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Letterer-Siwe's Disease (Case Report)

by

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Letterer-Siwe's disease or acute infantile reticulo-endotheliosis is an acute or subacute progressive systemic proliferation of differentiated histiocytes (Rappaport, 1966). The clinical features of this disease resemble those of acute leukemia, characterized by hepato-splenomegaly, hemorrhagic skin lesions, progressive anaemia with usually normal or decreased white blood cell and platelet count, generalized lymphadenopathy with a moderate degree of fever, and followed by progressive fatal course. This disease affects infants and young children, it rarely if ever, develops in children of more than three years of age.

Among the three clinical types of histiocytosis, Letterer-Siwe's disease is the least common; approximately 41 cases have been reported until 1955 by reviewing the literature. Thereafter 15 additional cases were reported by Batson et al. (1955). Burrows et al. in 1970 showed an incidence of 6 cases in a 1.500.000 population over a period of 10 years, with a mortality rate of 83%, a result very similar to that reported by Doede and Rappaport (1967) who found that 81% died within 2 years of diagnosis.

The present report concerns a case of Letterer-Siwe's disease which satisfies the clinical and pathological findings of acute non-lipid reticulo-endotheliosis. This is the third case reported in our clinic, the former two were reported by Kho et al. (1961) and Iskandar et al. (1966). Two other cases from other clinics were reported by Tangosaputra and Himawan (1970).

Case report

Ch, a 4½-month-old Indonesian boy was admitted on September 26,

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1973, with a 2-month history of limphadenopathy accompanied by intermittent fever, slight cough and mild diarrhea. One week before admission reddish papules were seen on the scalp, face and thorax. His parents had not noted any other abnormalities or considered him to have been unwell prior to the onset of the disease. Physical examination on the day of admission revealed a pale, weak and apathetic male infant, with a body weight of 4.900 gm, body length of 60 cm, and temperature of 38,1° C. Lungs and heart were normal. The abdomen was slightly distended, the liver was palpable for 3 fingers below the costal margin and the spleen was enlarged to Schüffner III. There was a moderate to severe enlargement of the cervical and axillary lymphnodes. A reddish papular rash was present predominantly on the thorax, scalp, palms and soles, and some papules were scattered on the abdomen and trunk. The chest x-ray revealed an enlargement of paratracheal lymphnodes with slight infiltration on both lungs. A slight generalized rarefaction of bones was found on a radiological survey of the skeleton. Routine hematological examination revealed as follows: haemoglobin 5,9 gm%, hematocrit 21%, reticulocytes 7%, MCH 27 uug, MCV 28 u^3, MCHC 98%. Platelet count was 35.000/cmm and leucocyte count was 7.800/cmm, with 2% band neutrophils, 59% segmented neutrophils, 36% lymphocytes and 3% monocytes. There was anisocytosis, poikilocytosis and hypochromia of the red blood cells. Bleeding time was 7,5 minutes and clotting time was 5,5 minutes. Serum cholesterol was 144 mg%. Bone marrow aspirate showed no abnormality. The Mantoux tests 1/2.000 and 1/100 were negative. The diagnosis of histiocytosis was confirmed by the phatological examination of the lymphnodes. The lymphnodes consisted of proliferated cells with eosinophilic cytoplasm, frequently without distinctive border and vesicular nucleus. The nuclear membrane and the nucleoli could be clearly seen. Mitosis was frequently found. There was diffuse hemorrhage and dilated sinuses, which were filled with nucleated erythrocytes, leucocytes and lymphocytes. The conclusion was histiocytosis.

The therapy consisted of intravenous vincristine, methotrexate, 6 mercaptopurine, prednison and antibiotics. Several blood transfusion was given due to low haemoglobin content.

