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Government Hospital, Kegalle, Ceylon, and Cancer Research Institute, Tata Memorial Centre, Parel, Bombay.

Bone Changes in Congenital Haemolytic Anaemias

Report of Cases in Ceylon

N. NAGARATNAM and P. K. SUKUMARAN

Clinical and radiological changes in the bones are not uncommonly seen in association with certain disorders of the blood. They tend to occur in conditions where there is either a compensatory hyperplasia of the erythropoietic tissue due to an increased red cell destruction or where there is an uncontrolled and widespread proliferation of the leucopoietic cells infiltrating the bone marrow. The former are represented by the hereditary or congenital haemolytic anaemias where the hyperplasia may result in radiological changes in the bones. The latter by the leukaemias and the non-leukaemic malignant diseases of the bone marrow. Radiological bone changes are only rarely seen in other blood diseases, though they have been described in association with iron deficiency [1, 2], pernicious anaemia and erythroblastosis foetalis [3].

This paper is an analysis of the radiological changes in the bones that occur in the congenital haemolytic anaemias as they are seen in Ceylon.

Material

Of the 20 patients under study, 11 had thalassaemia, 1 thalassaemia-Hb H disease, 4 thalassaemia-Hb E disease and 4 congenital non-spherocytic haemolytic anaemia.

Findings

The congenital haemolytic anaemias in Ceylon comprise the thalassaemia syndromes, the haemoglobinopathies and the non-spherocytic haemolytic anaemias.

Thalassaemias

Table I summarises some of the clinical and haematological data together with the bone changes in 11 cases. None of the cases showed

TABLE I

Summarises the Haematological, Clinical and Radiological Bone Changes in Patients with Thalassaemia

Case	Age (Years)	Hb	Hb-F	Hb (g%)	Retic (%)	Blood Picture	Liver	Spleen	Skull	X-rays Hands	Tub. bones
1	5/12	nil	36.4	4.2	6	N++++ T++	3f	3f	0	0	0
2	8/12	nil	73.5	3.3	6	N++++ T+	2f	4f	0	+	0
3	5	nil	6.2	11.0	3	T+	0	2f	0	0	0
4	9/12	nil	17.5	3.3	4	T±	2f	0	0	0	0
5	10/12	nil	14.0	3.7	8	N+++ T+	3f	2f	0	+	0
6	8/12	nil	70.0	5.2	–	N 0	0	0	0	+	0
7	11/12	nil	68.8	6.0	6	N+ T+	0	0	0	0	0
8	2/12	nil	40.0	8.4	–	N 0	0	0	0	0	0
9	4/12	nil	72.0	2.6	–	N++++ T++	2f	2f	0	+	+
10	3	nil	30.0	3.1	–	N+ T+	1f	splenectomy	0	0	0
11	5/12	nil	10.0	7.7	1	N+ T++	0	?	0	0	0

N = nucleated cells, T = target cells

any changes in the skull. Three had changes in the small bones of the hands and one of them in the tubular bones as well. One other had rarefaction of the bones of the hands and forearms.

All three that showed bone changes in the X-rays had alkali-resistant haemoglobin to the value of 70%. Two of them have since died. Two had palpable spleens and the haemoglobin levels were between 2.6 g% and 3.3 g% in the three cases. The youngest was 2 months old and the oldest 5 years.

Haemoglobinopathies

The abnormal haemoglobins that have so far been described in Ceylon are Hb. H [4] and Hb. E [5, 6]. Table II summarises the five

TABLE II

Summarises the Haematological, Clinical and Radiological Bone Changes in Patients with Haemoglobinopathies

Case	Age (years)	Hb	Hb-F	Hb (g%)	Retic (%)	Blood Picture	Liver	Spleen	X-rays Skull	X-rays Hands	X-rays Tub. bones
Hb H-thalassaemia											
1	5/12	H	–	2.2	–	N+++ T++	1f	0	0	0	0
Hb E-thalassaemia											
1	6½	EF	3.6	2.1	0.3	N++	4f	5f	0	++	+
2	13	EF	nil	2.1	17.2	0	3f	5f	0	rare-faction	0
3	10	EF	5	6.6	2.8	N+ T+++	3f	6f	0	++	+
4	4	EAF	4	6.9	4.0	N+ T+++	2f	0	0	++	0

N = nucleated red cells, T = target cells

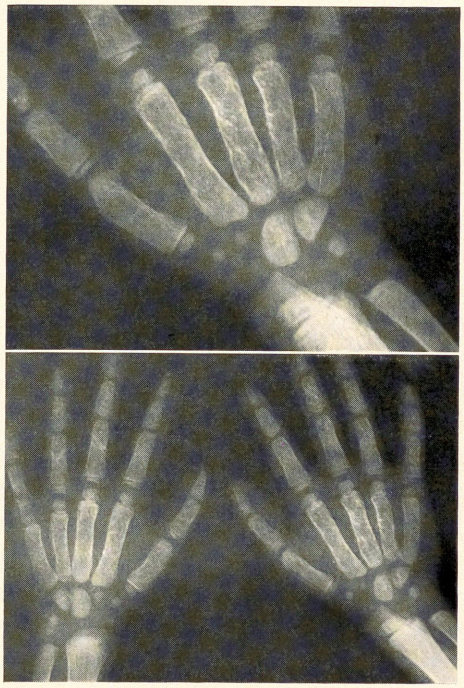
TABLE III

Summarises the Haematological, Clinical and Radiological Bone Changes in Patients with Congenital Non-spherocytic Haemolytic Anaemia

