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CASE REPORT

Osteopetrosis
A Report of Four Cases

by

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Abstract.

Four cases of osteopetrosis in infancy had been reported. All cases showed signs of anemia, thrombocytopenia and hepatosplenomegaly which at the beginning suggested the possibility of the diseases more commonly found in our country such as malaria, Cooley anemia, autoimmunne hemolytic anemia and malignancy. The authors then concluded that next to those diseases mentioned above the symptoms and signs of anemia, thrombocytopenia and hepatosplenomegaly especially in infancy should also lead to the possibility of the diagnosis of osteopetrosis. This latter is more obvious when it is accompanied by the difficulty in obtaining the bone marrow specimen.

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Introduction.

Osteopetrosis or marble bone disease or Albers Schönberg's disease is a rare congenital anomaly of the bones with obliteration of the bone marrow cavity, resulting in disorders of the blood forming organ. This congenital anomaly is an autosomal recessive entity. There is a block in the sequence of the chondro-osseous formation between primary and secondary spongiosa (Graham et al., 1973). Radiologically the epiphyses, metaphyses and diaphyses of the bones look very dense (Rubbin, 1964). Pathologically there is a persistent primary spongiosa (Stelling, 1967). It is a rare inherited autosomal recessive disease, usually manifests in infancy and early childhood. In severe cases it probably begins in utero and progresses after birth. However it sometimes appears in adults (Hinkel and Beller, 1955). The clinical course of this disease is variable from mild to rapidly lethal. As a result of the obliteration of the bone marrow spaces, anemia and thrombocytopenia of myelophtisic type develop. Therefore enlargement of the liver and spleen is common due to extramedullary hemopoietic proliferation occurring in these organs. Other manifestations such as lymphadenopathy throughout the body, optic atrophy and hydrocephalus may be present. This paper reports four cases of osteopetrosis in infants with symptoms of severe anemia and hepatosplenomegaly at the Department of Child Health, Dr. Cipto Mangunkusumo Hospital, Jakarta.

Case Reports.

CASE I, A two months old Indonesian boy was brought by her mother on August, 1968 to Dr. Cipto Mangunkusumo Hospital because of a very distended abdomen and frequent vomiting after each feeding.

The patient was the youngest child of eight children. There was neither history of having the same disease nor history of parental consanguinity in the family. Physical examination on the first day of hospitalization revealed a small, weak and pale infant with a body weight of 3.750 g, body length of 55 cm and a body temperature of 37,3°C. The head was normal. Ophthalmologic examination revealed papil and retinal atrophy. Heart and lungs were normal. Liver and spleen were both enlarged, 3cm and 6 cm below the right and left costal margin respectively. No signs of bleeding tendency were noted. Peripheral blood examination showed Hb level of 10.2 g/dl, R.b.C. count of 3 millions/ul, W.B.C. count of 11.400/ul with normal differential count.

As there was history of acute obstipation and frequent vomiting after each feeding, plain photo of the abdomen was done for the possibility of bowel obstruction. Rontgenographically the bowel didn't show any sign of obstruction but the radiographic density of the bones were clearly increased indicating the diagnosis of osteopetrosis. The skeletal survey made afterward supported the diagnosis of this disorder (Fig. 1, 2, 3 and 4) . On the 4th day of admit tance the baby looked paler but there was still no sign of bleeding tendency. Hb level decreased to 6,5 g/dl. A few normoblasts were found on the peripheral blood smears. Adequate bone marrow sample was very difficult to obtain. The specimen showed marked reduced erythropoietic and thrombopoietic system while the granulopoietic system showed almost normal activity. Blood transfusions were then administered. Two weeks later his general condition was getting worse and there were signs of subcutaneous bleeding throughout the body. Hb and platelets level fell to 3,7 g/dl and 3000/ul respectively while W.B.C. count increased to 28.000/ul. The child was treated by serial blood transfusions but the Hb and platelets level diminished steadily and the child died on the fifteenth day of hospitalization.

