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Ultrastructural Study of the Histiocytosis X.
—Report of two cases—

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Abstract

Two cases of Histiocytosis X, a Hand-Schüller-Christian disease and a Letterer-Siwe disease, are examined light and electron microscopically. Many of the histiocytes without appreciable lipid contained numerous rod-shaped structure identical to Langerhan's granules in the cytoplasm. The significance of this structure was discussed together with review of literature.

INTRODUCTION

Letterer-Siwe, Hand-Schüller-Christian, and Eosinophilic granulomas manifest clinically rather distinct features, but have a common basic morphologic component, namely histiocytic proliferation. Thus, Lichtenstein(1953) viewed them as single morphologic entity which he named Histiocytosis X. Other authors view Letterer-Siwe disease is separate from two others(Otani and Ehrlich 1940, Lichtenstein and Jaffe, 1940). Since the etiology of these disorders are not known, the final conclusion on the exact relationship among them is not yet available. Recently ultrastructural studies of the histiocytosis revealed so-called Langerhan's granules in about one-half of the cases of all three types of disorders, and this finding is an another suppartive evidence that these disorders are interrelated(Tarnowski and Hashimoto 1967, de Man 1968, Gianoti and Caputo 1969).

This report deals with the ultrastructural observations on skin lesions of a case of Letterer-Siwe and a case of Hand-Schüller Christian's disease.

MATERIALS AND METHODS

Two cases of Histiocytosis X, a case of Letterer-Siwe and a case of Hand-Schüller Christian type, diagnosed by histopathologic and clinical findings are studied. For electron microscopic examinations, rebiopsy of the skin was performed in the case of Letterer-Siwe disease and processed for routine electron microscopic preparations. Electron-microscopic preparation of the Hand-Schüller-Christian disease was made by reprocessing of the formalin fixed and paraffin embedded material. Ultrastructural examination was made with Hitachi HU-11E model scope.

RESULTS

A. Clinical history and light microscopic findings:

Case 1.

A 27 years old male complained of hearing difficulty on the right side. On physical examination, the right external auditory meatus was partially obstructed by non-tender movable mass. Excision biopsy of the lesion revealed granulomatous reaction principally composed of various types of histiocytes intermingled with large numbers of eosinophils and some lymphocytes, involving entire thickness of the skin from epidermo-demral junction to subcut-

aneous tissue(Fig. 1). Histiocytes were markedly pleomorphic from typical large mononuclear cell to multinucleated giant cells and spindle shaped fibroblastid cells. The cytoplasm were abundant, eosinophilic and variously vacuolated(Fig. 2). Possibility of Hand-Schüller-Christian disease was suggested and subsequent X-ray study of the skull disclosed a large round and well demarcated radioluscent lesion in the frontal bone with reactive slcerosis in the sphenoid bone.

Case 2.

An 11 month old male was admitted with complaints of vomiting and diarrhea with intermittent fever for two weeks. On physical examination, hepatosplenomegaly of 5 cm below costal margin, and the skin eruptions on the neck and abdomen were noted. Laboratory findings showed moderate anemia, leucocytosis and thrombocytopenia. The biopsy specimen from skin lesion disclosed patchy infiltration of large histiocytes in the papilla and upper dermis with occasional invasion into the epidermis(Fig. 5). The histiocytes were rather monotonous in shape and size, containing relatively large vesicular nucleus and abundant pale cytoplasm without vacuolization. However, a considerable number of lymphocytes were intermixed and eosinophils were observed. There was also moderate edema. The covering epidermis showed focal thining and mild parakeratosis, as well as focal infiltration of histiocytes. Subsequent bone marrow biopsy also disclosed infiltration of large numbers of atypical histiocytes(Fig. 6). A diagnosis of Histiocytosis X, Letterer-Siwe type, was made.

B. Ultrastructural findings

Ultrastructural observations were centered on histiocytes. The majority of histiocytes in Hand-Schüller-Christian disease were filled with large numbers of lipid vacuoles. Histiocytes with lesser amount of lipid showed many lysosomal granules, mitochondria, RER and other components of macrophages. In some of histiocytes, rod-shaped structure with periodicity of lining membrane and swelling of the end, closely resembling to Langerhan's granules were observed(Fig. 3, 4).

