HISTIOCYTOSIS X IN SINGAPORE CHILDREN

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The initial description of Letterer-Siwe Disease was ascribed to Letterer (1924) and Siwe (1933) and was characterised by fever osseous lesions, haemorrhage, progressive anaemia, hepatosplenomegaly, diffuse lymphadenopathy, and a fatal course. Hands described the first case of Hand Schuller Christian Disease in 1893 mentioning polyuria, exophthalmos, and skull defects in a patient thought to have tuberculosis. This disease concept was later described by Schuller in 1955 and Christian in 1920. The concept, Eosinophilic Granuloma of the bone was introduced by Lichtenstein and Jaffe in 1940. Lichtenstein (1953) grouped the three conditions under the generic term Histiocytosis X as he felt that all three conditions shared a common origin in proliferation of histiocytes.

Although many had agreed that the three conditions represent phases of the same disease (Avioli et al 1963, Oberman 1961, Avery et al 1957, Lichtenstein 1964), yet there are some who believe that the three conditions show entirely different patterns clinically and represent three distinct entities (Siwe 1949; Otani 1957).

In this paper 14 cases of Histiocytosis X are presented. Whilst recognising that Eosinophilic Granuloma, Hand Schuller Christian Disease and Letterer Siwe Disease are different phases of the same disease, yet because their course and prognosis are so different, these 14 cases are divided arbitrarily into these three clinical division. As a guide the following criteria are used in this subdivision. Eosinophilic granuloma denotes the mildest monosymptomatic stage, restricted to single or multiple skeletal lesion. Hand Schuller Christian disease refers to a chronic disseminated histiocytosis which is the chronic phase of the basic disorder in which multiple skeletal lesion are associated with systemic involvement of soft tissue and viscerae. Letterer-Siwe Disease which is also known as acute or subacute disseminated histiocytosis, represents the earliest and most acute form of a diffuse and more rapidly progressive form of disease.

AGE AND SEX INCIDENCE

Amongst these fourteen cases, the youngest was three months old and the oldest nine years when first seen at the Paediatric Unit. Figure 1 showed that 50% of the cases were within the first two years of life and the rest scattered between the second year and ninth year. Although two cases of Hand Schuller Christian Disease were aged three months and ten months respectively, all the cases of Letterer-Siwe Disease were within the first four years of life. The six cases of Hand Schuller Christian Disease were scattered between three months and seven years. The oldest patient was 9 years of age and had Eosinophilic Granuloma. Avioli et al (1963) mentioned that clinical manifestation usually appear within the first decade with the highest incidence in the 2-6 year age group. However, the disease may appear at any age. In Davidson's series (1933), eight patients were in the third decade and three in the fifth and eighth decades.

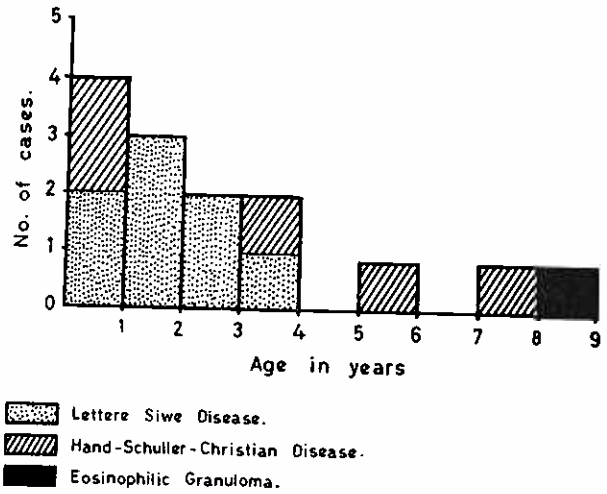

Fig. 1. Age incidence.

This study shows that the incidence in females is slightly higher than that in male. (Fig. 2). It is interesting to note that in the sex incidence mentioned by Avioli et al (1963), Avery et al (1957), the males predominate.

RACIAL INCIDENCE

The patients in this series were all Chinese. The racial distribution of patients admitted into the Paediatric Unit for a one year period revealed that only 75% were Chinese and the rest were Malays, Indian and others (Fig. 3). In other studies, the disease effected mainly the whites with occasional reports on Negroes. Avery et al (1957); Avioli et al (1963).

