A CHINESE GIRL WITH FEATURES OF LETTERER-SIWE DISEASE, HISTIOCYTIC MEDULLARY RETICULOSIS AND MONOCYTIC LEUKAEMIA

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SYNOPSIS

An 18 month old Chinese girl with the unusual features of Letterer-Siwe disease, histiocytic medullary reticulosis and monocytic leukaemia is presented, and the nosology of malignant histiocytic disorders discussed.

INTRODUCTION

The association of monocytic leukaemia with malignant histiocytosis is rarely encountered (Yu et al, 1960; Friedman & Steigbigel, 1965; Clark & Dawson, 1969). The association of monocytic leukaemia with Letterer-Siwe disease has been reported in one patient (Gray & Taylor). The association of all three features in the same patient has not been reported before. Such an association would lend support to the view that the heterogenous group of diseases known as the histiocytoses be regarded as manifestations of malignancy of increasingly immature histiocytes.

CASE REPORT

C.W.N. presented at age 18 months to the University Hospital, Kuala Lumpur, with the following features: prolonged fever, wasting, nodular skin rashes, gingival hypertrophy, lymphadenopathy, hepatosplenomegaly, anaemia and chronic diarrhoea (Figs. 1 & 2). She was the first and only child of Chinese parents. Pregnancy and delivery were uneventful. Birth weight was 3,100 gms. She received BCG and smallpox vaccination at 2 days old, and DPT and oral polio vaccines at age 3 months, and 4 months, without ill-effects. Low grade fever began at age 11 months.

The blood count revealed severe anaemia, thrombocytopaenia, neutropaenia and the presence of leukaemic monocytes (Hb 2.9 gm per cent, platelets 34,000/ μL, twbc 4,000/ μL, with 2 per cent neutrophils, 40 per cent lymphocytes and 58 per cent malignant monocytes). The watery stools contained >2 per cent reducing sugars. Large num-

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Fig. 1. Patient C.W.N. with brownish nodular rash.

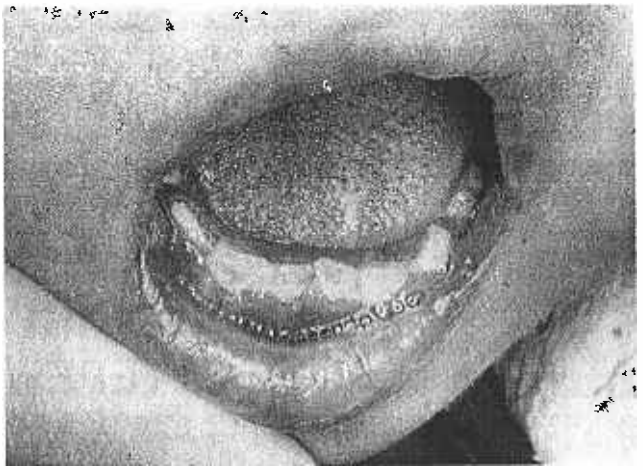

Fig. 2. Patient C.W.N.: gingival hypertrophy.

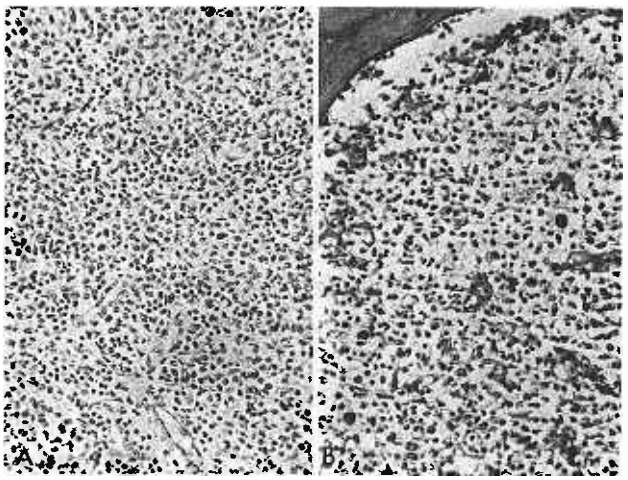

Fig. 3. (A) Thymus showing invasion by moderately differentiated histiocytes. Hassall's corpuscles are poorly formed. (B) Bone marrow with histiocytic replacement. Erythro- phagocytosis is not observed.