Histiocytes in Letterer-Siwe case showed three types. Majority of them showed irregular nuclear outline with deep infoldings of nuclear membrane and creating lobulations. The cytoplasm showed irregular surface outline, various degree of rough endoplasmic reticulum (RER) cisternal dilatation, abundant membrane bound and free ribosomes, and many dense body and few mitochondria. The other type of histiocytes contained many membrane bound dense material and some of them were crystaline (Fig. 7). The third type of histiocytes showed rod-shaped structure with periodicity of bounding membrane and terminal clubbing(Fig. 8). These structure closely resembled to Langerhan's granules in the epidermis.

DISCUSSIONS

Suprabasal clear cells of the epidermis, Langerhan's cells have been contraversial in nature and origin. They have both resemblance and difference from the melanocyte. Rod-like tubular structure by electron microscopy was first described by Birbeck(1961) followed by Breathnach(1965), and they were regarded as the characteristic morphologic feature of Langerhans' cells and named Langerhans' granules. Structure indistinguishable from Langerhan's granules has been observed in the histiocytes of Histiocytosis X, namely Letterer-Siwe disease, Hand-Schüller-Christian disease, and Eosinoplic Granuloma(Cancilla and Lahey 1967, Tarnowski and Hashimoto 1967, De Man 1968, Gianotti and Caputo 1969). The granules were found in the histiocytes is not only the skin lesion but also visceral and osseous lesions. The origin and function of the granules has been speculated variously. Cancilla and Lahey(1967) thought these granules are originated from cytoplasmic membrane and membranous channels of the endoplasmic reticulum of golgi system. Tarnowski and Hashimoto(1967) thought that these granules arise during the process of endocytosis of extracellular material. De Man (1968) discussed possibilities that these granules may represent either non-specific cytoplasmic reaction, storage of an organic material or an infective

agent, particularly viral particle. Gianotti and Caputo(1969) regarded Langerhan's granules not as phagocytized material but cell structure proper.

The first case of present report was 27 years old and rather older than ordinary case of Hand-Schüller-Christian disease when the biopsy was first examined. However, the skull X-ray revealed large osteolytic lesion and the diagnosis of histiocytosis became certain. The second case was a typical Letterer-Siwe disease both clinically and histopathologically. In both cases numerous rod-shaped tubular structure similar to Langerhans' granules were observed in histiocytes without appreciable amount of lipid, and the diagnosis of Histiocytosis X became more definite.

Although the exact nature and function of Langerhan's granules are not certain yet, the finding of these granules in histiocytes of Histiocytosis X provide following significance;

1) it support theory that Langerhans' cell in the epidermis is histiocytic origin,

2) it is another distinctive feature of diagnosing Histiocytosis X,

3) it support the concept that cellualr response in Histiocytosis X is basically same type of histiocyte indicating linkage of three variants of Histiocytosis X represent spectrum of single disease entity.

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Legends of figures:

Fig. 1. Cutaneous lesion of case 1. (Hand-Schüller-Christian disease) showing large numbers of histiocytes with several giant cell formation and an infiltrate in the mid dermis. H. & E. ×100.

Fig. 2. Higher magnification of fig. 1 showing large histiocytes intermingled with eosinophils and lymphocytes. H. & E. ×1, 000.

Fig. 3. Electron microphotograph of histiocyte in Hand-Schüller-Christian disease showing several lipid vacuoles and a large phagosome. ×22, 500.

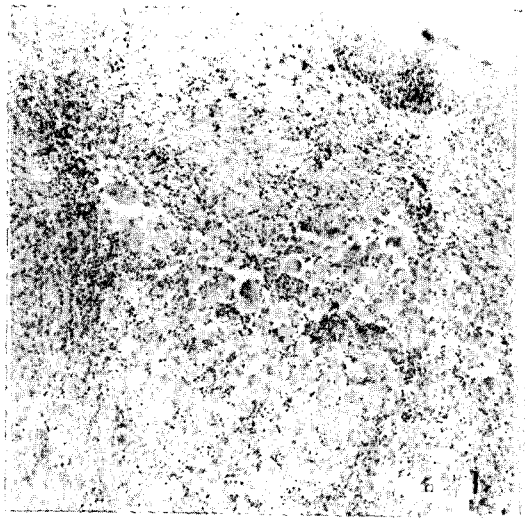
Fig. 4. Electron microphotograph of a portion of histiocytes showing perinuclear cytoplasm which contain large numbers of cross and longitudinal profiles of round, dumbell, and rod shaped tubular structures with terminal clubbing. Some of them show electron dense internal substance while others are less dense. ×22, 500.

