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A roentgenologic and genetic study of a rare osseous distrophy

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Some time ago a young medical doctor visited one of us (F. M. S.) inquiring about the mode of inheritance of a disease which affected several members of his family. One believed at first that the disease was osteopetrosis (Albers-Schönberg disease). Further studies of two of the affected persons, however, as well as of a description of the anomaly which afflicted a deceased member of the family (De Souza, 1927), showed that this was not the case. Its clinical picture shows several points of similarity with the Camurati-Engelmann disease and with hyperostosis corticalis generalisata familiaris, described by Buchem, Hadders and Ubbens (1955). Stimulated by the rarity of the condition a detailed study of this family was undertaken. The present paper is a report on the clinical and genetic data obtained.

The D. Family

Fig. 1 shows pertinent genetic information. The person who called our attention to this family is represented in the pedigree as being III-29. With regard to the affected persons the clinical and roentgenologic findings are the following (Roman numerals refer to the generation, while the arabic refer to the situation of the individual in this generation):

III-6 – G. L. M., male, 35 years, white, height 1.74 m., weight 80 Kg. He consulted with Dr. Franklin Verissimo because his fingers and nose seemed to become abnormally thick and the skull deformed due to the prominence of the parietals. The physical examination of the patient indeed accused thickened fingers, especially of the distal phalanges. There was an increase in volume of the mandible and of the temporoparietal bones. The ophtalmologic examination revealed a concentric diminution of the vision fields and incipient papillary atrophy. A hemogram was without pathologic findings. Chemical blood determination values were: non-proteic nitrogen: 510 mg%; glucose 1315 mg%; cholesterol 290 mg%; inorganic phosphorus 4.04 mg%; calcium 10.42 mg%; acid phosphatase 0.6% (Bodansky method); alkaline phosphatase 2.6% (Bodansky).

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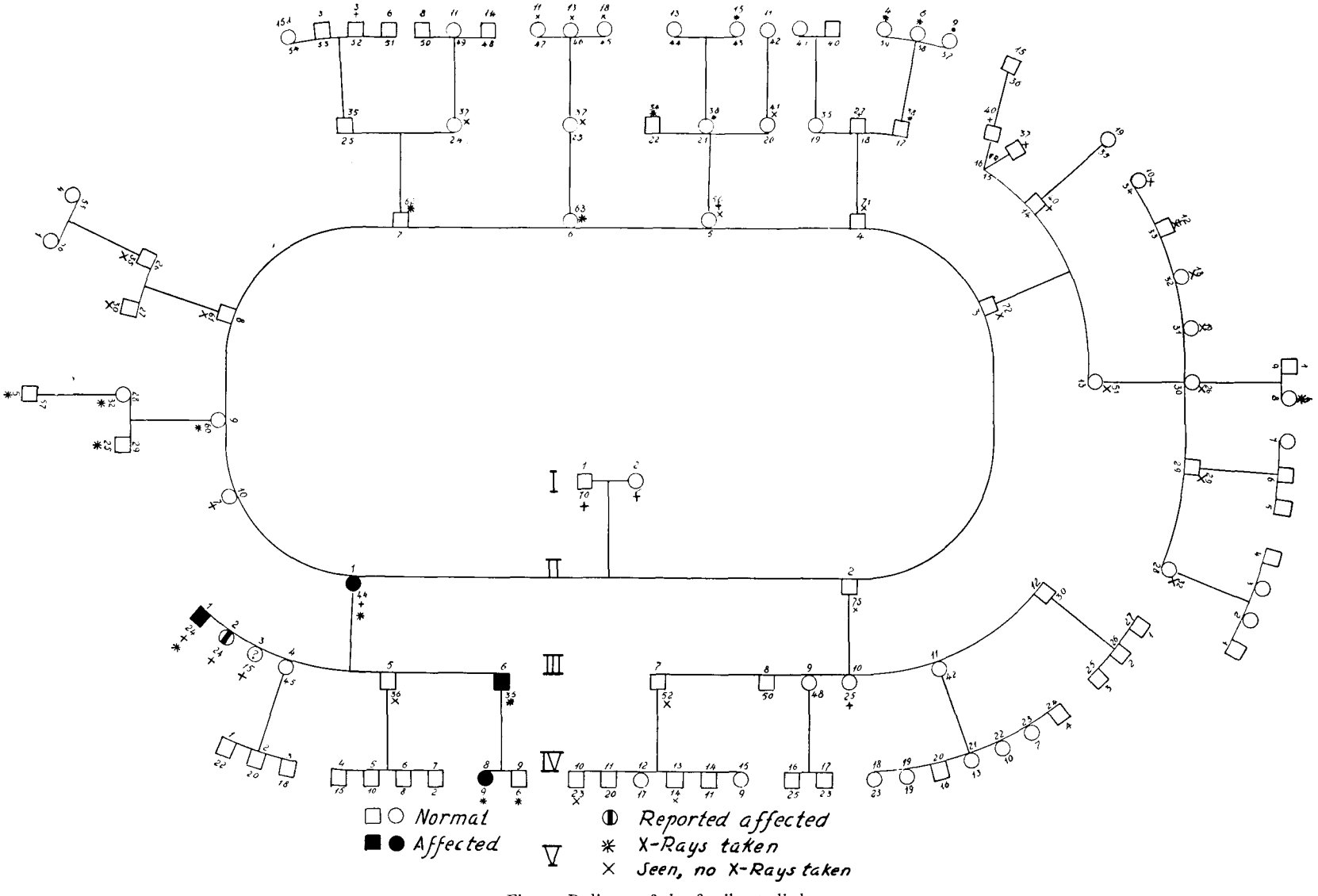

Fig. 1. Pedigree of the family studied.