Fig. 4. Lymph node showing histiocytic infiltration through the capsule.

bers of moderately differentiated histiocytes were found in skin and bone marrow biopsies. Bone lesions were absent on X-rays.

Immunologic studies prior to treatment showed elevated serum IgG (IgG 2000 mg per cent, IgA 82 mg per cent, IgM 80 mg per cent, IgD 2_2 Iu/ml). Uptake of tritiated thymidine by photohaemagglutin-stimulated lymphocytes was impaired (stimulation index = 0.4). Skin reactivity to p.p.d. was absent.

Therapy included blood transfusions for anaemia and intravenous hyperalimentation for intractable diarrhoea and malabsorption. Initial improvement following treatment with vincristine and prednisolone was not sustained. The course was inexorably downhill. Terminal causes of death were bronchopneumonia and disseminated intravascular coagulation eight weeks after admission.

AUTOPSY FINDINGS

At autopsy, the thymus was small and atrophic with absent Hassall's corpuscles (Figs. 3-7). Small clumps of moderately differentiated histiocytes infiltrated the following organs: skin, lymph nodes, liver, pancreas, adrenals, spleen, marrow, lungs, kidneys, oesophagus, stomach, small and large intestines. Erythrophagocytosis was not observed.

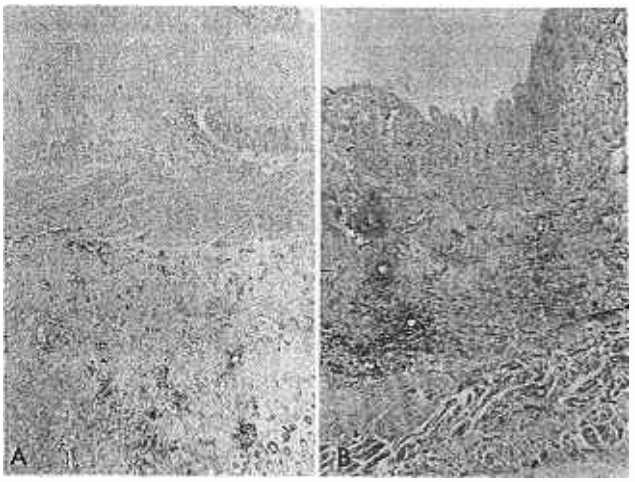

Fig. 5. (A) Small bowel with histiocytic invasion and necrosis. (B) Oesophagus with histiocytic infiltration, and mucosal ulceration.

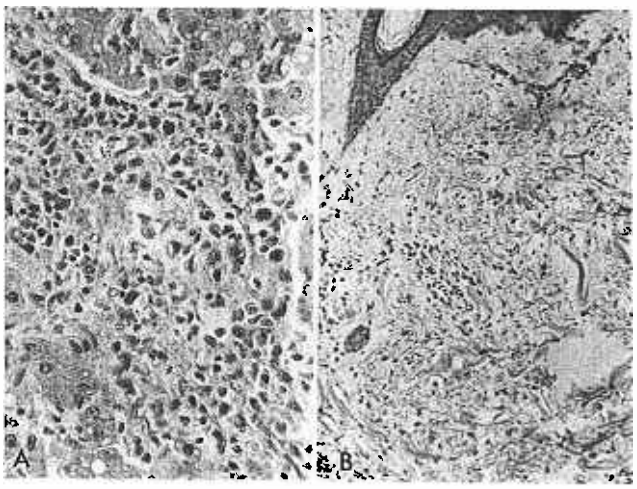

Fig. 6. (A) Histiocytic infiltration of the portal tract. (B) Disruption of dermis by infiltrating histiocytes.