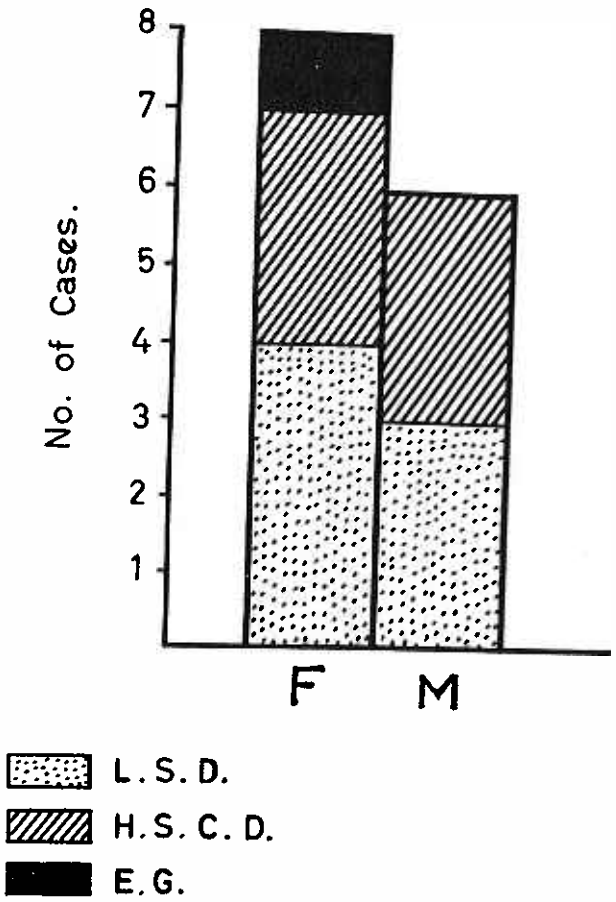

Fig. 2. Sex incidence.

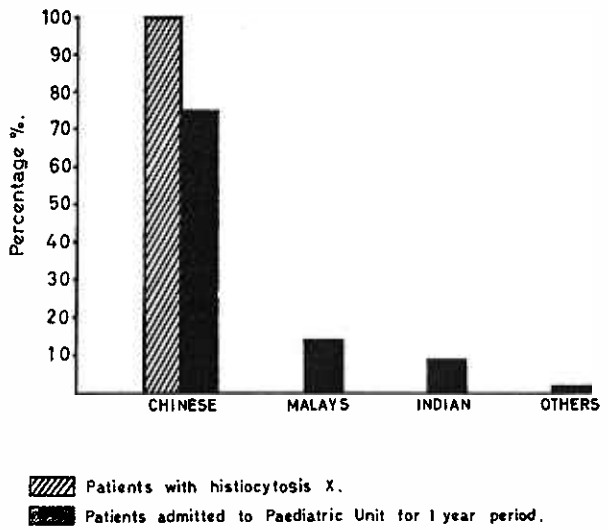

Fig. 3. Racial distribution.

CLINICAL FEATURE

The clinical manifestation were summarised in Tables I, II and III. There were seven cases of Letterer-Siwe Disease, six Hand Schuller Christian Disease and one Eosinophilic Granuloma.

CUTANEOUS MANIFESTATION

The skin lesion varies from seborrhoea eczematous lesion to yellow or reddish brown nodular rash. The cutaneous manifestation are frequently accompanied by widespread petechial eruption. The papular rash are usually located on the flexor surface of the extremeties and intertrigenous areas of the body. Seborrhoea eczematous lesion on the scalp is also common.

In this study four of the seven patients (57%) classified as Letterer Siwe Disease presented with skin eruptions and petechae on admission. With the exception of K.S.T. aged 4 years, the other three patients had seborrhoeic eczematous lesion on the scalp. Although none of the six patients classified as Hand Schuller Christian Disease had cutaneous manifestation, it should be noted that skin eruption in this group is not uncommon (Lichtenstein 1964). In approximately ten per cent of patients with Schuller Christian disease, the initial complaint involves cutaneous manifestation. Allen (1954) Lane and Smith (1939).

HEPATOSPLENOMEGALY AND JAUNDICE

Hepatosplenomegaly was present in all the seven cases of acute disseminated histiocytosis and was the initial presenting feature. It was less frequent in the chronic disseminated histiocytosis, hepatomegaly being present in only two out of six cases (33%) and splenomegaly three out of six cases. It was not present in the patient with Eosinophilic Granuloma. The hepatosplenomegaly was most marked in K.S.T. (Table I), who was admitted with a history of fever for four weeks, skin rashes for two weeks and an enlarged liver of five finger breadths and spleen of four finger breadths below the subcostal margin. In the Hand Schuller Christian disease group, T.C.E. (Table II) did not have hepatosplenomegaly when she was first seen with swelling of jaw, gingivitis and osteolytic lesions in the mandible. Three years later, the disease progressed rapidly with hepatosplenomegaly and infiltration to skull and long bones.

Jaundice which was a rare feature was present in two patients. They both had the obstructive type of jaundice, having bile in the urine and hyperbilirubinaemia. C.K.K. (Table I) presented with fever, anaemia and ear discharge for two months and jaundice for two weeks. On admission, the patient was jaundiced with a hepatomegaly of four finger breadths below the subcostal margin. She was also anaemic and had leucopaemia and thrombocytopaenia. The second patient T.C.E. (Table II) developed jaundice three years after the onset of her illness. The isocitricdehydrogenase was 360 units which is

