METAPHYSIAL DYSOSTOSIS

Report of a Case

J. A. P. CAMERON and W. B. YOUNG, SINGAPORE, MALAYA, and H. A. SISSONS, LONDON, ENGLAND

From the Departments of Orthopaedic Surgery and Radiology, University of Malaya, and the Institute of Orthopaedics, University of London, Royal National Orthopaedic Hospital

In 1934 Murk Jansen described an unusual case of skeletal growth disturbance under the title of "Metaphysial Dysostosis." No other example of the condition appears to be on record, although Fairbank (1951), in describing the features of Jansen's case, briefly referred to two others which had been brought to his notice by Dr Norah Walker and Mr G. M. Müller. These, though not strictly comparable with Jansen's case, showed widespread metaphysial lesions of a somewhat similar type. In an account of the second of these cases published later by Müller and Sissons (1951) it is stated that the radiographic changes present, although showing some similarity to those in Jansen's case, were consistent with a diagnosis of renal rickets, and that the histological findings in the abnormal bones were those of renal osteodystrophy with the high degree of secondary hyperparathyroidism that Gilmour (1947) described as characteristic of these cases.

The present case is published as an example of metaphysial dysostosis in which no evidence of a relationship to renal disease can be found on careful study, including clinical, radiological, biochemical and biopsy investigation. The case appears to be the only classical example of metaphysial dysostosis that has been described since Jansen's report in 1934, and is placed on record for this reason.

CASE REPORT

A Chinese boy aged seven years was seen on account of deformity of both lower limbs. The deformity had been noticed first after he began to walk at about the age of twenty months. Soon afterwards deformities of the chest and of the upper limbs were observed. The early history was that pregnancy was uneventful and went to full term. The infant raised his head at four months, sat up at six months, and walked at twenty months. He was breast-fed for seventeen days and then weaned because of fever and convulsions which lasted a week: artificial feeds were given for three years. Other illnesses recorded in his early life were pneumonia at six weeks and vesicles on both feet and palms without pyrexia at seven months. Family history—The mother and father were alive and apparently normal. There were two older brothers and a sister, all normal. There was no history of deformity in other members of the family.

Condition on examination—The child weighed 32\(\frac{1}{2}\) pounds and measured 33\(\frac{3}{4}\) inches in height. His general appearance is shown in Figures 1 and 2. The circumference of the skull was 20\(\frac{1}{2}\) inches. The head appeared to be slightly enlarged in its transverse diameter in the temporo-parietal region. The face was normal with slightly protuberant eyes. There was a tendency to nasal catarrh. Hearing was normal. There were no signs of thyroid enlargement. The ribs showed a "rosary" at the costo-chondral junctions. The fingers were "clubbed"; although the proximal ends of the phalanges were enlarged, the range of joint movements was full. The lower limbs showed marked genu valgum with anterior bowing of the femora, rotation of the tibiae, and angulation at the lower ends of the tibiae. The ends of all long bones were enlarged and deformed. Normal findings were obtained on examination of other systems.
Radiographic appearances—There was a marked disturbance of the normal processes of bone growth and development, and this was most pronounced in areas where growth is normally most active. The disorder appeared to be restricted to the metaphysial side of the growth cartilage and in the long bones extended into the adjacent terminal spongiosa. In the flat bones of the pelvis and shoulder girdle the bone in the neighbourhood of the acetabulum, sacro-iliac joints, crest of the ilium, and glenoid was most affected. In some bones the
Fig. 6
Skull.

Fig. 7
Thorax.
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**Fig. 8**
Pelvis and upper ends of femora.

**Fig. 9**
Figure 9—Left forearm and hand. The right side was similarly involved.

**Fig. 10**
Figure 10—Right tibia and fibula. The left side was similarly involved.

**Fig. 11**
Figure 11—Left foot. The right side was similarly involved.
metaphysis ended in a crenated line of increased density. The epiphysial bone centres that were visible had not been affected, nor had the bony centres of the bones of the tarsus and carpus that were present. The greater part of the spinal column was normal in appearance, and so was the vault of the skull.