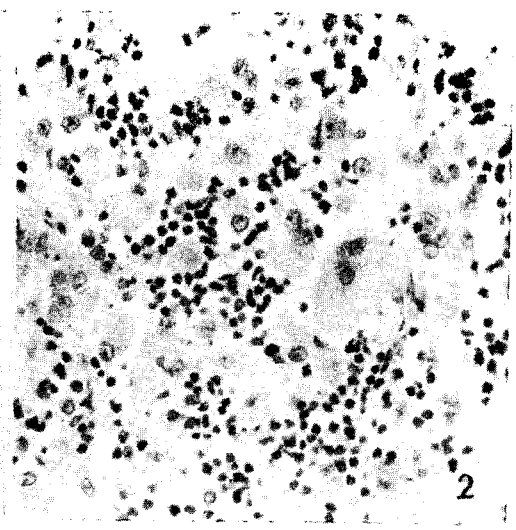
Fig. 5. Cutaneous lesions of case 2 (Letterer-Siwe disease) showing patchy infiltration of histiocytes at upper dermis partly invading into the epidermis, many extravasated red blood cells, interstitial edema and focal thinning of the epidermis. H. & E. ×450.

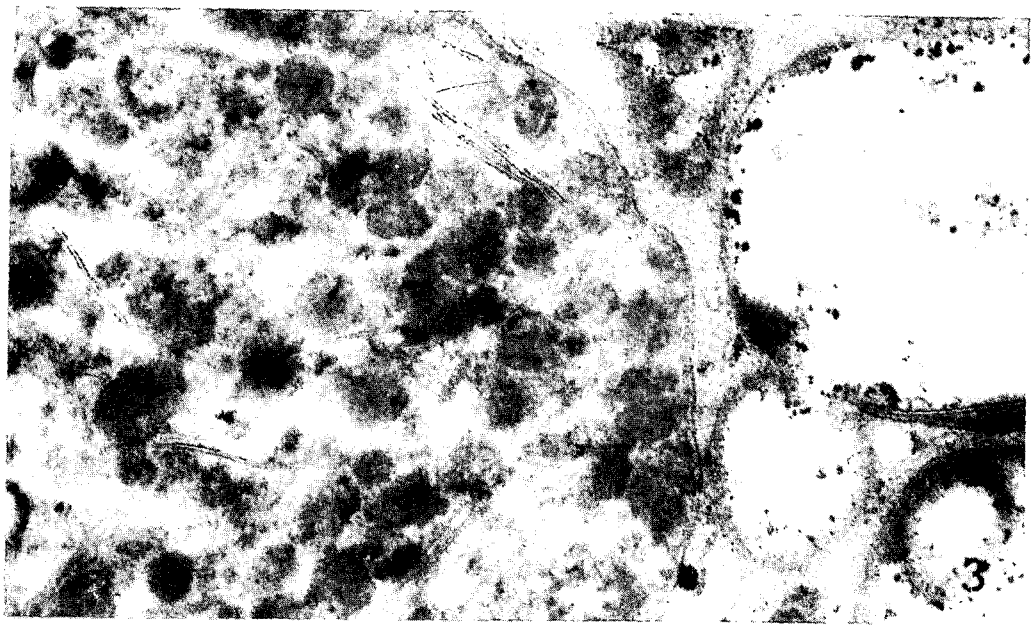
Fig. 6. Bone marrow section of case 2 showing proliferation of reticuloendothelial cells and several megakaryocytes. H. & E. ×1, 000.