CASE 2, A one and half months old Indonesian boy, was referred from the Department of Child Health, General Hospital, Ujungpandang, on July, 1980 with the history of high fever and severe anemia since two weeks prior to admission. He was the third child of three children; other siblings were healthy. His mother and father were first cousins. On admission to Dr. Cipto Mangunkusumo Hospital, Jakarta, the baby looked extremely pale with the body weight of 3.500 g, body length of 49 cm and body temperature of 38.6° C. The head was normal. Ophthalmologic examination showed no abnormality. Heart and lungs were also normal. Liver and spleen were both enlarged, 2,5 cm below the right and left costal margin respectively; there were petechiae over the abdominal wall and on the lower extremities. The initial blood examination revealed Hb level of 5,4 g/dl, R.B.C. count of 2,08 millions/ul, platelets count of 13.000/ul and W.B.C. count of 9.400/ul with normal differential count.

No malaria parasite was found; repeated bone marrow aspiration gave only a very small amount of specimen which showed a reduced erythropoietic and thrombopoietic system. Granulopoietic system showed normal activity without any evidence of malignancy. Serological examination didn't show any circulating antibody. The patient was treated by red packed cells suspension and antibody. On the 11th day of admission the clinical course was progressively deteriorating; the bleeding was more prominent and the abdomen was more distended. The spleen was larger than before and very hard on palpation that the possibility of a tumor mass in this area was suspected. Plain photo of the abdomen revealed only the presence of hepatosplenomegaly without any other mass but the bones showed signs of increased density and were sclerotic. The skeletal survey done thereafter, demonstrated the classical findings of osteopetrosis (Fig. 5, 6 and 7). Supportive treatment consisting of red packed cells and platelets suspension were readministered to the patient but he died a few weeks later.

CASE 3. A 5 months old Indonesian girl was referred from a Primary Health Center in Palembang, on March, 1982 with the history of anemia and hepatosplenomegaly. She was the youngest child of six children. Initial examination in Dr. Cipto Mangunkusumo Hospital, Jakarta revealed an undernourished and pale female infant with the body weight of 5300 g, body length of 60 cm and body temperature of 37° C. The head was normal. Ophthalmologic examination showed no abnormality. Lungs and heart were also normal. Liver and spleen were palpable 3 cm and 6 cm below the right and left costal margin respectively. No signs of bleeding tendency were noted. Peripheral blood examination revealed Hb level of 6 g/dl, R.B.C. count of 2.29 millions /ul, reticulocytes count of 15.000/ul, platelets counts of 126.000/ul and W.B.C. count of 6.400/ul with normal differential count. As in the two cases presented above.

The bone marrow sample of this patient was also difficult to obtain. The specimen showed profound hypoactivity of both erythropoietic and thrombopoietic system. The Granulopoietic system was normal. No evidence of malignancy was noted. On the 3rd. day of admission the patient looked paler and the hemoglobine content fell to 5.4 g/dl. Red packed cells was then administered to the patient. The presence of anemia and hepatosplenomegaly suggested a diagnosis of thalassemia major. However, the fetal hemoglobine determination showed a level of only 10%. While investigating other possible causes for these clinical and hematological picture, a skeletal survey was done disclosing the diagnosis of osteopetrosis involving the skull, vertebral, pelvic and phalageal bones (Fig.8 and 9).
The patient died at the age of 2 years.