TABLE I

CLINICAL FEATURES OF LETTERER SIWE DISEASE

Patient	Age (Yrs.)	Sex	Dermatitis	Petechae	Hepato-megaly	Spleno-megaly	Adeno-pathy	Otitis	Jaundice	Gingivitis	Exoph-thalmus	Diabetes Inspidus	Lung Lesion	Skeletal Lesion	Anaemia	Result
K.C.C.	17/12	M	+	+	+	+	+	0	0	0	0	0	0	+	+	Alive (1 yr.)
Y.K.K.	1½	F	—	—	+	+	+	0	0	0	0	0	0	0	+	Alive (2 yrs.)
T.S.Y.	3/12	F	—	—	+	+	+	0	0	0	0	0	+	0	+	Died
K.S.T.	4	F	+	+	+	+	+	0	0	0	0	0	+	0	+	Died
N.P.H.	1	M	+	+	+	+	+	+	0	0	+	0	+	+	+	Died
C.K.K.	3	F	—	—	+	+	—	+	+	0	0	0	0	+	+	Died
L.K.T.	2	M	+	+	+	+	+	0	0	0	0	0	0	0	+	Died
Total	7		4	4	7	7	6	2	1	0	1	0	3	3	7	
Percentage	100%		57%	57%	100%	100%	89%	29%	14%	0	14%	0	46%	46%	100%	

TABLE II

CLINICAL FEATURES OF HAND SCHULLER CHRISTIAN DISEASE

Patient	Age (Yrs.)	Sex	Dermatitis Petechae	Cranial Nerve Lesion	Hepato-megaly	Spleno-megaly	Adeno-pathy	Otitis	Jaundice	Gingivitis	Exoph-thalmus	Diabetes Insipidus	Lung Lesion	Skeletal Lesion	Anaemia	Result
C.Y.Y.	3	F	0	0	0	0	+	0	0	+	0	0	0	0	+	Alive (6 yrs.)
O.K.C.	3/12	M	0	0	+	+	+	0	0	+	0	0	0	+	+	Alive (8 yrs.)
N.S.L.	4	F	0	0	0	+	+	+	0	+	0	0	0	+	0	Alive (12 yrs.)
S.Y.C.	6	M	0	+	0	0	0	+	0	0	0	0	0	+	0	Alive (4 yrs.)
C.K.W.	10/12	M	0	0	0	0	+	+	0	+	+	0	+	+	+	Died
T.C.E.	7	F	0	0	+	+	+	0	+	+	0	+	0	+	+	Died
Total	6		0	1	2	3	5	3	1	5	1	1	1	5	4	
Percentage	100%		0	17%	33%	50%	83%	50%	17%	83%	17%	17%	17%	83%	66%	

TABLE III

CLINICAL FEATURES OF EOSINOPHILIC GRANULOMA

Patient	Age (Yrs.)	Sex	Dermatitis Petechae	Hepato-megaly	Spleno-megaly	Adeno-pathy	Otitis	Gingivitis	Exophthalmus	Diabetes Insipidus	Skeletal Lesion	Anaemia	Result
L.L.J.	9	F	0	0	0	+	0	0	0	0	+	0	Alive (4 yrs.)
Total	1		0	0	0	1	0	0	0	0	1	0	

within normal limits. Unfortunately autopsy could not be obtained in these two patients to determine the cause of the obstructive jaundice.

Oberman (1961) mentioned hepatomegaly in 8 out of 17 cases of Hand Schuller Christian Disease and noted jaundice in one case only. Avioli (1963) noted the infrequency of hepatomegaly in the chronic disseminated form of histiocytosis. In Avery's series of twenty-nine cases, hepatomegaly was noted in three cases. Rowland (1928) described one out of twenty six cases reviewed. In some cases of jaundice, the liver function tests are consistent with parenchymal damage, whereas in other instances liver function tests were within normal limits. Kabat (1961), Renzetti (1957). Adenopathy in the region of the hepatic hilum may account for the obstructive jaundice in some cases. (Hampton 1942).

LYMPHADENOPATHY

Lymphadenopathy was present in 89% of Letterer Siwe Disease (Table I) and 83% of Hand Schuller Christian disease (Table II). The lone case of Eosinophilic Granuloma also had small cervical lymphadenopathy over the same side of the skull osteolytic lesion. The most common site of the lymphadenopathy were the cervical areas. Other sites such as submandibular, occipital axillary and inguinal lymph nodes were also affected. Generalised lymphadenopathy were seen in three patients, *viz.* K.S.T. N.P.H. of the Letterer Siwe Disease group and C.K.W. of the Hand Schuller Christian Disease group, all of them had a fatal course.

Avioli (1963) mentioned that lymphadenopathy, a consistent finding in the Letter Siwe variety of disseminated histiocytosis is variably present in Schuller Christian disease. Lichtenstein (1964) listed three instances in which a lesion of Eosinophilic Granuloma of bone apparently extended to regional lymph nodes.

OTITIS MEDIA

Chronic otitis media was a common manifestation among the Hand Schuller Christian disease accounting for 50% of the cases. Among the Letterer Siwe Disease group there were only two cases (29%). Of the five cases with chronic ear discharges. three had granulomatous lesion in the meatus and biopsy from these granuloma showed proliferation of histiocytes, foam cells and eosinophils. Four of the five cases had associated radiological changes in the mastoid or petrous portion of the temporal bones. One patient S.Y.C. (Table II) had been treated for ear discharge for two years with antibiotics without success. Exploration biopsy which was done when he developed a seventh cranial nerve palsy and an aural polyp revealed evidence of histiocytosis. X-ray of skull showed erosion of the mastoid. N.S.L. (Table II) had a history of ear discharge for 1 year and presented with gingivitis and granulomatous lesion of palate and right aural meatus. Biopsy of the granulomatous lesion from the palate and right meatus revealed histological picture of histiocytosis.