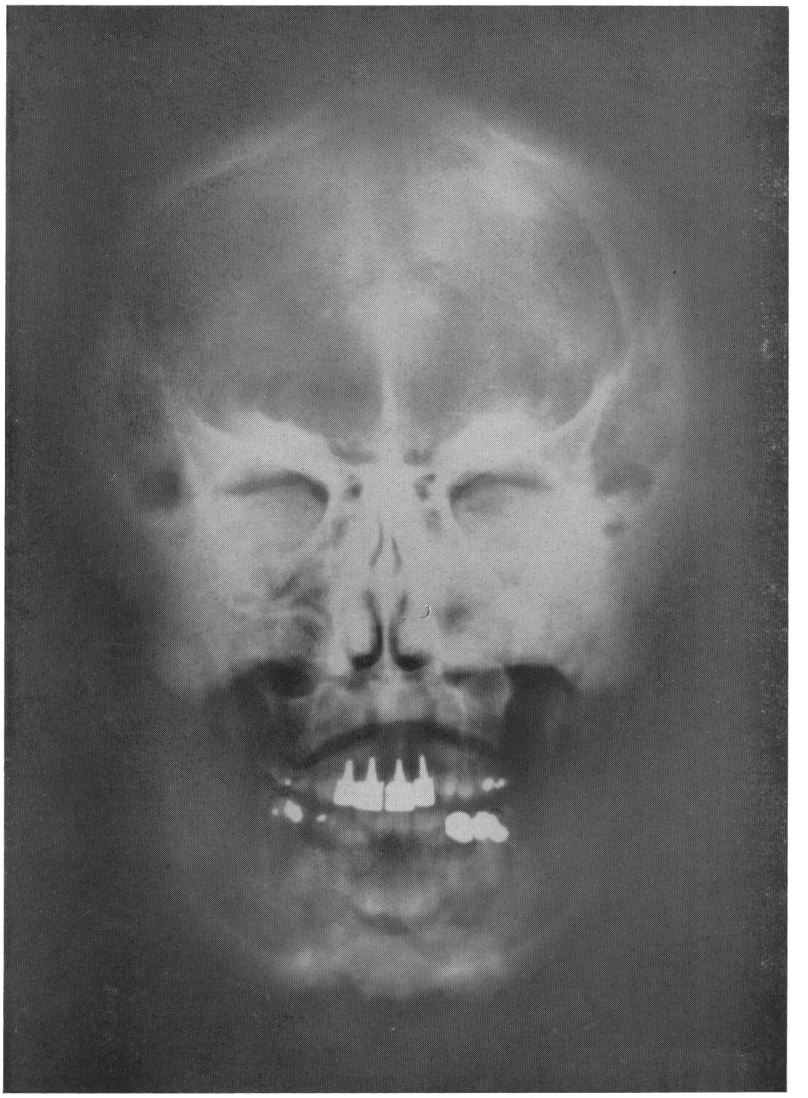

Fig. 2. Frontal radiogram of the skull and face of III-6. Accentuated bone hyperostosis.

Radiologic findings: a) *Skull bones* (Figs. 2 and 3). Intense osteosclerosis of all the skull bones coupled with considerable thickening. There is a very pronounced lateral protuberance in the temporoparietal region of both sides. Osteosclerosis and hyperostosis involve, as mentioned, bones of the cranial base; there is, however, no reduction in the opening of the optic canals; b) *Facial bones* (Figs. 2 and 3). Osteosclerosis involves all the facial bones, particularly the mandible. This bone presents an