During the first 10 days of hospitalization, the lymphnodes became enlarged and the spleen became Schüffner VI (fig. 1). The skin manifestation was more prominent and purpura appeared. During his stay in the hospital the body temperature ranged between 37° C and 39° C. Three weeks after treatment, the infant showed clinically some improvement. The enlarged lymphnodes and spleen

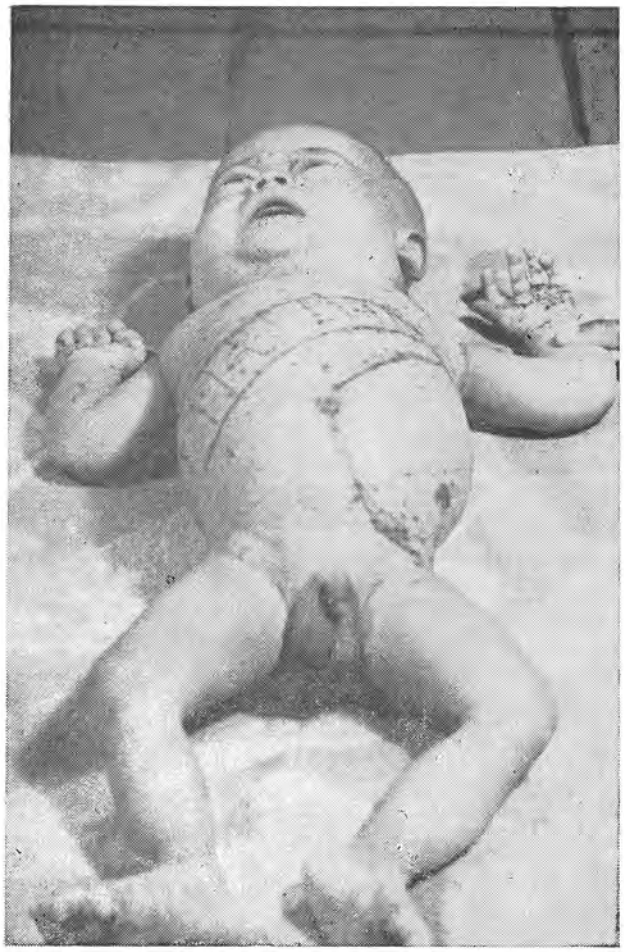

Fig. 1A. *Note the distribution of the typical skin lesions.*

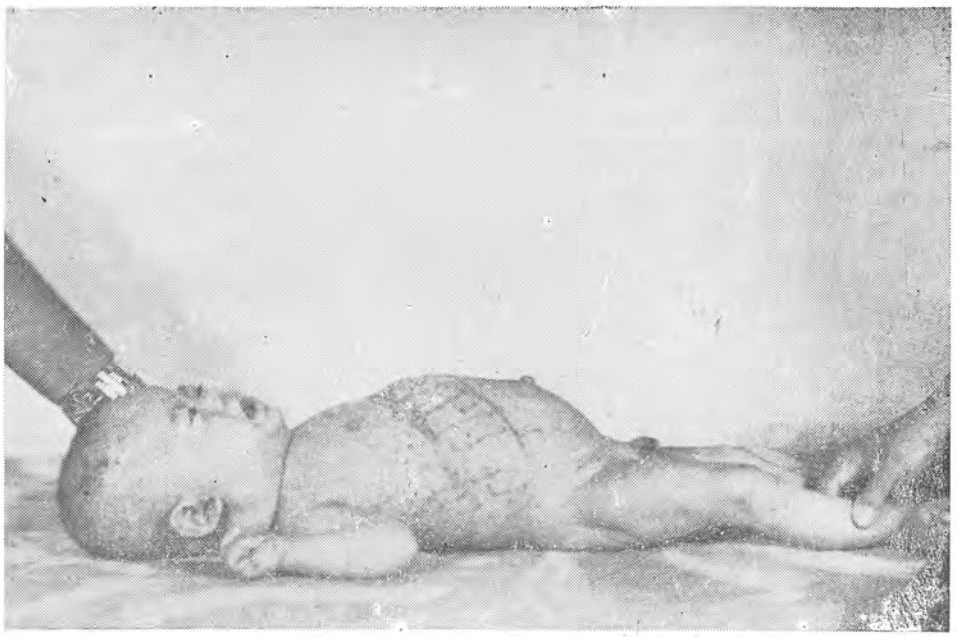

Fig. 1B. *Lateral view.*