CASE 4. A 3½ months old Indonesian girl was taken by her mother to Dr. Cipto Mangunkusumo Hospital with the chief complaint of abdominal distention since the age of one week. The mother noted also that the child looked pale. The baby was the 13th child of 13 siblings; three of her siblings died at the age of 2 months, 4 months and 6 months respectively due to the same condition. Examination revealed a pale baby with a body weight of 4.000 g, body length of 56 cm and body temperature of 36.7° C. The abdomen was distended with significant hepatosplenomegaly. No sign of hemorrhagic diathesis were seen. Initial peripheral blood investigation showed Hb level of 9 g/dl, W.B.C. and platelets number were 9.500/ul and 180.000/ul respectivelv with normal differential count. Bone marrow specimen was difficult to obtain and showed signs of erythropoietic hypoplasia. On the 7th day of hospitalization the patient looked paler. The peripheral blood showed a decrease level of Hb and platelets to 6,4 g/dl and 12.000/ul respectively. Investigations to the possibilities of diseases presenting with anemia and hepatosplenomegaly gave negative results. Based on those findings and the difficulty in obtaining the bone marrow specimen, the radiological examination of the bones was done for the possibility of osteopetrosis which showed sign of increase density of the bones clearly indicating the diagnosis of this disorder (Fig. 10, 11 and 12). Consultation to the Ophthalmologic Department revealed an optic atrophy of both eyes.

Discussion.

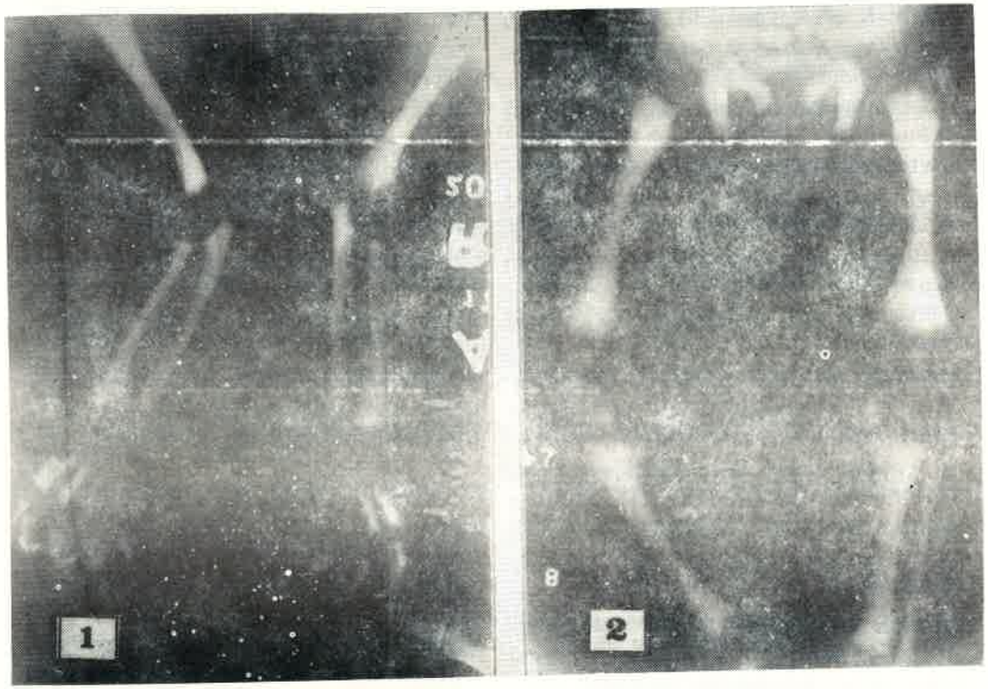
The presence of severe anemia and hepatosplenomegaly in our cases warrant the authors to think about the possibility of the diseases more commonly found in our country such as malaria, Cooley anemia and other hemolytic anemias. The peripheral blood of these cases showed also thrombocytopenia. This finding made the authors also think about malignancy. But the peripheral blood, Hb analysis, bone marrow as well as serological examination didn't support the possibility of those disorders. The diagnosis of osteopetrosis in the first, second and third cases was then established accidently by rontgenographic examination. In the first case the indication of performing this procedure was the suspicion of bowel obstruction while in the second and the third ones were the suspicion of tumor mass and Cooley anemia respectively. The authors then concluded that next to hemoglobinopathia, malaria and malignancy, signs and symptoms of anemia, thrombocytopenia, and hepatosplenomegaly should also lead to the possibility of osteopetrosis especially in infancy. This latter is more obvious when it is accompanied by the difficulty in obtaining the bone marrow specimen as seen in our cases. Due to the experience in the diagnosis of the first three cases mentioned above, the authors were aware that the last case also suffered from osteopetrosis. However since this disorder is rare, the authors suggested to do the radiological investigation for the possibility of osteopetrosis after having done the routine examinations such as bone marrow aspirations, Hb analysis and serological test. The anemia and thrombocytopenia in our cases were of the myelophtisic type as shown by the bone marrow examination. According to Sjölin (1959) and Gamsu et al. (1961) in addition to the decreased red cell production, the anemia and thrombocytopenia might be also due to secondary hypersplenism.