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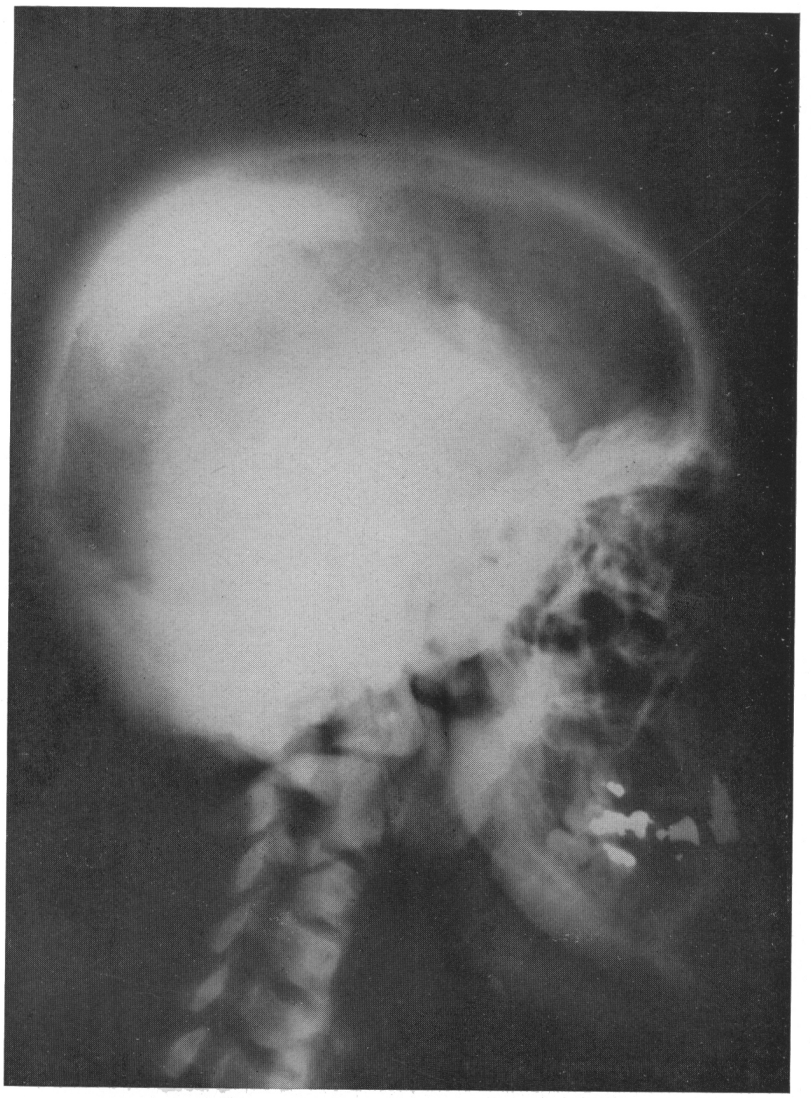

Fig. 3. Lateral radiogram of the skull and face of III-6. The findings are similar to those found in Fig. 2.

increase in proportion due to the accentuated thickening of the compact portion. Intense lateral procidentia occur on both sides at the level of the mandible's angle which, together with the temporoparietal knobs, give a very peculiar aspect to the patient's head; c) *Spinal column* (Figs. 4, 5 and 7). The elements of the cervical, dorsal, lumbar and sacral segments present intense and homogeneous osteosclerosis which attains in a uniform way the structure of the vertebral bodies and archs. The

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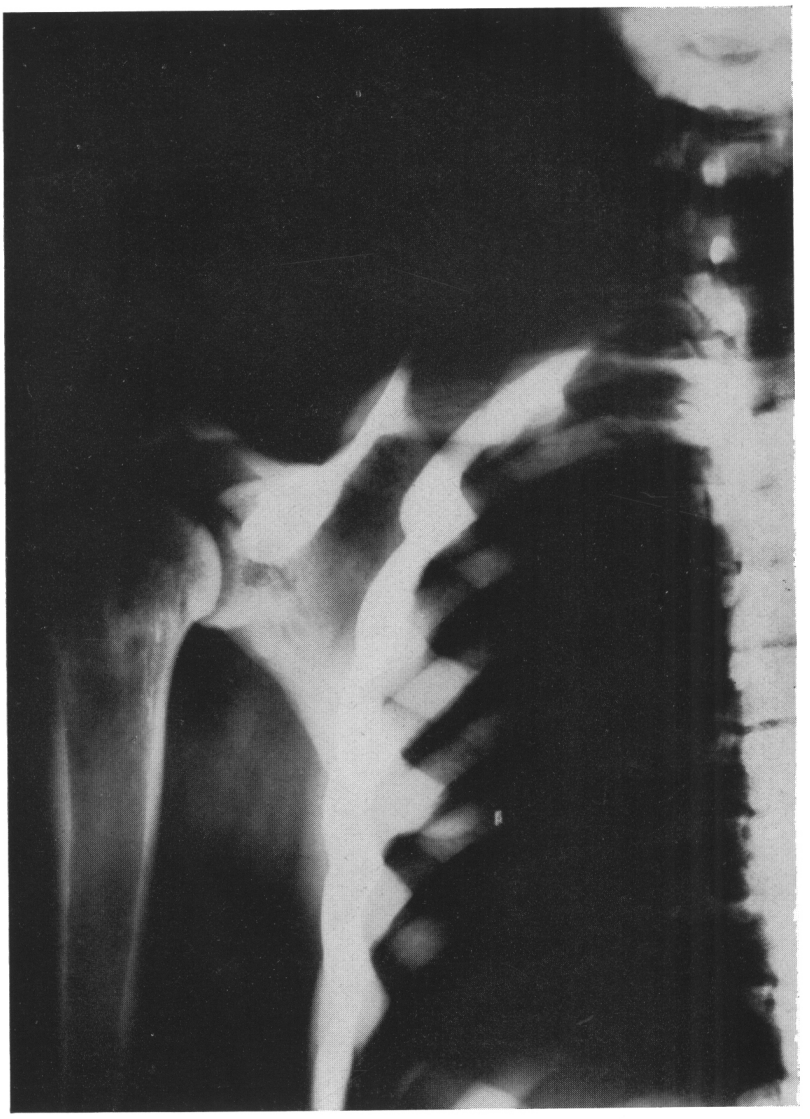