ORAL AND DENTAL LESIONS

Lesions involving the gums were observed in five out of six cases (83%) of Hand Schuller Christian Disease, but was not seen among the Letterer Siwe Disease in the series. The oral involvement may present as swollen sore gums some of which bled and had ulceration. In the older children the gum lesions were associated with loosening of teeth. Granulomatous lesion of the palate was seen in only one patient N.S.L. (Table II). The recognition and familiarization of gum and dental lesion is important from the diagnostic and therapeutic point of view as they may be the only presenting feature in the early phase of the disease. It is interesting to mention that three of these five cases were referred to the Paediatric Unit by the dental surgeons who were consulted by these patients for dental complaints.

EXOPHTHALMUS

Exophthalmus was noted in only two patients in this study. One of them N.P.H. (Table I) presented with unilateral proptosis whilst the other patient C.K.W. (Table II) had bilateral exophthalmus. Both the patients died, within two months and one and a half years respectively of their illness. The exophthalmus is caused by retroorbital accumulation of granulomatous tissue. Osteolytic lesion at the orbital apex may facilitate the displacement of the globe. Osseous destruction of the orbital bone was not seen in these two cases. Although both of them had osteolytic lesion in other parts of the skull and skeleton, diabetes insipidus was not noticed in either, thus the classic triad of exophthalmus. diabetes insipidus and membranous bone lesion initially described by Hand was not present in this series.

Avioli et al (1963) noted exophthalmus in 89 of their 180 cases and approximately one half of them also exhibited lytic bone lesions and diabetes.

DIABETES INSIPIDUS

Diabetes Insipidus was present in one patient T.C.E. (Table II) three years after she presented with swelling of jaw and gums. The diabetes responded favourably to pitressin therapy. Associated destruction of the sella-turcica was not present.

Although diabetes insipidus was not universally present in the disseminated form of histiocytosis, it was noted in as high as 57% of Avioli's (1963) series. The lack of diuretic hormone resulted more from involvement of the tubercinereum and hypothalamus rather than local infiltration of the posterior pituitary gland.

PULMONARY INVOLVEMENT

The lungs were involved in three patients (46%) from the Letterer Siwe Disease group and one patient from the Hand Schuller Christian Disease. Three patients N.P.H., T.S.Y. and C.K.W. had positive radiological changes in their chest X-rays. Two of them showed fine reticular infiltrations which were bilateral and symmetrical. In the other case T.S.Y. the infiltration appeared in several localised patches simulating the appearance of bronchopneumonia. K.S.T. presented with pyrexia for one month, night sweats dyspnoea, pleural pain, toxicity and signs of pleural effusion which on aspiration revealed haemorrhagic pleural effusion.

The incidence of pulmonary involvement varies. It was documented in 14% by Avioli et al (1963) and approximately 35% by Avery et al (1957). In this study it accounted for 31% of the disseminated form of histiocytosis. The clinical manifestation also varies from one extreme which could be very mild and symptomless apart from positive radiological changes to the other extreme where the patient could be very toxic and ill presenting with pyrexia, nights sweats, cough, chest pain and dyspnoea. The radiological picture generally showed a bilateral and symmetrical reticular or reticular-nodular infiltration. Sometimes it could appear as larger nodules with several localised patches, Honeycomb or cystic appearance had also been described (Lichtenstein 1964).

SKELETAL LESION

The chronic disseminated group had more frequent skeletal involvement. In this study. five out of six patients (83%) of the Hand Schuller Christian disease had skeletal involvement against 3 patients (46%) among the Letterer Siwe Disease group. The lone case of Eosinophilic Granuloma had osteolytic changes confined to the temporal bone.

The skull was infiltrated in most of the patients in this series where eight out of nine patients showed positive radiological changes. The commonest site is the calvarium which was involved in six of the eight cases. The osteolytic lesion varies from single to multiple areas of destruction and they also vary in size. The typical irregular 'geographic' areas were seen in only two patients.

The osteolytic lesions were associated with palpable defect over the scalp in five patients, two from the Letterer-Siwe group and three from the Hand Schuller Christian Disease group. The palpable skull defects were pulsatile in two cases.

Other bone lesions were detected in the mandible (2 cases) long bones (3 cases); Vertebrae (2 patients) and ribs (one patient). Multiple skeletal lesions were seen in only three patients. *viz.* C.K.W., T.C.E. (Table II) and K.C.C. (Table I). Figures 4 to 10 showed radiological changes in the skull, long bones, vertebrae, ribs and chest from patient C.K.W.