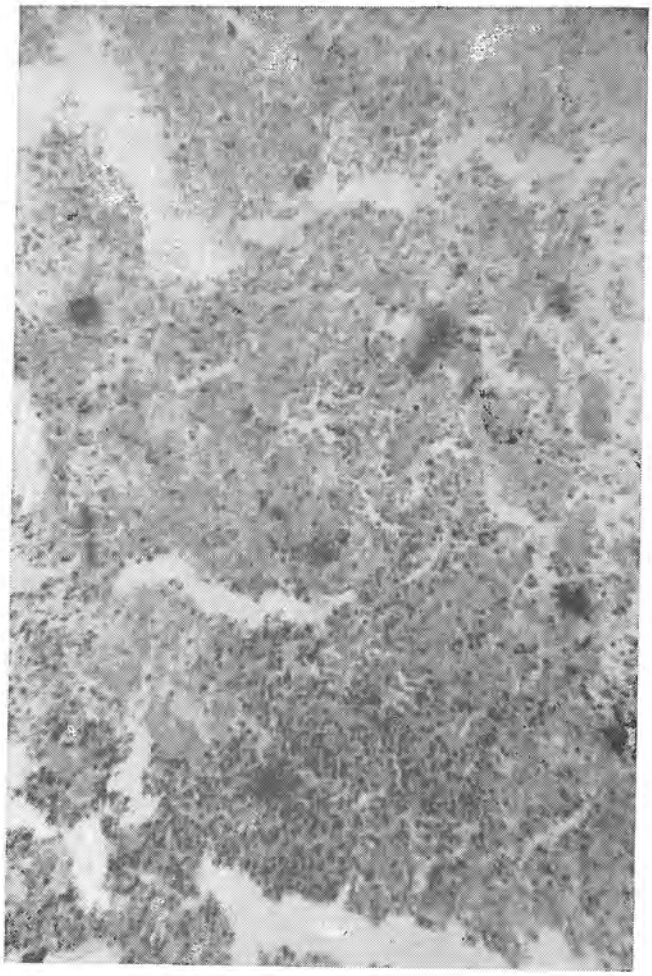

Fig. 2A. *Photomicrograph of cervical lymphnode showing proliferation of histiocytes pushing the normal lymphoid tissue aside. H.E., reduced from X 80.*

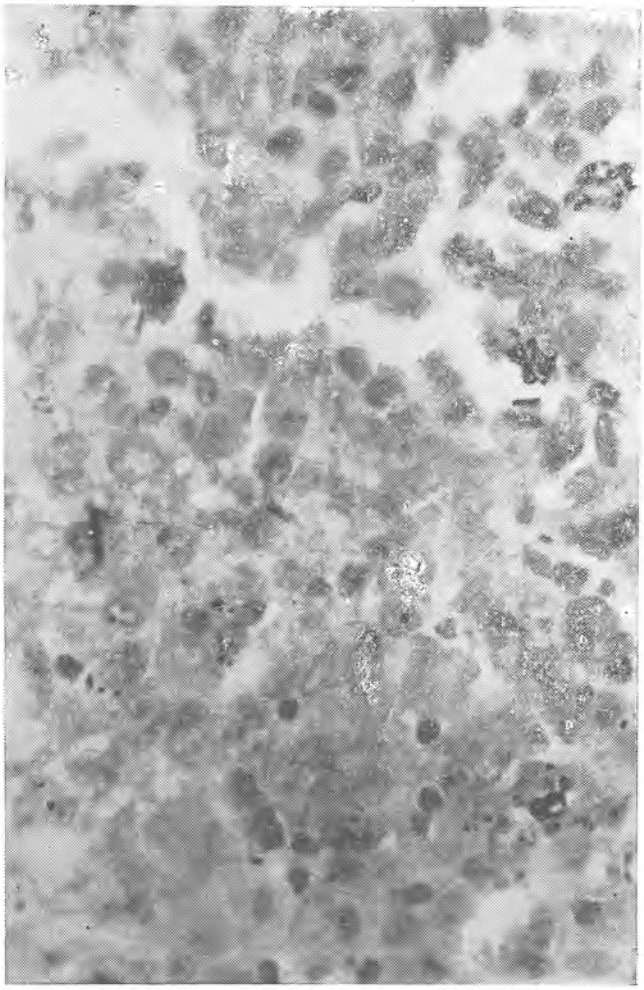

Fig. 2B. *Photomicrograph of cervical lymphnode showing phagocytic activity of histiocytes H.E., reduced from × 360.*

became smaller, the appetite improved, the skin lesions diminished and the haemoglobin content rose to 8 gm%, but unfortunately the child died due to bronchopneumonia, after one month of hospitalization.

