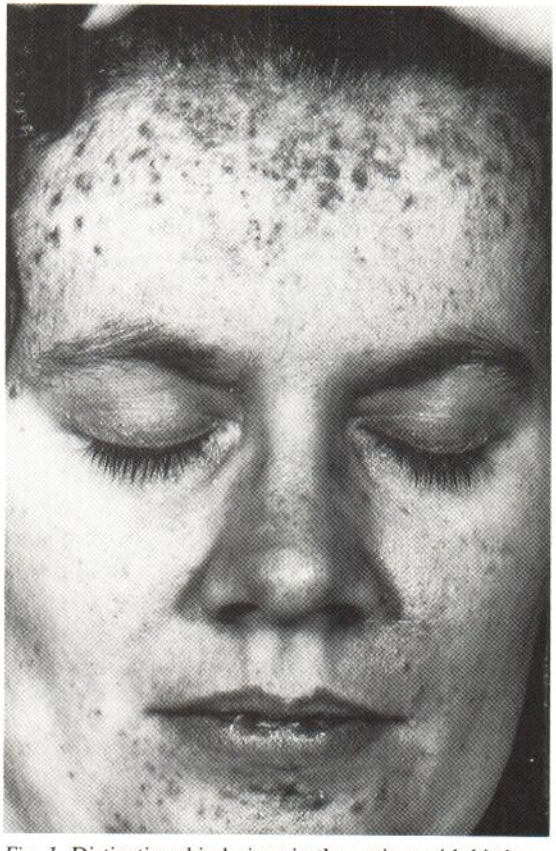

Fig. 1. Distinctive skin lesions in the patient with histiocytosis X.

Before the diagnosis of histiocytosis X at the age of twenty-four the patient had only received treatment with various topical preparations containing corticosteroids and antibiotics. After the diagnosis, between the ages of twenty-four and thirty, she had received a total of 150 PUVA treatments on scalp, axillary, and inguinal areas. At the same sites she had also been treated with two courses of soft X-rays consisting of 29 and 43 kV, half value depth in tissue 3 to 7 mm. Two Gy was given five times. During this period she also received seven courses of chemotherapy with vinblastine alkaloid (Velban). Between the ages of thirty-one to thirty-two because of inadequacy of the PUVA treatment she received grenz ray therapy. The PUVA treatment had moderately improved the lesions in the axillae and the inguinal regional, but not in the scalp. For two years the patient received a total of six courses of grenz ray therapy consisting of 10 kV, half-value layer in tissue of 0.5 mm. The good results of this type of treatment have recently been published (3). During these latter two years the patient had also received one course of chemotherapy with teniposid (Vumon) and cytarabine (Cytosar-U). At the age of thirty-three the patient suddenly developed large reddish-brown papules in the submammary region. Biopsy showed a dense infiltrate of histiocytes in dermis. Irregularly shaped multinucleated giant cells were seen frequently. Electron microscopic examinations showed numerous Langerhans' cells in dermis with rodlike and racquet-shaped granules (Fig. 2). The most striking finding was the large number and the length of the Langerhans' cell granulae. We have never before observed such long Langerhans' cell granulae in any condition. Immunohistochemical investigations (4) of the tissue with antibodies directed towards CD1, substance P (SP), calcitonin generelated peptide (CGRP), galanin, somatostatin, vasoactive intestinal polypeptide (VIP), peptide histidine amide (PHI), neuropeptide tyrosine (NPY), neurofilament, neuronspecific enolase (NSE), protein S-100, γ-melanocyte stimulating hormone (γ-melanocyte stimulating hormone (γ-MSH), and methionine-enkephalin were performed. All neuronal markers, sensory as well as autonomic, showed a normal pattern with the exception of CGRP which did not show any immunoreactivity at all. Dermis was infiltrated with γ-MSH-positive neutrophilic granulocytes. The dentritic population of the epidermis, stained with protein S-100 antiserum and CD1 had an atypical morphology with short and swollen dendrites. A large population of protein S-100 and CD1 cells was also found in the dermis (Fig. 3).

Because of the eruption of new lesions the oncologists decided to treat her with Interferon α-2b, 3 millions IE daily (5). After two months of treatment with a moderate result the patient suddenly developed a hemiplegia and cerebral infarctus cerebri. Histiocytic changes were found in liver and spleen but not in the brain.