The ends of all the long bones were expanded to a greater or lesser degree as if the process of remodelling had failed (Figs. 8, 9, and 10). In some bones this expansion was very pronounced and the bone had the shape of a club. The expanded ends were cupped, the amount varying in different bones, but in some cases being sufficient to enclose the greater part of the corresponding epiphysial bone centre. The walls of the cup were formed of sclerotic thickened bone and in some bones appeared to be fragmented or possibly fractured. The bottom of the cup was formed by a zone of fairly dense irregular interlacing trabeculae, which seemed to be compressed so that an area of increased density demarcated the abnormal bone from bone of apparently normal structure in the diaphysis. The cupped expanded ends of the bones appeared to contain a material of soft-tissue density in which there were scattered irregular areas of density which in some bones resembled isolated fragments of dense bone; in others amorphous calcification; and in others punctate calcification. In the lower end of the radius and ulna there was a mosaic pattern of soft-tissue densities separated either by irregular transradiant lines or lines of increased density (Fig. 9). The femora were bowed anteriorly to a marked degree. The tibiae and fibulae also appeared to be bowed, but the deformities were caused not so much by bowing of the shafts as by angulation at the junction of the disordered hyperplastic metaphysis and the shaft. At sites where angulation had occurred there was increased bone density most marked on the concave side. The shafts of the long bones were thicker than normal; but their cortices were not particularly thickened, except at sites of bowing where there was definite buttressing, as in the tibiae where cortical buttressing extended all along the posterior and medial parts of the shafts (Fig. 10).

The distal bones of the limbs appeared to be a little short relative to the length of the proximal bones, and the fibulae appeared short in relation to the tibiae. The small long bones of the hands and feet were shorter and broader than normal so that the hands had a stumpy trident appearance and the feet appeared wide and short (Figs. 9 and 11). They exhibited metaphysial changes similar to those occurring in the long shaft bones, and were interesting in that, although in the distal and middle phalanges cupping and loss of density were the most marked features, in the proximal phalanges islands of slight density could be seen within the cups, and in the metacarpals these islands appeared still denser as if bone had at last been laid down in them.

The anterior ends of the ribs and the inner ends of the clavicles were expanded and cupped and showed changes similar to those described in the long bones (Fig. 7). The spinal column was of normal length, and the vertebral bodies and discs were of normal size and shape except for a localised section of the spine—T.11, 12; L.1, 2—in which there was an irregular increase in the density of the anterior borders and the anterior thirds of the upper and lower margins of the vertebral bodies. In the pelvis the acetabula were deformed and enlarged and there was a marked irregularity of its bony margins which seemed to be composed of dense nodules of bone and thickened interlacing trabeculae intermingled with clear areas (Fig. 8). The triradiate cartilage was thicker than normal and the femoral capital epiphyses were separated from the bony bases of the acetabula by distances greater than normal. The bone bordering the sacro-iliac joints and along the crests of the ilia showed similar changes. There was a wide separation between the ossified ramus of the ischium and the inferior ramus of the pubic bone.

The skull was large and brachycephalic. The calvarium was of normal thickness (Fig. 6). The mastoids were fairly well pneumatised but the body of the sphenoid was opaque and showed no evidence of pneumatisation. Although there was a suggestion of the rudiments of the anterior clinoid processes there was no evidence of a pituitary fossa, dorsum sellae or
posterior clinoids. There was an abnormal separation of the bones at the sphenoid-occipital suture. The frontal and maxillary air sinuses were underdeveloped, and, although the orbits were separated more than usual, the posterior and middle ethmoid cells were underdeveloped.

Figure 12

Figure 13

Figure 14

Figure 12  Histological appearance of the abnormal cartilage present in the metaphysial region. Note the irregular arrangement of the cartilage cells, and the absence of basophilic staining of the intercellular matrix. (× 105.) Figure 13  Histological appearance of the abnormal cartilage present in the metaphysial region. Occasional clusters of cartilage cells surrounded by basophilic matrix are present, and patchy vascularisation is seen in the lower part of the field. (× 105.) Figure 14  Bone and bone-marrow. Bone trabeculae do not show osteoid borders, and there is no "osteitis fibrosa" in the marrow spaces. (× 105.)

The development of epiphysial and other centres of ossification in the hands and feet was markedly retarded. Although the child was seven years of age only four tarsal bones were visible—the calcaneum, talus, cuboid and third cuneiform. The epiphysial centres for
most of the phalanges were present but centres for the metatarsals, other than the first, had not appeared. In the hands the centres for the capitate and hamate were well developed but no other carpal bones were visible. The epiphysial centres of the phalanges were all apparent. This degree of development corresponds to that of a normal Chinese boy of two and a half years; epiphysial centres of the long bones that were present in our patient also correspond with this skeletal age. An interesting feature is that all the epiphyses and bone centres that were present were well developed, as if development had proceeded normally up to the age of about two and a half years and that subsequent endochondral bone growth had become disordered and no further epiphysial bone centres had appeared.