Fig. 4. Frontal radiogram of the right clavicle, scapula, ribs and humerus of III-6. Definite osteosclerosis and hyperostosis of the several structures seen.

coccyx is affected also by osteosclerosis, though to a lesser degree; d) *Ribs* (Figs. 4 and 5). All ribs show intense osteosclerosis coupled with a slight increase in the proportions of these structures; e) *Clavicles* (Figs. 4 and 5). Osteosclerosis involves the compact bone as well as the spongiosa, which has a coarse structure. Both clavicles, although not generally deformed have, however, proportions clearly larger than normal; f) *Scapulae* (Figs. 4 and 5). The scapulae present obvious osteosclerosis which

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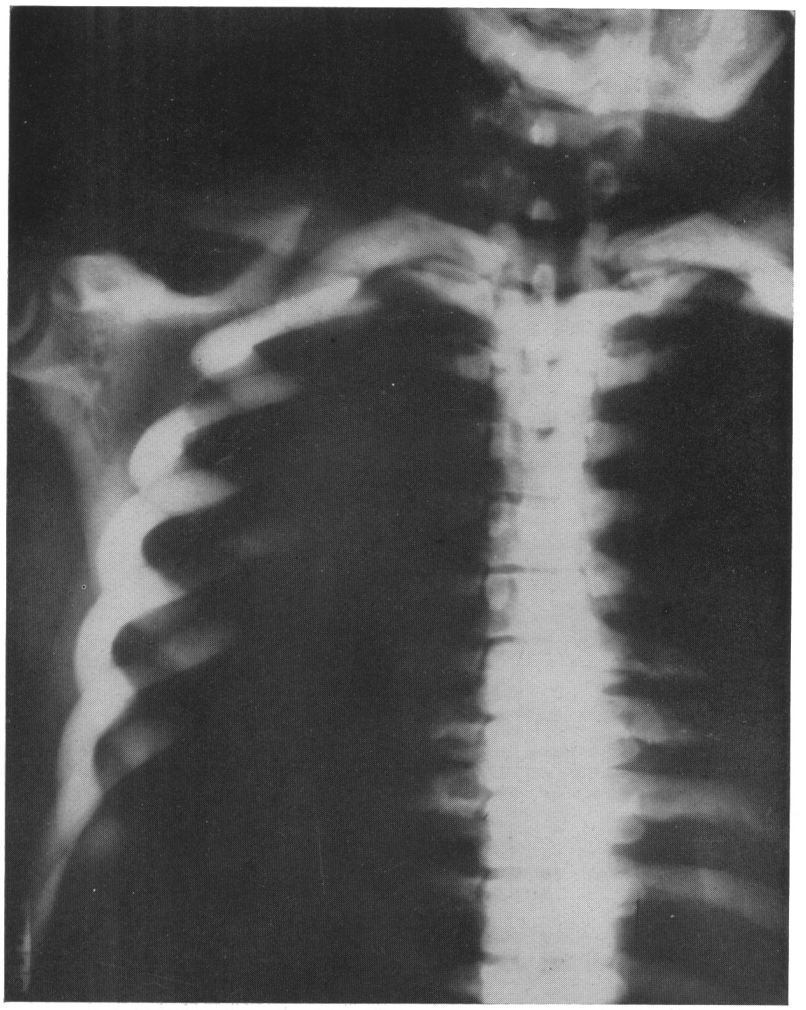

Fig. 5. Frontal radiogram of the cervicodorsal spinal column and right clavicle, scapula and ribs of III-6. Intense osteosclerosis of the vertebrae and ribs, hyperostosis of the clavicle.

involves both trabecular and compact portions. Of the long bones of the upper limbs (Figs. 4 and 6) the diaphyses are particularly affected. In them the thickness and density of the compact bone is clearly increased by periosteal apposition. The external profile of the compact region is wavy and slightly irregular. The medular space is modified not only by the apposition of the enostosis bone, but by the presence of large areas of compact bone. Metaphyses and epiphyses are involved to a lesser degree; the dense and coarse aspect of the spongiosa in these regions is nevertheless obvious, as well as the increased density and thickness of the articular cortices. The carpal bones (Fig. 6) present dense and coarse trabeculae and thickened and more