Therefore splenectomy has been performed with apparent benefit in some patients suffering from osteopetrosis associated with life threatening anemia (Sjölin, 1959 and Besselman, 1966). But since the spleen may be a major source of red cell production in this disorder the effect of removal of this source must be balanced against the severity of hemolysis and thrombocytopenia. Radioisotope studies may be of help in evaluating the necessity for removing this organ (Schwartz, 1974). As mentioned above the enlargement of the liver and spleen in osteopetrosis is common with extramedullary hemopoietic proliferation occurring inside them. This condition can cause release of normoblasts and leucocytes into the peripheral blood of patients with osteopetrosis as found in our cases. Ragab et al. (1975) stated that the encroahment on the bone marrow space and the subsequently disturbed marrow microenvironment by osteoid tissue cause the migration of the immature cells of the bone marrow. This would also explain the presence of leucocytosis and several normoblasts in the peripehral blood of these patients. The first and the fourth cases showed signs of optic and retinal atrophy. Alter et al. (1931) found that as a result of the thickening of the bones, the optic foramina distinctly narrowed. They assumed that the atrophy was due to the compression of the optic nerve. Craniotomy with optic nerve decompression has been applied on a few instances with different results (Hill and Charlton, 1965). As a matter of fact beside optic atrophy, hearing loss is also a common feature of osteopetrosis when it involves the temporal bone. Several mechanisms of the pathogenesis of this disorder has been postulated among others expessive bone formation involving the tympanic cavity and ossicles (Hamersma, 1970) and recurrent otitis media (Hawke et al., 1981). Nussey (1938) found that 20% of the cases of osteopetrosis occur in consanguinous marriages as it was found in our second case.

Acknowledgement.

The authors would like to thank Dr. Taslim Sutomenggolo for the clinical and laboratory informations of the first case.

Case I.



Case I :

Fig. 1 – 2 : The extremities show a generalized but uneven amorphous sclerosis, in which the individual component-cortex, epiphyseal plates, spongiosa and medullary cavity are obliterated.