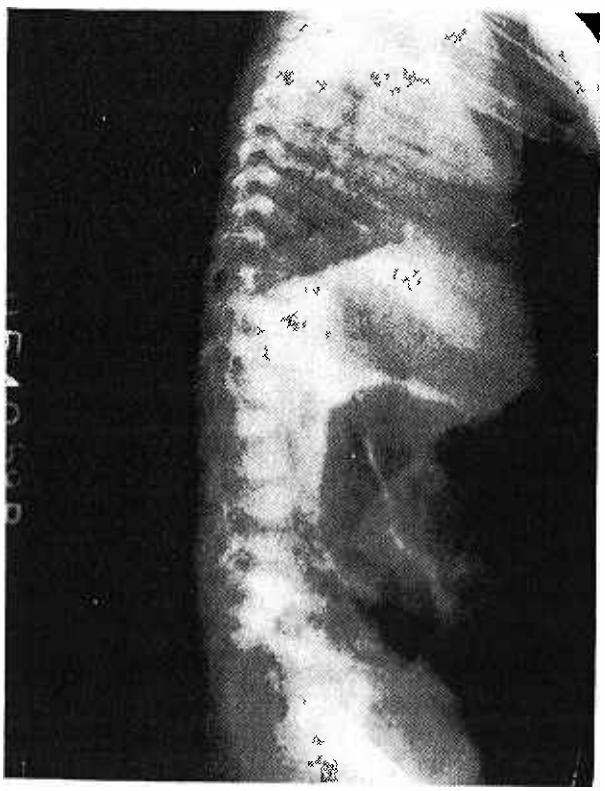

Fig. 7. Shows infiltration in vetebrae with collapse of lumbar vetebrae.

In Avioli's series (1963) 80% of Hand Schuller Christian disease developed bone lesion. They also found that the skull was

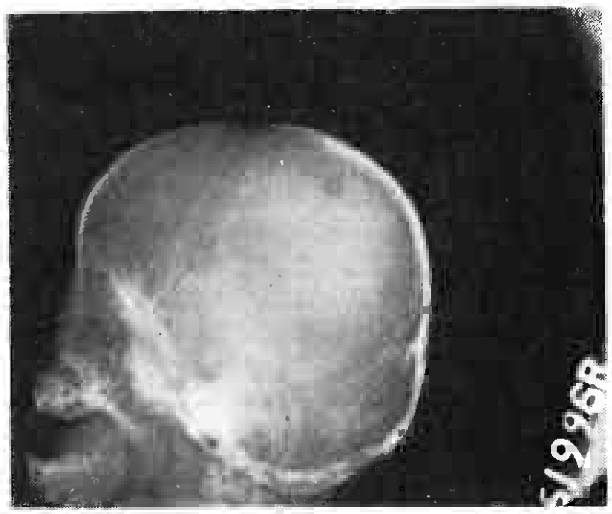

Fig. 4. Skull X-ray of C.K.W. shows a few osteolytic lesion in August 1964.

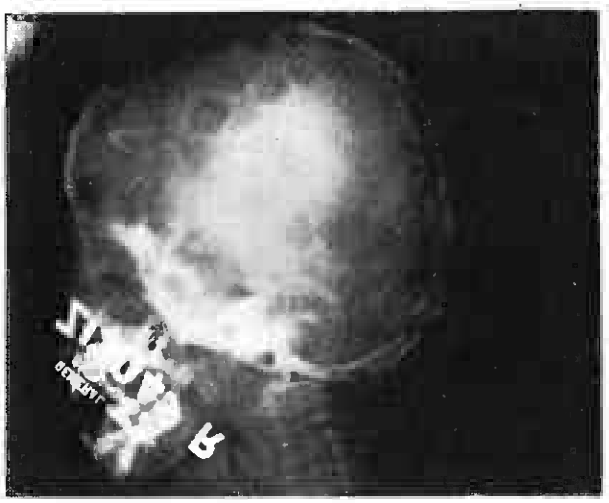

Fig. 5. The osteolytic lesions increased to give an irregular 'geographical' picture in March 1965.

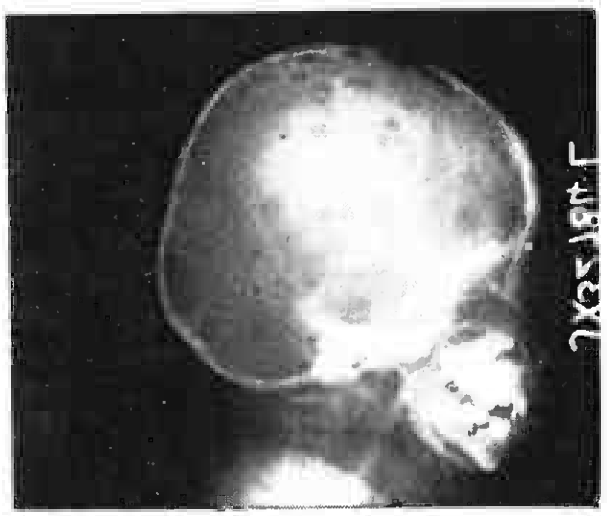

Fig. 6. Three months after steroid therapy, the osteolytic lesion became smaller. Taken in June 1965.