Discussion

The non-lipid reticuloendotheliosis is usually considered to include Hand Schüller-Christian's disease, eosinophilic granuloma of the bone and acute disseminated reticuloendotheliosis (Letterer-Siwe's disease). Perhaps it would be more correct to use the term "histiocytosis-X" as suggested by Lichtenstein in 1953. His classification of Hand Schüller-Christian's disease as chronic disseminated histiocytosis-X, Letterer-Siwe's disease as acute disseminated histiocytosis-X and eosinophilic granuloma as histiocytosis localized in bone, indicates the predominant cells common to all three conditions.

The classic diagnosis of non-lipid reticuloendotheliosis was first outlined by Siwe in 1933, based on clinical and phatological findings which included hepato-splenomegaly, a hemorrhagic tendency, lymphadenopathy, anaemia, osseous involvement, generalized hyperplasia of the reticuloendothelial system and non familial nor hereditary disease in infancy and childhood. All the characteristic symptoms were observed in the patient described above. The radiological findings of the lungs are still to be differentiated from other possible causes of bronchopneumonia rather than caused by this disease, although Melhem et al. (1964) found the lung lesions resembling bronchopneumonia in some of his serial cases of histiocytosis.

Winkelman (1969) pointed out that skin lesions in Letterer-Siwe's disease are characteristic and noteworthy for their constant appearence as individual, brown, scaling papules occuring in crops on the scalp, face, neck and trunk. The consecutive stages consist of infiltrated papules, vesicles, ulcerations, haemorrhage and scarring. The accumulation of scales and crusts and accentuation of the eruptions on the scalp and skinfolds have often caused confusion of Letterer-Siwe's disease with seborrhoic dermatitis. Batson (1955) pointed out the frequency of infiltrated crusted eruptions in patients having the acute disease in 10 out of 15 patients. All but 2 of his 15 cases died at follow-up. It has been stated that the existance of skin lesions is a sign of serious disease. Unusual locations of the lesions such as the palms and soles are considered to be a grave sign. According to the observation of Nezelof and Guibert (1963) purpura is the most serious sign. The histopathological findings in cutaneous lesion of histiocytosis-X is a typical histiocytic infiltration of large, pale histiocytes with homogenous nuclei and clear, slightly granular cytoplasm. In general, the proliferative reaction with its almost pure

histiocytic infiltrate is typical for Letterer-Siwe's disease, whereas the granulomatous reaction of eosinophilic granuloma and the xanthomatous reaction for Hand Schüller-Christian's disease (Lever, 1967). In the patient described in this report, the pathological picture of the skin was not typical for Letterer-Siwe's disease, but the pathological findings of the lymphnodes showed a typical picture of histiocytosis (fig. 2).

The value of steroid therapy in histiocytosis has long been known and in critical situation may be life saving (Bass, 1953; Cox, 1953; Prouty, 1959; Doede and Rappaport, 1967). Remission following antibiotics have been reported (Aronson, 1951; Fisher, 1953). More recent work has suggested the use of cytotoxic agents such as vinblastine sulphate and nitrogen mustard as giving better results (Winkelman and Burgert, 1970; Bor and Smith, 1969), but Lichtenstein (1963) was of the opinion that such drugs should be avoided in acute disseminated histiocytosis-X since they might seriously injure an already damaged bone marrow. Gianotti and Caputo (1971) demonstrated that mitosis was arrested in anaphase after giving vinblastine intravenously.

In this patient the therapy resulted in a clinical improvement, but nonetheless the prognosis of Letterer-Siwe's disease is fatal as shown by various authors (Batson et al., 1955; Avery et al., 1957; Doede and Rappaport, 1967; Burrows et al., 1970).

Summary

A case of Letterer-Siwe's disease in a 4½-month-old Indonesian boy has been presented. The patient has fulfilled the clinical and pathological criteria of Siwe, and was treated with antibiotics, cytotoxic agents and corticosteroid. The result of the therapy showed some clinical improvement, but unfortunately the patient died due to bronchopneumonia after one month of hospitalization.

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