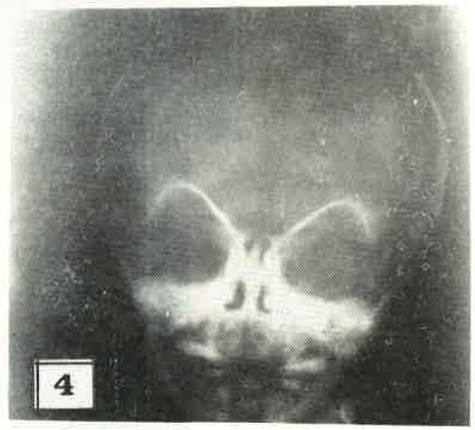
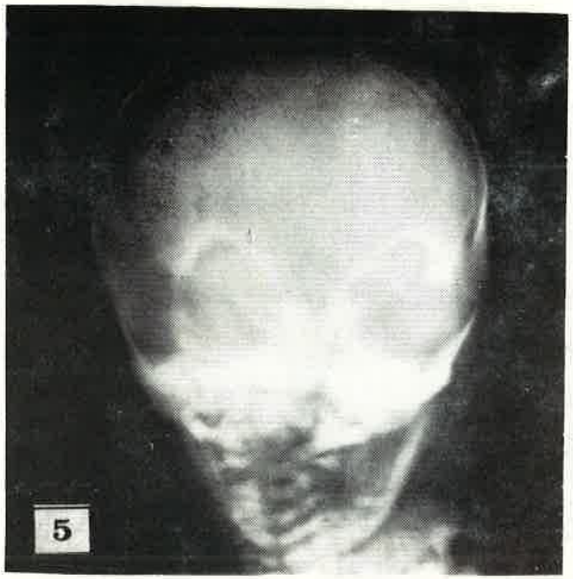
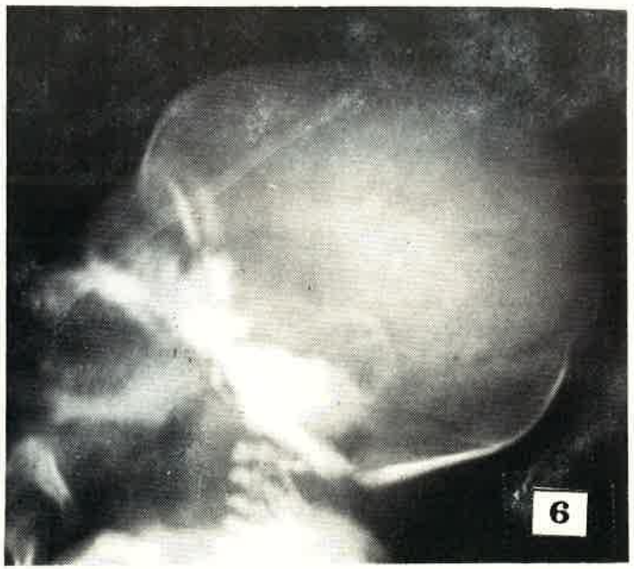


Fig. 3 – 4 : The base of the skull looks extremely dense, which on frontal projection gave the image of "glasses" ("spectacles").





Case II :

Fig. 5 – 6 : The base of the skull shows also the "spectacle" sign on frontal projection.