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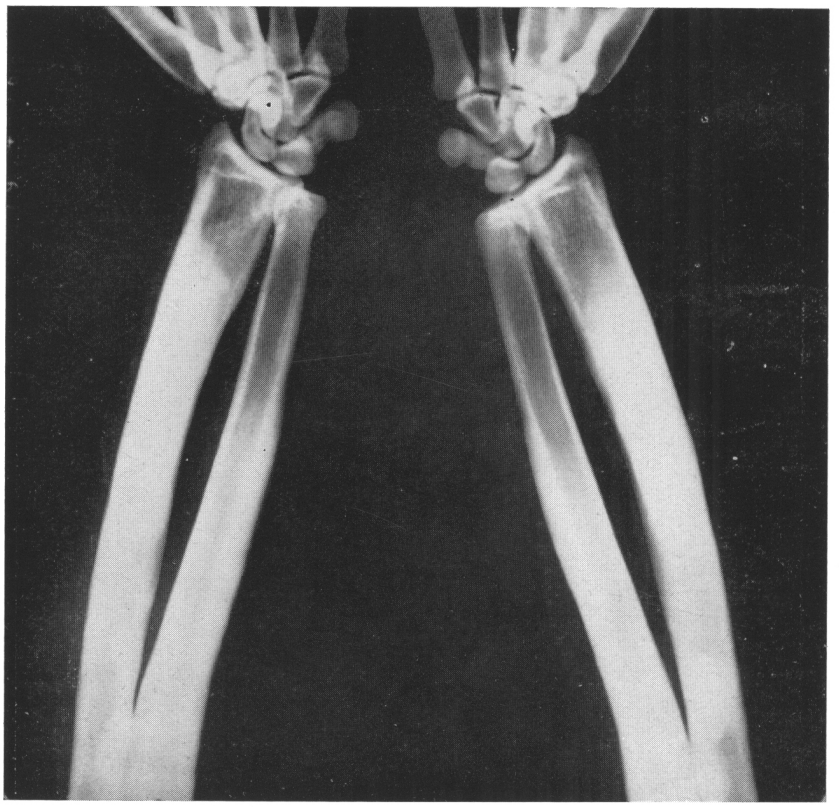
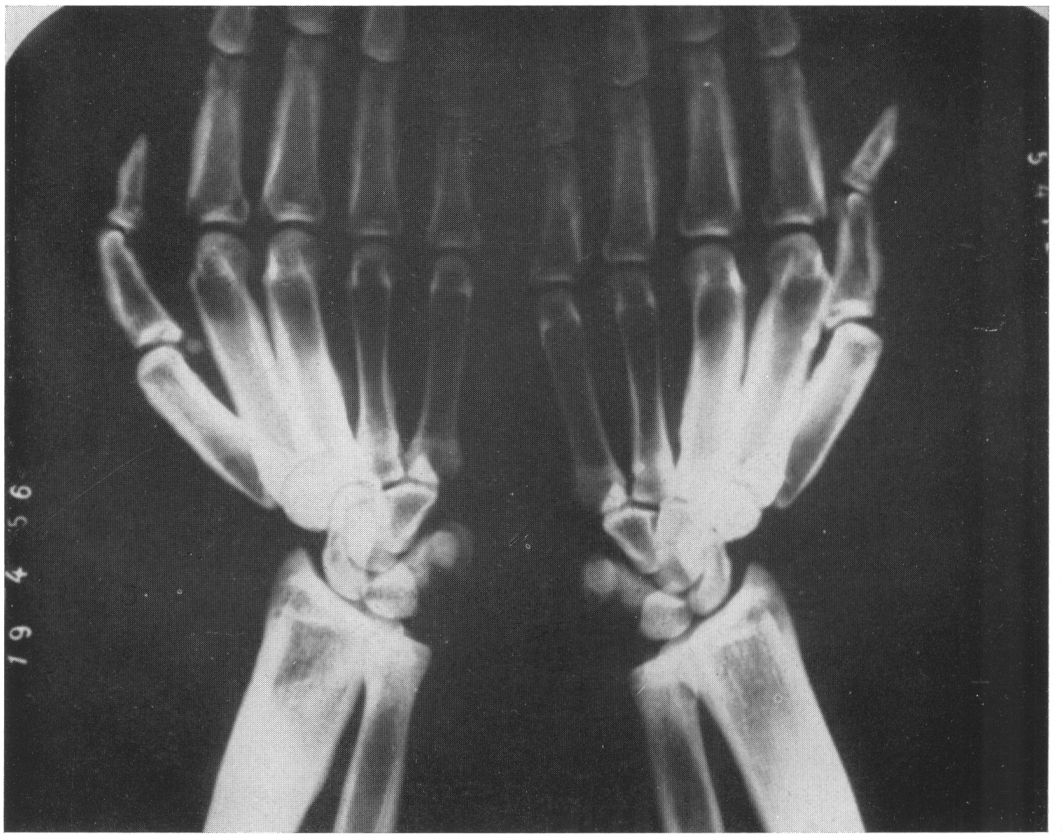


Fig. 6. Frontal radiogram of both forearms, wrists and hands of III-6. Notice the dominant involvement of the diaphyses of the long bones, as well as the absence of definite spindle-like deformation.