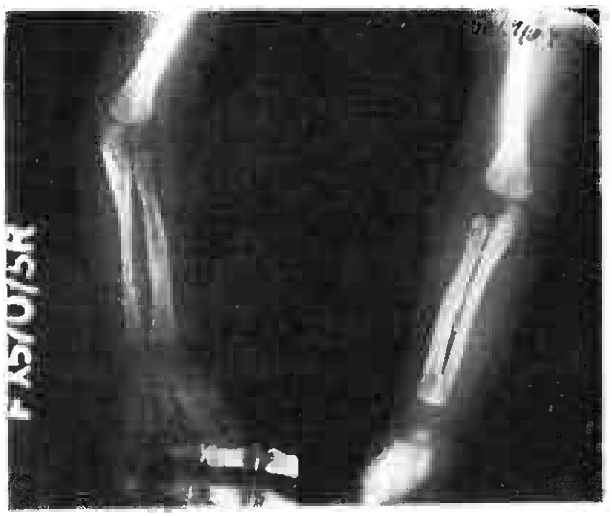

Fig. 8. Infiltration of Ulna and Radius.

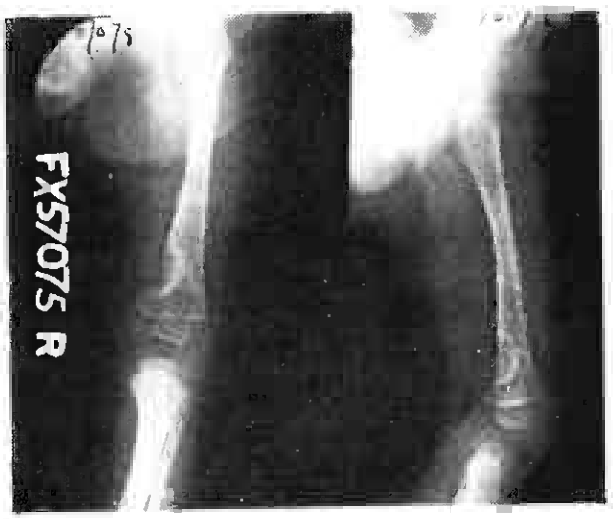

Fig. 9. Lesion in Femur.

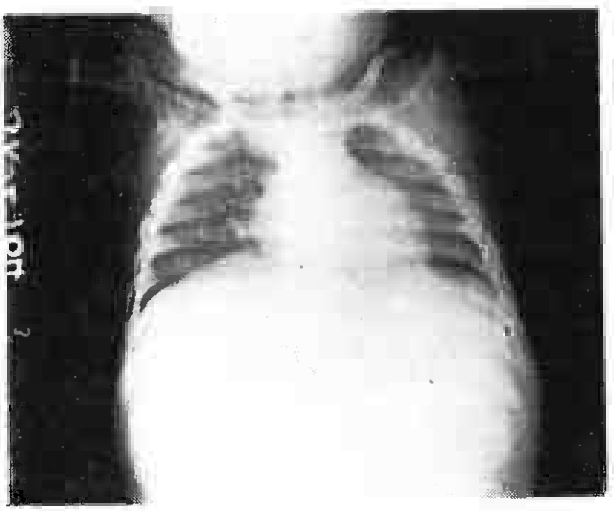

Fig. 10. Shows lesion in ribs and reticular infiltration in both lungs.

involved most frequently with temporoparietal region showing the highest incidence. The lesions are typically osteolytic but dense osteoblastic lesions may occur.

CRANIAL NERVE LESION

Involvement of cranial nerve lesion is rare. In this study one patient S.Y.C. presented with right facial nerve palsy with granulomatous lesions in the right aural meatus following a history of right ear discharge for two years.

Bender (1958) reported a case with involvement of fifth, seventh, eight, and nineth cranial nerves, along with many of the usual manifestations in a woman of forty-three.

HAEMATOLOGICAL FINDINGS

Anaemia was noted in all the cases classified under Letterer-Siwe Disease. Their haemoglobin level ranged from 4·4 gm.% to 8·8 gm.% with a mean of 6·8 gm.%. In the Hand Schuller Christian Disease group, anaemia was present in four patients only. Two patients N.S.L. and S.Y.C. had haemoglobin level of 10·3 gm.% and 14·0 gm.% respectively. The case of Eosinophilic Granuloma had a haemoglobin level of 13·5 gm. %.

The total white blood cell count was normal in all the patients except two cases K.S.T. and C.K.K. (Table I) who had white blood cell count of 3,200/c.mm. and 2,500/c.mm. respectively. Both these patients had a fulminating course and did not survive.

Thrombocytopaenia was also noted in three patients. Two of them K.S.T. and N.P.H. had the acute disseminated form of histiocytosis and presented with skin petechae. Both the patients had platelet counts of 20,000/c.mm. each and died within two months from the onset of their illnesses. The third patient O.K.C. had a platelet count of 30,000/c.mm. which returned to normal when the disease went into remission.

The cause of the anaemia was uncertain. In some cases it may be associated with chronic suppurative infection or malnutrition. It was not uncommonly seen in the advanced stage of the disease. A suggestion that marrow accumulation of lipid interfering with haemotopoeisis was made by Rowland (1928). Rarely aplastic anaemia may be found with the normal marrow being replaced by histiocytes (Baber 1960). Among the cases of anaemia seen in this series none had aplasia of the bone marrow. Two patients C.Y.Y. and O.K.C. had chronic suppurative infection associated with the anaemia.