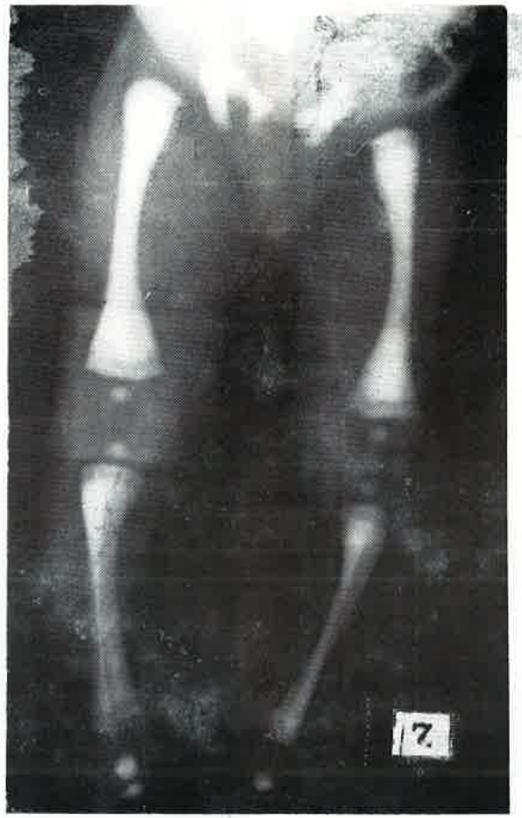
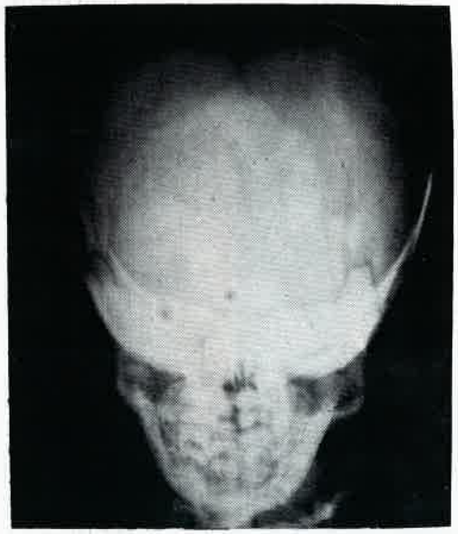
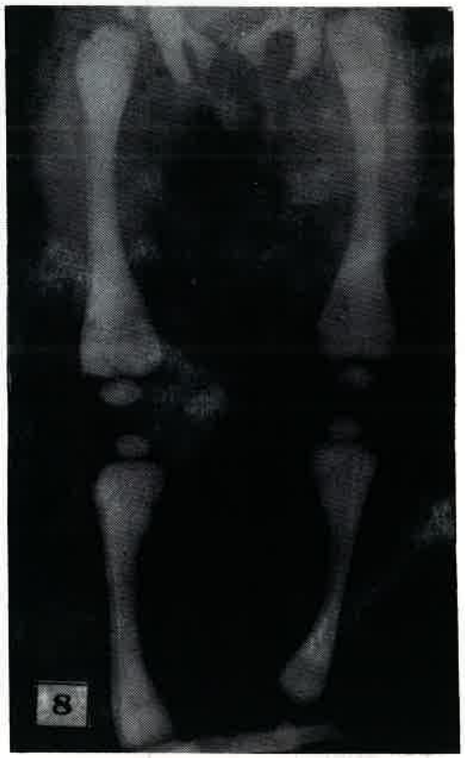


Fig. 7 : The ends of the tubular bones are sclerotic and widened.

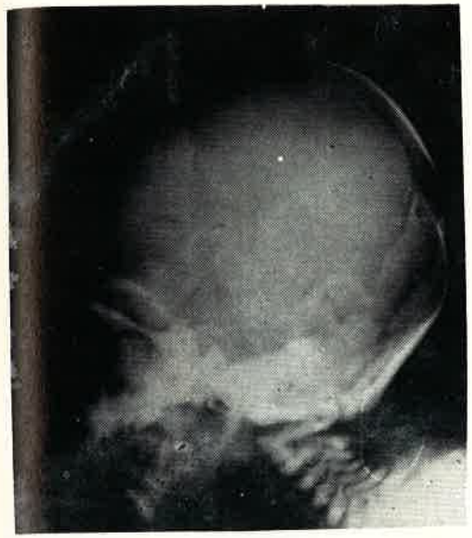




Case III :

Fig. 8 :

Invariably there is failure of construction of the shafts and they appear swollen and splayed at the ends with transverse bands of relatively diminished density.