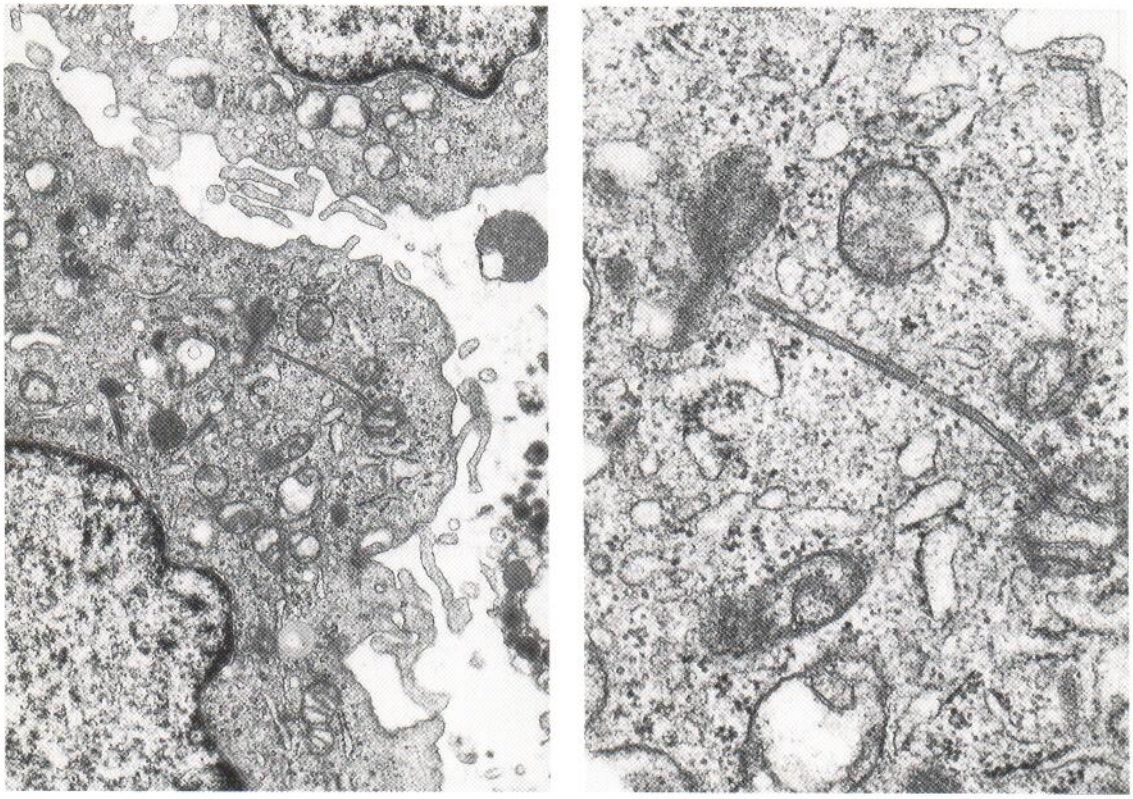

Fig. 2. Electron micrograph illustrating a dermal histocytosis X cell. (a: x14 400 b: x50 000).

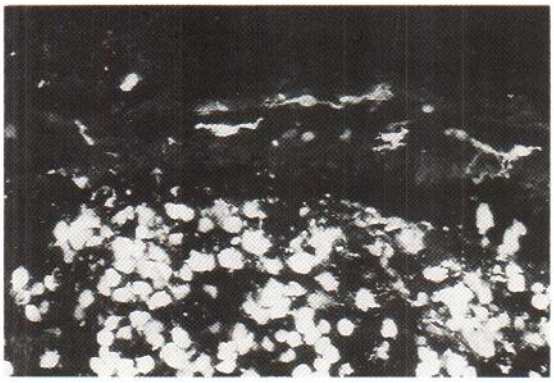

Fig. 3. Skin biopsy specimen showing S-100 positive cells in dermis. (x170).

DISCUSSION

Our patient manifested the clinical and histologic features of histiocytosis X. It has been recommended that this term should be abandoned and replaced by Langerhans' cell histiocytosis (6). Since this disease most often occurs in children (1), the age of onset in our patient was unusual.

Histiocytosis X may represent of disorder of the dendritic Langerhans' cell of the bonemarrow derived monocyte-histiocyte-macrophage series. In the electron microscope, the Langerhans' cells and the cells found in histiocytosis X have the same morphologic features, including the characterstic Langerhans' cell granula (7). The ultrastructural changes of our patient were similar. However, the length of the Langerhans' cell granulae were impressive (Fig. 2).

Both Langerhans' cells and histiocytosis X cells possess the S-100 antigen, a protein that is found in brain glial cells, Schwann cells, melanocytes, and other dendritic cells, such as the lymph node interdigitating reticulum cells. This antigen is not found in macrophage-type histiocytes which lends support to the concept of different populations of histiocytes (8, 9).

The treatment of histocytosis X depends on staging. In patients with bone lesions, local surgery and radiation are used. In severe histiocytosis X systemic treatment with alkylating agents or plant alkaloids is used (1). Our patient received radiation therapy, chemotherapy, PUVA and Grenz rays. These treatment modalities could control her disease in such way that she was able to work full-time for more than 15 years. Eventually she got a serve eruption and interferon therapy was tried. The role of interferon-therapy in her death has to be further evaluated, since no signs of histocytosis-X in her brain were found post mortem. However, CNS involvement in histiocytosis X is not rare but is sometimes difficult to diagnose (10).

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