ERYTHROCYTIC SEDIMENTATION RATE

The E.S.R. was done on eight patients. Four of them K.C.C.; Y.K.K.; T.S.Y. and K.S.T. all classified as Letterer Siwe Disease had E.S.R. which ranged from 10 mm. to 27 mm. The other four patients C.Y.Y., O.K.C.; C.K.W.; and T.C.E. who were classified as Hand Schuller Christian disease had E.S.R. which ranged from 92 mm. to 106 mm.

DIAGNOSIS

The diagnosis of Histiocytosis X was based on clinical manifestation; radiological changes and finally histological examination of biopsied specimens from gums, lymph glands, skin or granulomatous lesion. All the patients in this series had their diagnosis of histiocytosis X confirmed by histology.

One patient T.S.Y. who gave a history of fever for one month presented with only hepatosplenomegaly and cervical lymphadenopathy. She was treated as a case of pyrexia of unknown origin with Sigmamycin (Tetracycline and oleandomycin). Autopsy revealed infiltration of liver by multiple histiocytic nodules. L.L.J. the lone case of Eosinophilic Granuloma had her diagnosis confirmed after exploration of the mastoid revealed some fatty substances in the bone erosion. Histology of the fatty substance showed proliferation of histiocytes with foam cells and eosinophils.

TREATMENT

All the patients received prednisolone therapy for varying periods except for three patients *viz.* L.L.J., S.Y.C. and T.S.Y. The latter case received only broad spectrum antibiotics because she was diagnosed as pyrexia of unknown origin before death. The former two patients L.L.J. and S.Y.C. received deep X-ray therapy.

Out of eleven cases treated with prednisolone, six cases succumbed giving a mortality of 55%. When these cases were subdivided into their respective groups it was shown in Table IV that of the six cases of Letterer-Siwe Disease given prednisolone four were fatal giving a mortality of 66% whilst in the Hand Schuller Christian Disease group five patients received prednisolone and two died resulting in a mortality of 40%.

TABLE IV

TREATMENT

		Mortality
a) PREDNISOLONE		
Letterer Siwe Disease	(6 cases)	66%
Hand-Schuller Christian Disease	(5 cases)	40%
Total	(11 cases)	55%
b) ENDOXAN		
Letterer Siwe Disease	(1 case)	100%
c) RADIOTHERAPY		
Hand-Schuller Christian Disease	(1 case)	0%
Eosinophilic Granuloma	(1 case)	0%
d) ANTIBIOTIC		
Letterer Siwe Disease	(1 case)	100%

Endoxan was used in one patient K.S.T. after she did not show any response to high doses of prednisolone (40 mgm. per day). This did not alter the fatal course of her illness.

Of the two cases who received deep X-ray therapy, one case was classified as Eosinophilic Granuloma and the other Hand Schuller Christian Disease. The latter case had mild symptoms *viz.* chronic ear discharge, cranial nerve involvement, granulomatous lesion in the right aural meatus and osteolytic lesion in the temporal bone. Both patients showed clinical as well as radiological remission of symptoms for four years.

COURSE OF ILLNESS

The mortality in this series was 50%. Subdividing it into age groups revealed that within the first year of life three out of four patients succumbed, giving a mortality of seventy five percent (see Table V). Seven patients who were within one to five year age group had three deaths resulting in mortality of forty three percent. In the older age group (above 5 years) the mortality was thirty three percent.

TABLE V

Age		Mortality
0 - 1 yr.	(4 cases)	75%
1 - 5 yrs.	(7 cases)	43%
5 - 10 yrs.	(3 cases)	33%

Separating the patients into the various phases of disease it was shown that the Letterer Siwe Disease group had a mortality of 71%; Hand Schuller Christian Disease 33% and Eosinophilic Granuloma 0%. (Table VI)

DISCUSSION

As stated before, because of the variable nature of the clinical course and for prognostic reasons, the cases in this study were divided into three entities, although realising that they in fact represent different phases of the same disease. Even so, detail study will reveal that in some cases it was difficult to separate them as they were transitional between two phases. Eosinophilic Granuloma was classified as a localised form of histiocytosis as seen in the only case in this series. However Oberman (1961) noted that although in the majority of his cases of Eosinophilic Granuloma the skeletal involvement was the sole manifestation of the disease, yet two of his patients subsequently developed diabetes insipidus and one had otitis media. In his paper he attempted to classify forty cases of histiocytosis into its three entities by clinical as well as histopathological findings and concluded that it was difficult to separate them. However he added that the most accurate guide to the ultimate outcome is the assessment of the rapidity of progression of the disease for several months.

The classic triad *viz.* Exophthalmus, Diabetes Insipidus and membranous bone lesion was not present in this study. Oberman (1961) mentioned that it is rarely seen. Avery et al (1957) noted the triad in three out of twenty nine patients reviewed.