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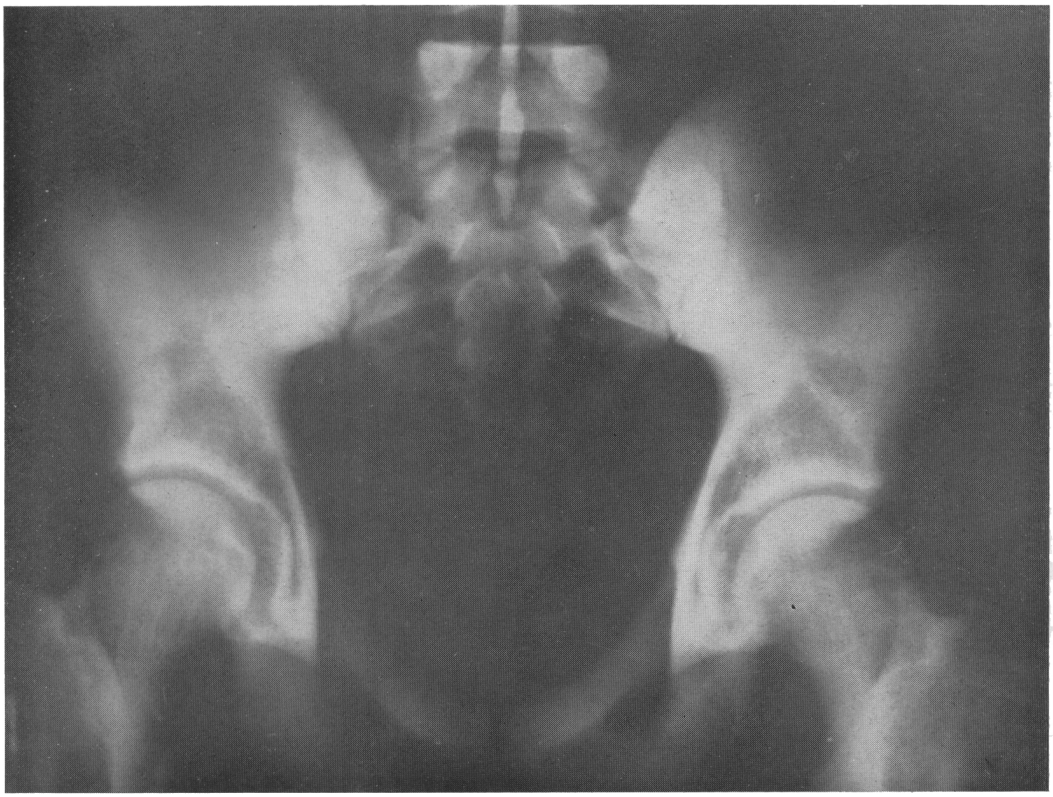
dense cortices. Metacarpals and phalanges present changes similar to those of the other long bones of the upper limbs. Some phalanges present a slight spindlelike aspect. The iliac bones (Fig. 7) present intense osteosclerosis of all portions. In the iliac wings a less dense central portion is noticeable among the high density of medial and lateral parts. The proximal extremities of the femora (Fig. 7) present modifications similar to those described for the long bones of the upper limbs.

IV-8 – L. L. M., female, 9 years, white. No detailed clinical examination is available but the two radiograms taken indicate that she suffers from a disease similar to the one which affected her father. There is definite osteosclerosis of facial and skull bones, including the mandible. The skull shows (Fig. 8) a more intense sclerosis in the base structures and parietals. Vertebrae, ribs, clavicles and scapulae (Fig. 9) are clearly and homogeneously osteosclerotic. Both humeri (Fig. 9) present sclerosis in the diaphysis which have a tubular aspect. The alterations are similar

Fig. 7. Frontal radiogram of the pelvic girdle bones of III-6. Notice in the iliac wings the less dense central portion which is enhanced by the osteosclerosis of the medial and lateral portions.



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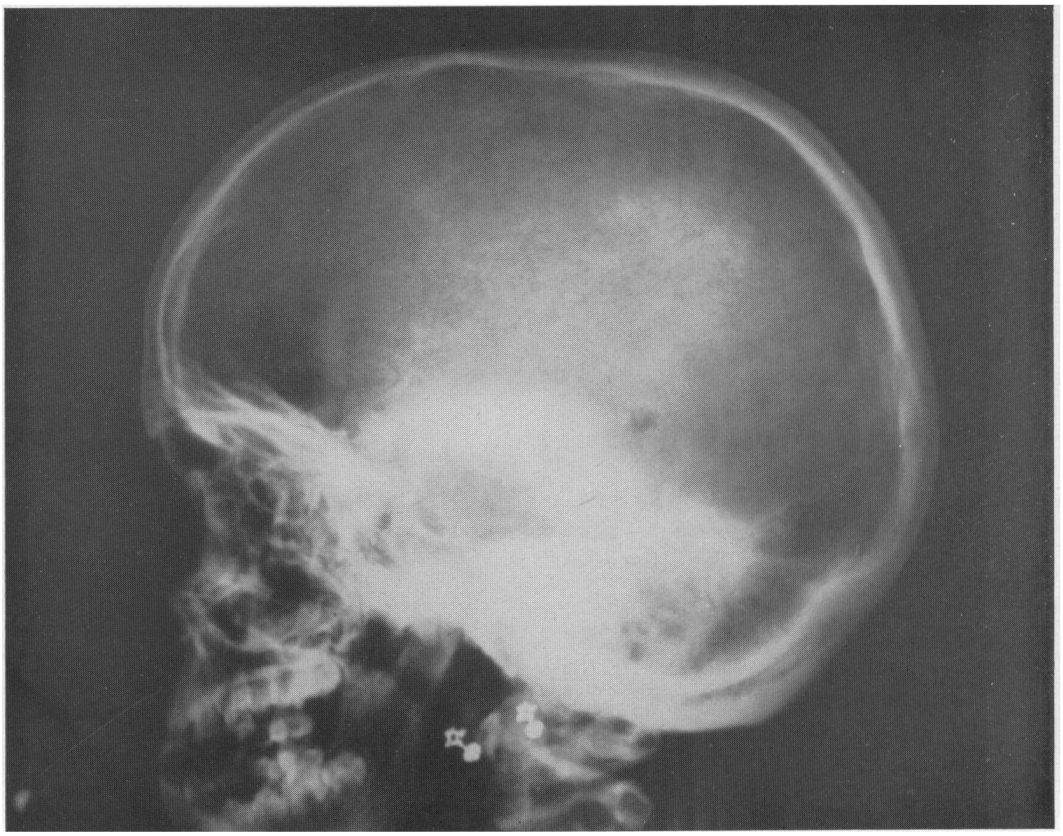
for the cranial halves of the radii and ulnae (Fig. 9). The epiphyses of these bones present slightly coarse and dense trabeculae; changes at the diaphyses level, however, are undoubtedly more important.

