PYCNODYSTOSIS

BY

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It was in 1904 that Albers-Schönberg (1904), a radiologist from Hamburg, Germany, described the first condensing bone disorder unassociated with an underlying disease. For a number of years his name was given to the condition characterized essentially by increased thickness and density of the cortical and spongy portions of the entire osseous system. Osteopetrosis seems to be the current term in favour to describe this syndrome (McCune and Bradley, 1934; Kneal and Sante, 1951). It is under this label that some disorders have been included that seem to be a different disease, or at least a distinct variant.

Pycnodysostosis (pyknos, Gk. = dense) is a term coined by Maroteaux and Lamy (1962a, b) to describe one such variant. This is definitely a condensing bone disorder such as that described by Albers-Schönberg and others, but in addition one finds specific skeletal anomalies and a distinct clinical picture.

The two cases reported below are further examples of the syndrome of pycnodysostosis.

Case Reports

I.D., male, age 7½ years. This is the only child of healthy, unrelated, English parents. His birth weight was 3 kg. and he thrived well; developmental milestones were achieved in normal fashion. Medical opinion was obtained at the age of 2 years because of a widely patent anterior fontanelle. Since then he has been followed because of short stature, peculiar appearance of the hands and feet and excessive fractures (three). School progress has been satisfactory despite a hearing deficit.

Both the father and paternal uncle are congenitally deaf.

Examination showed a short, stocky lad, height 107.5 cm., weight 19 kg., with peculiar facial characteristics (Fig. 1). Slight frontal and occipital prominence of the skull is apparent, the chin is receding, the fontanelles are widely patent as are the sutures. Mandible and maxilla are hypoplastic and there is partial anodontia with abnormal implantation of teeth (Fig. 2).

The fingers and toes are short, wrinkled and blunt on the distal end where the nails tend to override (Fig. 3). Bilateral hearing loss is present.

The following investigations were completed and found normal: haemoglobin (11.8 g./100 ml.), white blood cell and differential count, reticulocyte count (1%), platelet count, blood smear, prothrombin time, thromboplastin screening test, electrolytes and blood urea, 24-hour urine for reducing substances and amino acids, urine mucopolysaccharides and routine urine concentration and dilution test, liver function tests (bilirubin, transaminases, serum proteins and electrophoretic pattern), cholesterol and protein-bound iodine. In addition

Fig. 1.—I.D., age 7½ years.

FIG. 2.—Partial anodontia with abnormal implantation of teeth.

FIG. 3.—Fingers are short, wrinkled and the nails tend to 'fold over' the end of the fingers.

FIGS. 4a and 4b.—Long bones to show increased density.

FIG. 5.

FIG. 6.

FIGS. 5 and 6.—Absence of fusion of sutures and fontanelles with remaining 'lakes of bone' and dense base of skull. Mandible and maxilla both hypoplastic, note virtual disappearance of angle of mandible.

FIG. 7.—Hypoplasia of distal phalanges and increased density.

serum iron and total iron-binding capacity and clearance of radioactive Fe^{59} were normal. Red blood cell

utilization of radioactive iron was normal. Surface counting carried out during the study revealed a normal pattern. A five-day calcium, phosphorus, nitrogen and fat balance study was normal. Serum calcium, phosphorus, acid and alkaline phosphatase levels were repeatedly normal. Chromosome culture of the peripheral blood showed a normal male karyotype. Audiogram confirmed a bilateral high frequency loss. Psychometric evaluation placed intelligence in the average or normal range for his age.

Radiographs show a generalized increase in density (Figs. 4a and 4b) with enlargement of the cortex of the long bones and associated anomalies. In the skull (Figs. 5 and 6) the absence of fusion of sutures and fontanelles with remaining 'lakes of bone' and dense base of skull is obvious. The mandible and maxilla are hypoplastic, and there is virtual disappearance of the angle of the mandible. Distal phalanges are hypoplastic (Fig. 7). The acromial end of the clavicle (Fig. 8) is also hypoplastic. The spine is dense and the pelvis is normal.

A *bone biopsy* of the anterior surface of the left tibial shaft was taken, and the bone was extremely hard and

FIG. 8.—Hypoplasia of acromial end of clavicle.

FIG. 9.—Photomicrograph ($\times 73$), showing small Haversian canals and dense lamellar bone.

FIG. 10.—J.D., age 43 years.

FIG. 11.—Fingers are short and wrinkled.

FIGS. 12 and 13.—Absence of fusion of sutures and fontanelles and a dense base of skull. Mandible and maxilla are hypoplastic and the angle of mandible is virtually absent.

difficult to remove. A piece of cortical bone 1.3 cm. $\times$ 0.7 cm. was submitted for histological examination. On microscopy the sections showed abnormally dense cortical bone with very small Haversian canals (Fig. 9). No cancellous bone was included.