**Biochemical investigations**—Urine and blood analyses were carried out on a number of occasions, with the following results. The urine showed no abnormality except for a trace of albumin. There was no evidence of glycosuria or amino-aciduria. Urea concentration tests gave normal results. Excretion of 17-ketosteroids was normal for age. Haemoglobin was 98 per cent, and white blood corpuscles 7,400 per cubic millimetre. Differential blood count was normal. Blood urea was 23–31 milligrams per cent; serum calcium 10–0–13·7 milligrams per cent; serum inorganic phosphorus 3·4–4·9 milligrams per cent; and serum alkaline phosphatase 16–20 King-Armstrong units per 100 millilitres. The Kahn test was negative.

**Histological examination**—The biopsy specimen (about 1 × ½ inch in size) from the metaphysial region of the lower end of the femur consisted of irregular masses of abnormal epiphysial cartilage, together with some adjacent cortical and cancellous bone. The abnormal cartilage (Figs. 12 and 13) showed wide areas of degenerated matrix—much of which failed to show the normal basophilic staining reaction of this tissue—in which were set occasional cartilage cells. In some sparsely-cellular areas the matrix was eosinophilic and fibrotic. The normal regular columnar arrangement of cartilage cells was lacking, and the tissue was, on the whole, avascular. At some points on the periphery of the cartilage masses groups of cartilage cells were "hypertrophied," the basophilic staining reaction of the intercellular matrix was locally intensified, and there was some patchy vascularisation with irregular endochondral ossification. The remainder of the abnormal cartilage, however, was uncalcified. Both at the margin of the cartilage and in the nearby cortical bone the surfaces of bony trabeculae were devoid of any excess osteoid tissue, and the spaces between them were occupied by normal marrow (Fig. 14).

The main histological abnormality in the present case consists in the presence of irregular masses of abnormal cartilage in the metaphysial region. The appearance of this cartilage is similar to that present in the case described by Müller and Sissons (1951). No excess osteoid, which would indicate active rickets or osteomalacia, is present. No "osteitis fibrosa" is present, there being no histological evidence of the hyperparathyroidism that was suggested in the case described by Müller and Sissons.

**Treatment and progress**—Corrective osteotomy was done at the lower end of each femur, the material for histological examination being obtained during this procedure. Both osteotomies united normally, and the patient has subsequently been followed for two years without any new clinical development (Figs. 3, 4 and 5).

**DISCUSSION**

In the case described, an abnormality of ossification has produced interference with skeletal growth and development. Skeletal age is greatly retarded, and in many situations the normal replacement of proliferating cartilage by endochondral bone has failed to occur, masses of partly calcified cartilage accumulating and being responsible for the conspicuous radiological abnormalities in the metaphysial regions of the long bones. Secondary angulation at the site of the abnormal tissues has occurred in the bones of the lower limb, and in all situations the margin of the abnormal cartilage is marked by abnormally dense bone tissue. These changes, restricted as they are to the metaphyses, are remarkably similar to those...
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put on record by Jansen in 1934, and described by him as "metaphysial dysostosis," while the present case fails to show any abnormality of the shafts of the long bones which in Müllermuller and Sisson's case was evidence for a diagnosis of renal osteodystrophy from both the radiological and pathological viewpoints. The changes in the present case are quite distinct from dysplasia epiphysialis punctata; although there is some similarity to the metaphysial lesions of dyschondroplasia, the changes in the bones of the hand—in particular—contrast with this condition in that no isolated cartilaginous masses are present in regions remote from the metaphyses.

Although the outline of the pituitary fossa could not be seen in radiographs of the skull in the present case, no clinical evidence of pituitary disorder was present and the radiological changes in long bones in no way resemble those found in pituitary dwarfism.

On the basis of the material presented, and of a comparison of it with the literature, the present authors regard "metaphysial dysostosis" as a distinct entity among the chondrodystrophies (in which group are included achondroplasia, dyschondroplasia, diaphysial acasis, dysplasia epiphysialis multiplex, dysplasia epiphysialis punctata, Morquio-Brailsford disease, and gargoylism), and put forward the present case as an example of this condition. Metaphysial dysostosis appears to have certain affinities with dyschondroplasia and with achondroplasia, although ignorance of the pathogenesis of these conditions makes it impossible to assess the precise significance of such similarities, or of the exact criteria to be adopted in classification of atypical examples of these conditions.

SUMMARY
1. Details of clinical, radiological, biochemical and histological investigations of a case of metaphysial dysostosis are presented.
2. The patient was a boy of seven years, and showed widespread lesions (involving long bones of limbs, small bones of hands and feet, pelvis, clavicles, and ribs) characterised by retardation of growth and ossification with masses of partly calcified tissue in the metaphyses.
3. No radiological, clinical or histological evidence of renal osteodystrophy was found in the case described.
4. Metaphysial dysostosis is discussed in relation to other chondrodystrophies.

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REFERENCES