III-1 – A. M., male, white, deceased at the age of 24. A detailed clinical and roentgenological description of his disease is available through a publication of de Souza (1927), who examined him at the age of 18. Several photographs illustrate the gradual skull changes, especially of the mandible, which was enormous at the date of the examination. Bone alterations are similar to the ones described in the present paper. The changes at the mandible level are, however, coarser, and one of the long bones (humerus) presents less intense osteosclerosis in the diaphyses.

II-1 – L. A. M., female, white; she comitted suicide at the age of 44. No clinical examination is available, but one of her fibulae was obtained by one of her nephews

Fig. 8. Lateral radiogram of the skull and face of IV-8.
Accentuated osteosclerosis of the skull base bones and parietals.



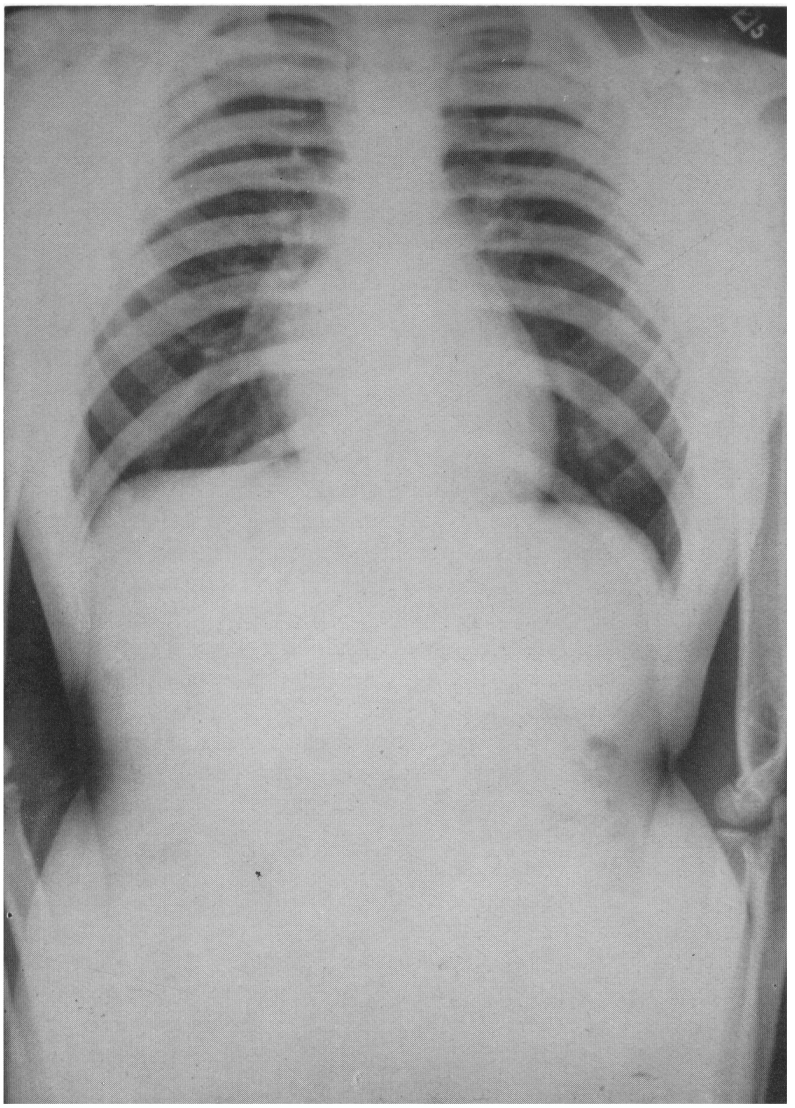


Fig. 9. Frontal radiogram of the thorax, scapular girdle and long bones of part of the upper limbs of IV-8. Diffuse osteosclerosis of the bones seen and absence of the spindle-like deformation of the long bone diaphyses.

for study. Radiologic alterations of this fibula are the same as those which affected III-6, despite more intense changes in the median portion of the diaphyses.