TABLE VI

STAGE OF HISTIOCYTOSIS

		Mortality
Letterer Siwe Disease	(7 cases)	71%
Hand-Schuller Christian Disease	(6 cases)	33%
Eosinophilic Granuloma	(1 case)	0%

The prognosis of histiocytosis X depends on various factors. The phase of the disease is significant, as can be seen in this study where the acute disseminated form had 71% mortality as compared with 33% in the chronic disseminated group and 0% in the localised form (Table VI). Oberman's (1961) series showed a mortality of 66% among the Letterer Siwe Disease as compared to 53% and 12% among the Hand Schuller Christian disease and Eosinophilic Granuloma respectively. He further explained that among the two deaths in the Eosinophilic Granuloma group, one death was not related to the disease and the other was due to location of the lesion rather than dissemination. In Avery's series (1957) the mortality rates were, Letterer

Siwe Disease 100%; Hand Schuller Christian Disease 13% and Eosinophilic Granuloma 0%. Although the prognosis in Letterer Siwe Disease is poor, the disease is not invariably fatal. This study and longer follow up studies by others (Oberman 1961; Lichtenstein 1964; Bass et la 1953; Cox, 1953; Lightwood and Tizard 1954) supports the impression that with adequate therapy acute disseminated histiocytosis need not necessarily be serious.

The prognosis is worse in infants than in older children probably because the acute disseminated form occurs more frequently during infancy. In this study, of the three deaths in the infant age group, two were classified as Letterer Siwe Disease and one Hand Schuller Christian Disease. Table V showed that the infants had the highest mortality rate.

It is generally stated that those cases where the disease was confined to the skeleton at onset has a favourable outcome, whereas those with involvement of soft tissue or viscerae and skeletal lesion have a less favourable outlook, particularly when the lesions progressed rapidly. Jaundice which is an unusual finding, was seen in two patients in this study and both succumbed. Oberman (1961) also reported poor prognosis when jaundice sets in. He also considered hepatomegaly as a poor prognostic sign. In this study of the nine patients with hepatomegaly the mortality was 67%. Anaemia which was present in all the cases of Letterer Siwe Disease in this study has poor prognosis particularly when associated with leucopenia and thrombocytopenia.

Oberman (1961) stated that histologically there was inconstant correlation of foam cells, tissue eosinophilia and fibrosis with clinical course. Nevertheless, it was suggested that the presence of a homogenous histiocytic infiltration with no eosinophils or foam cells pointed to a poor prognosis, whereas the presence of large aggregates of eosinophils augured a more favourable one.

The clinical effectiveness of steroid had been reported by many observers. The action of steroid is probably a result of its anti-allergic, antiphlogistic potencies. It reverses not only the histiocytosis proliferation but also the cholesterol accumulation which characterise the xanthomatous phase of the disease. The result of steroid varies with the stage of disease. Avioli (1963) treated ten cases of Hand Schuller Christian Disease with high doses of steroid for six to eight weeks and reported that steroid was capable of reversing all the skeletal and viscerae manifestation of the disease. A number of papers also reported on the success of steroid on Letterer Siwe Disease. (Bass et al 1953; Cox 1953; Lightwood and Tizard 1954; Oberman 1961).

Radiotherapy is generally used for localised skeletal lesion, but it had been used with success on mucocutaneus lesion (Avery et al 1957). These groups of workers also recorded irradiation on sixteen cases of Hand Schuller Christian Disease and reported improvement in eleven patients. Spontaneous remission of Hand Schuller Christian Disease had been reported in some papers (Thomson et al 1959; Panner 1959).

There was no experience of spontaneous remission in this series. T.C.E. (Table II) was not treated with steroids when she first presented with swelling of jaw and gingivitis at the age of three years. The lesion disseminated quite rapidly three years later when steroid was used but with no effect. T.S.Y. (Table I) also did not receive steroid because the diagnosis was not made before death. Her condition deteriorated rapidly in spite of broad spectrum antibiotics. The result of steroid therapy was shown in Table IV. In those who survived there was evidence of remission in skeletal as well as soft tissue and viscerae infiltration.

It is concluded that it would be useful to use large doses of steroid early in the acute and chronic disseminated form of Histiocytosis X once the condition is diagnosed to aid remission and increase the survival rate.

SUMMARY

This paper describes fourteen cases of Histiocytosis X seen at the Paediatric Unit (East), General Hospital. All the patients were Chinese. Their age group ranged from 3 months to nine years old.

There were seven cases of Letterer-Siwe Disease or Acute Disseminated Histiocytosis, six cases of Hand Schuller Christian Disease or Chronic Disseminated Histiocytosis and one case of Eosinophilic Granuloma. Whilst recognising that these three entities represent different phases of the same disease, the subdivision was made because of their variable clinical course and different prognosis.

Their clinical features such as cutaneous manifestation, Hepatosplenomegaly, Lymphadenopathy, Otitis media, Oral and Dental lesions, Exophthalmus, Diabetes Insipidus, Lung and Skeletal lesions were discussed.

The treatment consisted of steroid (eleven patients) deep X-ray therapy (2 patients) and broad spectrum antibiotic (one patient).

The prognosis was poor in infancy and those with the acute disseminated form of Histiocytosis particularly in those where the lesion progressed very rapidly.

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