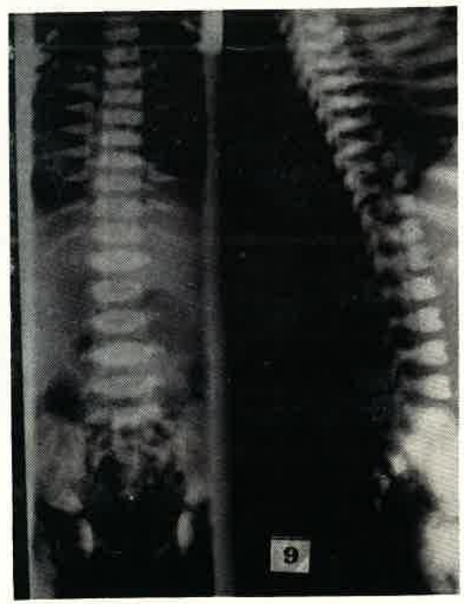
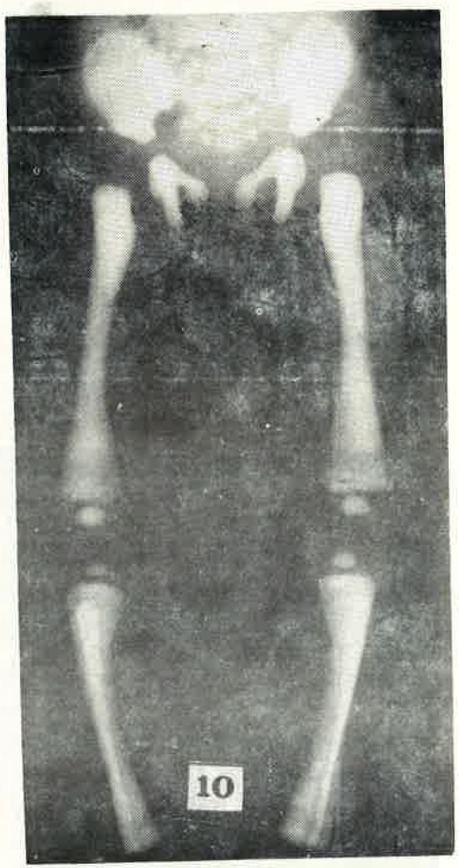
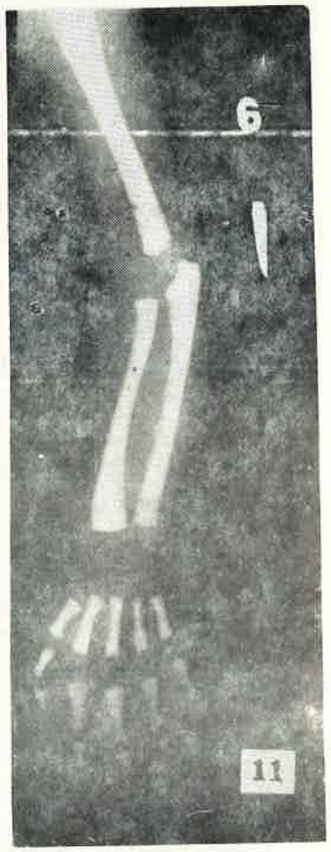


Fig. 9 :

Although the entire spine looks dense, there is a central inset of diminished density, which suggest that the sclerosis began at or near birth.





Case IV :

Fig. 10 – 11 :

Dense extremities with obliteration of the medullary cavities and radiolucent transvere bands at the ends of the shafts.

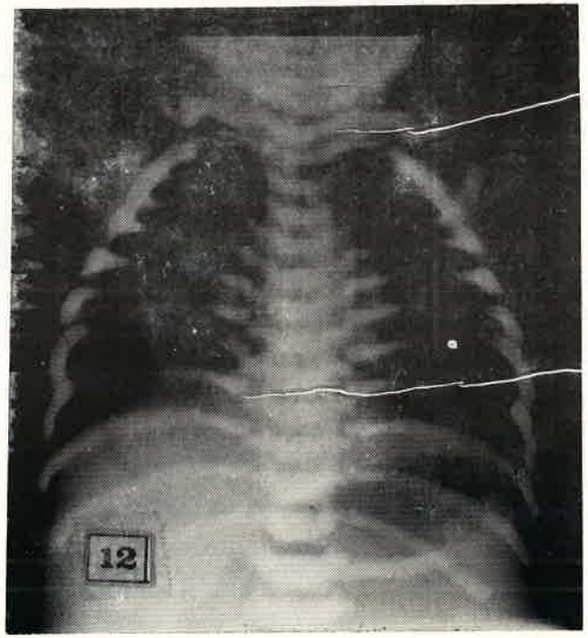


Fig. 12 : Unusual dense throracic cage.

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