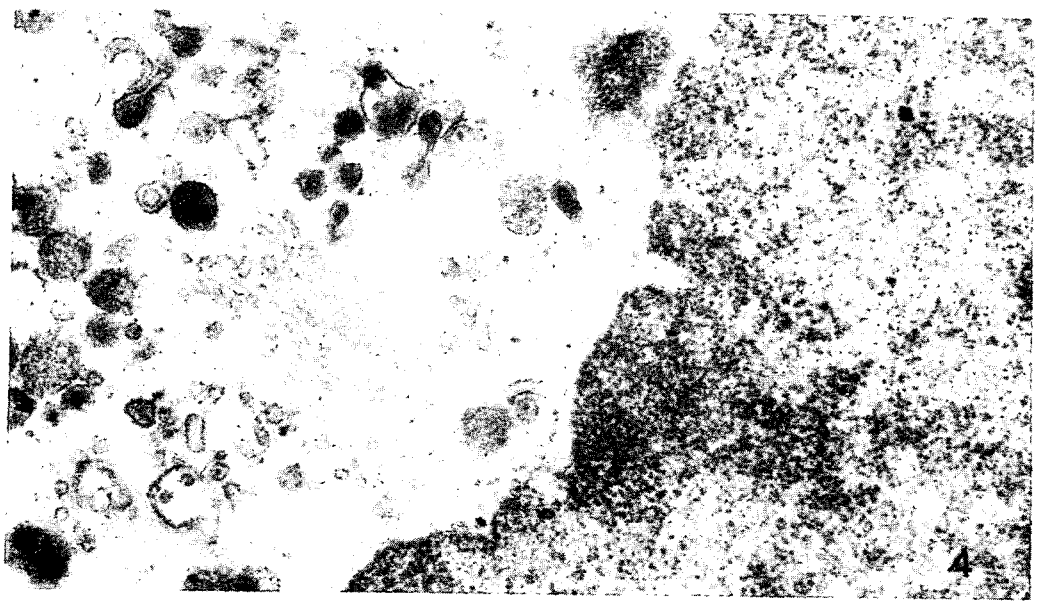
Fig. 7. Electron microphotograph of histiocyte in Letterer-Siwe disease showing many rod shaped tubular structure with slightly swollen and electron dense terminal end. No appreciable lipid is noted. ×20, 000.

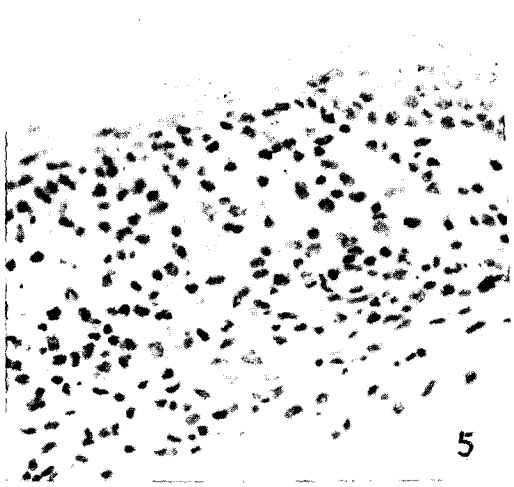
Fig. 8. Electron microphotograph of another type of histiocyte in Letterer-Siwe disease showing many membrane bound dense bodies with crystal line appearance in some of them, which are probably cholesterol accumulation. ×22, 500.











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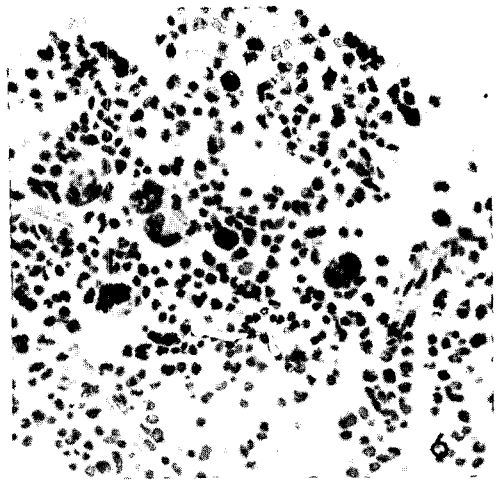