Case	Age (years)	Hb	Hb-F	Hb (g%)	Retic (%)	Blood Picture	Liver	Spleen	X-rays Skull	X-rays Hands	X-rays Tub. bones
1	1	nil	0	6	4	mac.	0	0	++	++	++
2	2	nil	0	4.8	3	N+	0	0	0	0	0
3	18	nil	0	2.8	4.5	N 0	2f	3f	0	0	0
4	30	A_2 sl. raised	0	3.3	5	N 0	2f	4f	0	0	0

N = nucleated red cells, T = target cells

cases. The only case of Hb. H-thalassaemia did not show radiological evidence of bone changes. All four cases of Hb. E-thalassaemia had bone changes, 3 had the characteristic changes in the bones of the



1a

1b

Fig. 1. X-ray of the hands showing bone changes from a case of Hb. E-thalassaemia disease.

hands (Fig. 1), two in the tubular bones and one showed rarefaction of the bones of the hands. None showed changes in the skull.

Congenital non-spherocytic haemolytic anaemias

Of the 4 cases of atypical congenital haemolytic anaemias which had been described in detail by one of us [7] only one showed the characteristic changes in the skull, hands and tubular bones. Clinically, there was considerable bossing of the frontal and parietal bones of the skull. X-rays done at the end of 3 years showed none of the changes seen earlier. Table III summarises the clinical and haematological data in relation to the bone changes.

Discussion

Caffey [8] has described in detail the radiological bone changes in thalassaemia. The first site of detectable changes are in the small

bones of the hands. There is widening of the medullary cavities with thinning of the cortex and decreased density of the medulla. The trabecular pattern in contrast appears prominent. Owing to broadening, the small tubular bones assume a rectangular rather than a linear shape. In the membrane bones of the skull there is broadening of the diploe with separation of the tables resulting in thickening of the vault of the skull especially of the frontal and parietal bones. The outer table is thinned and the bony trabeculae traversing the widened space give it an appearance of "hair on end" or "brush" appearance. The expansion of the marrow in the malar bones gives rise to a mongoloid appearance. Growth as a whole is often retarded.

These changes usually develop early in life and as the child grows older they tend to regress in the extremities but may persist in the skull and pelvis. According to *Lie-Injo Luan Eng* [1] in thalassaemia major occurring in Indonesia the bone changes are more pronounced in other parts of the body than in the skull. Our findings are very similar to hers. Besides the characteristic changes seen in the three cases in this series, one showed rarefaction of bone. Rarefaction of bone is also seen in sickle-cell anaemia [9] and in Hb. E-thalassaemia disease [6]. Spontaneous fractures have been known to occur in the bones occasionally [10] but none of our cases showed any spontaneous fracture.

According to *Astaldi et al.* [11] bone changes are conspicuous especially in the less severe and milder forms of thalassaemia major. In our series, however all 3 that showed bone changes appear to have been affected severely as the clinical, haematological and the level of the alkali-resistant haemoglobin indicate. In thalassaemia major more often than not there are large amounts of Hb. F though low percentages have also been observed. However, according to *Fessas* [12] and others the proportion of Hb. F cannot be correlated with the clinical severity of the disease.

Bone changes are also seen in the haemoglobinopathies but are usually less marked. The single case of Hb H-thalassaemia in our series did not show bone changes, but all the cases of Hb E-thalassaemia showed changes in the extremities but not in the skull. Changes in the bones are similar to those that occur in thalassaemia, X-ray examination of the skull and long bones in 17 cases with haemoglobin E and α-thalassaemia in Thailand showed widening of the medulla typical of thalassaemic diseases in only one and in two they were only suggestive [13].

Changes in hereditary spherocytosis are rare still more so in the

congenital non-spherocytic anaemias. They have also been described by others [14, 15].

Summary

Twenty cases of congenital haemolytic anaemias were studied in relation to the bone changes. Of the 11 cases of thalassaemia only 3 showed bone changes and these occurred only in the peripheral bones. The 4 cases of Hb. E-thalassaemia also showed similar changes and distribution. One case of non-spherocytic haemolytic anaemia showed well marked changes in the skull, hands and tubular bones.

Zusammenfassung

Bei 20 Fällen von kongenitaler hämolytischer Anämie werden die damit verbundenen Knochenveränderungen untersucht. Nur 3 von 11 Fällen von Thalassämie wiesen Knochenveränderungen auf, und auch diese betrafen nur die peripheren Knochenabschnitte. 4 Fälle von Hb E-Thalassämie zeigten ähnliche Veränderungen und Verteilungsmuster. Bei einem Fall von nichtsphärozytischer, hämolytischer Anämie bestanden ausgeprägte Veränderungen am Schädel, an den Händen und den Röhrenknochen.

Résumé

Vingt cas d'anémies hémolytiques congénitales ont été étudiés du point de vue osseux.

Sur onze cas de thalassémie, il n'y eut que trois cas de modifications osseuses, survenues sur les os distaux.

Dans les quatre cas d'Hb – E thalassémie, les modifications furent semblables et leur distribution fut identique.

Dans un cas d'anémie hémolytique non sphérocytaire, on observe des modifications osseuses marquées au niveau du crâne, des mains et des os longs.

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Authors' addresses: N. Nagaratnam, M.D., Government Hospital, *Gampaha, W. P.* (Ceylon) and P. K. Sukumaran, Cancer Research Institute, Tata Memorial Centre, Parel, *Bombay* (India)