III-2 – B. M., female, white, deceased at the age of 24 completely blind. Several informants mention that she also suffered from the disease and was completely deformed when she died. De Souza (1927) saw a fotograph of this person and noted an increase in volume of the upper maxillae.

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Some members of the family mention that perhaps III-3 was also affected which could, however, not be confirmed. As shown in the pedigree chart it was possible to gather information from radiograms taken from 15 persons of the family. In all 15 members no sign of the disease could be found. In addition medical information was obtained in relation to 26 other persons from whom no radiograms could be examined. Almost all of these medical examinations were performed by the family's physician Dr. Romeu Muccillo to whom we owe thanks for making these examinations available. As the persons affected present great physical deformations they would be recognized even without radiograms. There exists therefore medical confirmation of the fact that at least 41 of the 107 persons who constitute the family do not present the disease.

Discussion

In a differential diagnosis of the entity which affects these patients several diseases could be considered, for instance, osteosclerosis congenitalis diffusa or Albers-Schönberg disease, osteomielosclerosis, hyperostosis generalisata with pachydermia (Uehlinger, 1941), Camurati-Engelmann disease (Neuhauser et al., 1948; Ribbing, 1949) and hyperostosis corticalis generalisata familiaris (Buchem et al., 1955).

The aspect and distribution of the alterations here described place this affection in an intermediary position between the Camurati-Engelmann disease and hyperostosis corticalis generalisata familiaris. This conclusion is justified by the existence of symmetrical osteosclerosis, more accentuated at the level of the diaphyses of the long bones and phalanges, changes similar to those present in the Camurati-Engelmann disease; and extensive and intense involvement of the vertebrae, skull and facial bones; a less precise separation between changes of the epiphyses and diaphyses of the long bones, and absence of the spindle-like deformation of the diaphyses of the long bones, all these characteristics being similar to those present in hyperostosis corticalis generalisata familiaris.

In relation to the pattern of inheritance in this family, it is clearly of the autosomic dominant type. Both males and females are affected, afflicted persons always presenting one affected parent. It is interesting to note, however, that the disease was restricted to one familial line only. Although II-1 has had five brothers and four sisters (all examined with the exception of the deceased sister), only she was affected. Therefore, despite of the fact that no medical information is available for I-1 and I-2, it is highly probable that the disease which affected II-1 was due to a mutation which occurred in the sex cells of her parents.

The only report available about the inheritance of hyperostosis corticalis generalisata familiaris concerns the cases studied by Buchem et al. (1955) of two affected fraternal twins of different sex, with normal genetically unrelated parents. Camurati-Engelmann disease is stated by Schinz et al. (1951) to be inherited through a dominant gene. In Ribbing's (1949) cases there were six siblings, four of which affected.

While the mother was normal the father presented pain in the legs which could perhaps be attributed to the disease. These cases would therefore also be compatible with dominant inheritance. Summing up the pattern of inheritance in the condition here reported is similar to that found in the Camurati-Elgemann disease and could be different of the one reported for hyperostosis corticalis generalisata familiaris. More genetic studies, however, are needed for this last condition in order to clarify its mode of inheritance.

Summary

Description is made of a family of which in three generations five members presented a rare osseous distrophy. Medical information was obtained for about 46 individuals of the 107 who constitute the family. The affection shows resemblances with both the Camurati-Engelmann disease and hyperostosis corticalis generalisata familiaris. It is inherited through a dominant gene.

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RIASSUNTO

Descrizione di una famiglia nella quale cinque componenti, in tre generazioni, presentavano una rara distrofia ossea.

Si ottennero informazioni mediche a proposito di 46 individui dei 107 membri della famiglia. La malattia mostra alcune rassomiglianze tanto con il morbo di Camurati-Engelmann quanto con la hyperostosis corticalis generalisata familiaris. Viene trasmessa mediante un gene dominante.

RÉSUMÉ

Description d'une famille dans laquelle cinq membres sur trois générations présentaient une rare dystrophie osseuse. L'on a obtenu des informations médicales sur 46 des 107 individus qui constituent la famille. L'affection présente des ressemblances avec la maladie de Camurati-Engelmann et avec l'hyperostosis corticalis generalisata familiaris. Elle est transmise par un gène dominant.

ZUSAMMENFASSUNG

Beschreibung einer Familie in welcher fünf Mitglieder in drei Generationen eine seltene Osteodystrophie hatten. Wir erhielten ärztliche Informationen über 46 der 107 Angehörigen dieser Familie. Das Leiden hat Ähnlichkeiten mit der Krankheit von Camurati-Engelmann wie auch mit der Hyperostosis Corticalis Generalisata Familiaris. Sie wird durch ein dominantes Gen vererbt.