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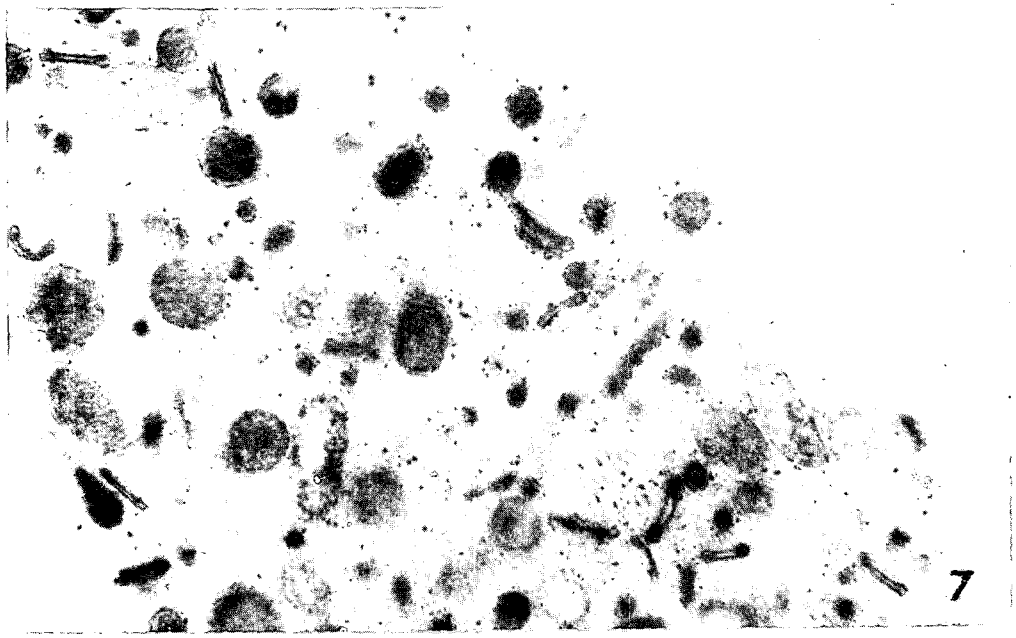

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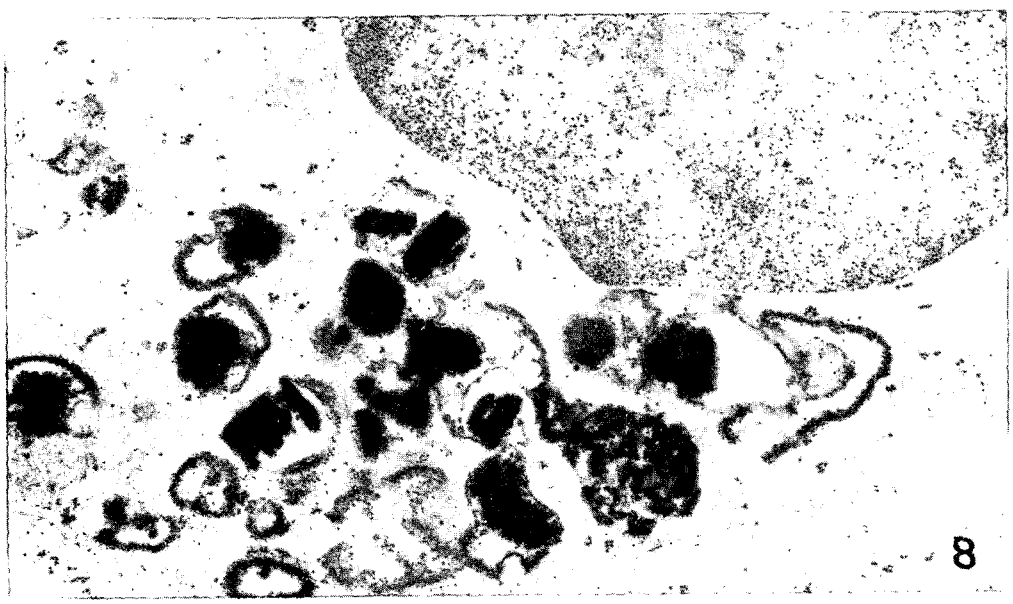

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