J.D., male, age 43 years. This is the maternal uncle of the child just described. He was the shortest member of all his family. It was for this reason that he was asked to come in for investigations. The other siblings were all of average or above average height, including the mother of the first case. She had previously been x-rayed and found to have normal bones.

Mr. J.D. is a skilled labourer of somewhat above average intelligence. He has been an extremely healthy person: the only medical care that he has ever required

was for a fractured left clavicle following a severe blow. He has no hearing difficulty.

Examination revealed a short stocky man, height 155 cm., with a facial expression resembling I.D. (Fig. 10.) Slight frontal prominence of the skull is apparent and the maxilla is hypoplastic. Fontanelles and sutures are clinically open. Dentition is normal. The fingers are short and the nails on the index fingers tend to override (Fig. 11).

The only investigation completed was a blood count: haemoglobin 14.1 g./100 ml., reticulocytes 0.9%, platelets 170,000, blood film normal, white blood cells 7,200, differential normal.

Radiographs showed changes that are not as obvious as those in the first case but are definitely present. Bones show increased density. There is absence of fusion of sutures and fontanelles (Figs. 12 and 13) and a dense

FIG. 14.

FIG. 15.

FIG. 14.—Hypoplasia affects the index fingers predominantly, i.e. distal phalanx.

FIG. 15.—Acromial end of the clavicle is hypoplastic, note old fracture of left clavicle.

base of the skull. Mandible and maxilla are hypoplastic and the angle of the mandible is virtually absent. Hypoplasia of the distal phalanges (Fig. 14) is noted mainly in the index fingers. The acromial end of the clavicle is hypoplastic (Fig. 15). The pelvis is normal and the spine is dense.

Discussion

The predominant features of these cases are: (1) a generalized osteodystrophy with clinical findings limited mainly to the head and hands plus stunting and a tendency to fracture, (2) radiologically specific changes that seem, as a group, to differ from most well-recognized bone disorders, and (3) a genetic predisposition.

Maroteaux and Lamy (1962a, b) have reviewed the literature and separated out cases that fulfilled their criteria. They documented 26 cases in their report. Certainly those cases reported by Abboud, Abidin and Alfay (1954) as well as the ones reported by Palmer (1960) and Palmer and Thomas (1958) seem to show the pycnodysostosis syndrome.

Dental abnormalities as seen in the first case (I.D.) have been reported. Stunting is usually of a greater degree than in the second case, the adults in most cases reaching heights of only 1.35-1.5 metres. Though there is a tendency to fracture easily it is not so severe as in osteogenesis imperfecta, and this is not a great problem as healing is apparently normal.

In 10 of the families reported by Maroteaux and Lamy (1962a, b), a brother and/or sister were similarly affected. This type of family pattern

suggests that those affected are homozygous for an autosomal recessive gene. In this family, however, a mother's brother is similarly affected, strongly suggesting that the gene responsible is sex-linked.

The second patient in this report, now 43 years old, is haematologically normal and has no cranial nerve problems. Thus far there have not been any reports of bone marrow hypoplasia or cranial nerve compression in cases of pycnodysostosis. Deafness was noted in the first case (I.D.), which could be related to his bony abnormality, but in view of the strong family history of deafness on the paternal side of the family (grandfather, uncle and father) this could be unrelated.

Microscopy in the first case showed abnormally dense cortical bone with very small Haversian canals. From this specimen it is impossible to state whether this is a different disease from osteopetrosis, the same or a variant. Certainly the sections are compatible with the diagnosis of osteopetrosis.

Differential diagnosis is limited primarily to osteopetrosis. The differentiating features are mainly the skeletal anomalies in the skull, mandible and distal phalanges. In addition the bones tend to be more dense in osteopetrosis, and the presence of alternating bands of greater and lesser density arranged parallel to the epiphyseal line is a characteristic radiological finding. Modelling of the metaphyses is not seen in pycnodysostosis. There is also the tendency to develop progressive hypoplastic anaemia from obliteration of the marrow spaces with secondary extramedullary haematopoiesis and hepatosplenomegaly in osteopetrosis. As previously

mentioned, cranial nerve compression is not an uncommon finding in osteopetrosis.

Cleidocranial dysostosis, Engelman's disease, idiopathic hypercalcaemia and vitamin D intoxication should be mentioned in passing, but should cause little problem in differential diagnosis.

Summary

Two cases of a generalized osteodystrophy with associated anomalies in the skull and digits are described. It appears that this condition is a variant of osteopetrosis. Clinically the condition presents as stunting, a tendency to fracture easily or failure of the fontanelles or sutures to close. In addition the fingers are short and wrinkled because of the hypoplasia of the terminal phalanx. There is a genetic predisposition. The prognosis seems to be excellent from the knowledge available at the present time.

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