DISCUSSION

The onset in early childhood and features of wasting generalized non-pruritic rashes, hepatosplenomegaly, lymphadenopathy and bone marrow failure favour the diagnosis of Letterer-Siwe disease (Rappaport, 1966). However, epidermal involvement by histiocytic cells, considered as characteristic of Letterer-Siwe by Rappaport was not observed, although disruption of the dermis occured extensively. Widespread gut involvement with malabsorption is a rare feature of malignant histiocytosis (Clark & Dawson, 1969; Marshall, 1956), but the other feature of this disease—erythrophagocytosis (Lynch & Alfrey, 1965; Natelson et al, 1968; Zawadski et al, 1969) was not demonstrable in tissue sections. Monocytic leukaemia has been reported as a very unusual accompanying feature of both Letterer-Siwe (Gray & Taylor, 1953) and malignant histiocytosis (Yu et al, 1960; Friedman & Steigbigel, 1965; Clark & Dawson, 1969).

With the increasing understanding of macrophage development and function, the heterogenous group of disorders known as the histiocytoses—monocytic leukaemia, reticulum cell sarcoma, Letterer-Siwe disease, malignant histiocytosis, Hand-Schuller—Christian syndrome, eosinophilic granuloma and localized histiocytoma—may be regarded as manifestations of malignancy of increasingly mature histiocytes (Kline & Golde, 1973). In this context, the clinicopathological entities of Letterer-Siwe disease, malignant histiocytosis and monocytic leukaemia are manifestations of malignancy of the immature, moderately differentiated histiocyte, and the concurrence of these disorders in our patient would support this view.

Recent reports (Ochs et al, 1974; Cederbaum, 1974) indicate that the syndrome of combined-immunodeficiency with graft-versus host disease mimic the Letterer-Siwe syndrome. Although immuno-deficiency has been demonstrated in our patient, this finding is probably secondary to the disease process. In support of this interpretation is the history of this child's ability to tolerate vac-

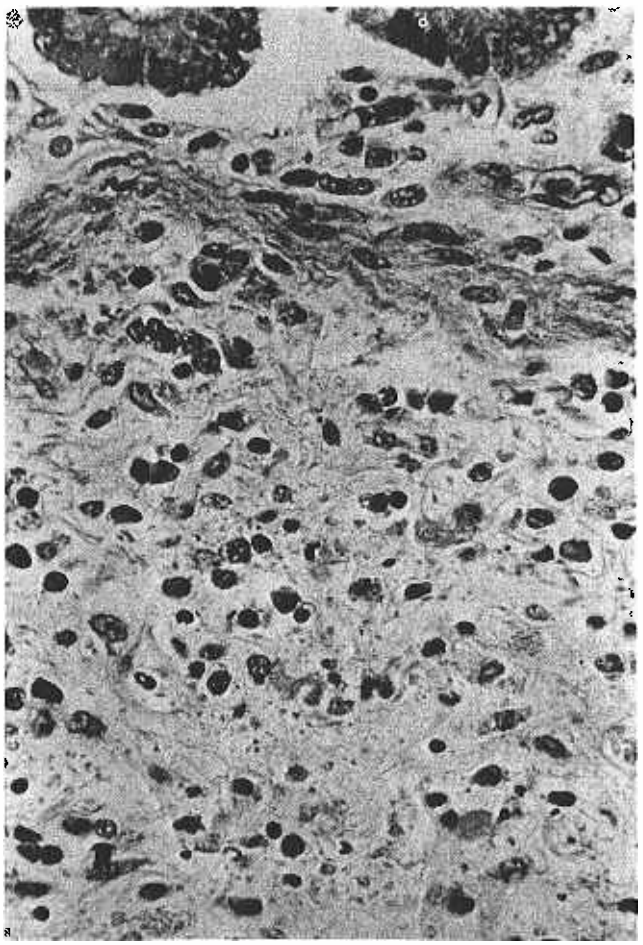

Fig. 7. High power view of histiocytes in submucosa of colon.

cination with smallpox and BCG soon after birth, and the observation of invasion and disruption of lymphatic organs by histiocytes.

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