METAPHYSIAL DYSOSTOSIS (JANSEN TYPE)
REPORT OF A CASE WITH LONG FOLLOW-UP

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A case of the Jansen type of metaphysial dysostosis, followed for fifteen years from childhood to the age of nineteen, is reported. Radiographs taken at five years revealed the characteristic metaphysial changes in all the tubular bones, especially those of the hands and feet. The acetabular and glenoid areas, the costochondral junctions and the sternal ends of the clavicles were also involved. Radiographs taken at nineteen years, however, showed only marked deformities, which shows that the involvement of the metaphyses can regress by the end of growth. Biopsy of the lower end of radius at the age of twelve revealed changes in the growth plate or physis, especially in the zone of resting cartilage. This finding suggests that cellular function in this zone is disturbed by some unknown mechanism. Hence, the term physial dysostosis may be more accurate than metaphysial dysostosis.

Since Murk Jansen’s report on metaphysial dysostosis further reports of differing degrees of severity have been presented. In fact this disease has many variant forms. Weil (1957) classified it into Jansen and Schmid types and Sutcliffe (1966) found seven types. The Jansen type is the most severe and is rare, only five cases having been reported so far (Jansen 1934; Cameron, Young and Sissons 1954; Weil 1957; Gram, Fleming, Frame and Fine 1959; Silva 1966). There has been no case reported in Japan. Two of the cases were reviewed after a long interval and the radiographic findings at skeletal maturity were reported (Weil 1957; Haas, Boer and Griffioen 1969). So far as the pathology is concerned, pertinent reports are very few. In particular we have found no detailed description of the histological features of the metaphysial region.

This paper reports a patient with metaphysial dysostosis followed throughout the period of growth and describes the findings of a biopsy of the lower end of radius at the age of twelve.

CASE REPORT
A man aged twenty complained of multiple deformities of the limbs. He had been admitted to our hospital three times at the age of five, twelve and nineteen years for detailed examinations, the records of which were available.

TABLE 1
PHYSICAL MEASUREMENTS

<table>
<thead>
<tr>
<th></th>
<th>At 12 years</th>
<th>Normal</th>
<th>At 19 years</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>126.0</td>
<td>145.2</td>
<td>156.2</td>
<td>169.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>25.0</td>
<td>37.0</td>
<td>47.0</td>
<td>59.8</td>
</tr>
<tr>
<td>Chest (cm)</td>
<td>62.5</td>
<td>70.1</td>
<td>80.0</td>
<td>87.0</td>
</tr>
<tr>
<td>Sitting height (cm)</td>
<td></td>
<td>84.8</td>
<td>90.8</td>
<td></td>
</tr>
<tr>
<td>Length of arms (cm)</td>
<td></td>
<td>63 and 63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of legs (cm)</td>
<td></td>
<td>83 and 83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm span (cm)</td>
<td></td>
<td>140.0</td>
<td></td>
<td></td>
</tr>
</tbody>
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The family history was not remarkable. As for the patient, he started to lift his head at the age of twelve months and to walk at eighteen months, when his gait was thought to be normal. His intelligence was good enough to enable him to pass through a high school.

Examination at the age of five revealed multiple symmetrical swelling of joints, with clubbing of the fingers specially noticeable, but the range of joint movement was not restricted. The facial appearance was normal at the age of six. At the age of twelve, deformities of the extremities including the fingers had persisted and his height was much below normal (Fig. 1 and Table I). At the age of nineteen years he was still short; the extremities were short compared with the trunk, and the distal segments (forearms and legs) appeared to be shorter than the proximal segments (upper arms and thighs) (Fig. 1). Rotational and angular deformities were found at the lower ends of the tibiae. The fingers and toes were greatly deformed (Fig. 2). The ribs showed a "rosary" at the costo-chondral junctions, and the sternal ends of the clavicles were prominent.

Radiographic features—Radiographs taken at the age of five revealed the characteristic metaphysical change in all the tubular bones, especially those of the hands and feet. The acetabular and glenoid areas, the costo-chondral junctions and the sternal ends of the clavicles were also involved. At the age of twelve these bone changes persisted but with some improvement. By the age of nineteen the changes of bone structure had almost completely resolved, leaving marked deformities. The characteristic findings in various kinds of bone were as follows.

Short and long tubular bones—The most striking and exactly symmetrical changes were found at the metaphyses in the hands and feet. These bones were shorter and broader than normal, with a wide space between epiphysis and diaphysis outlined irregularly by expanding cortex. Patchy streaks and stipplings of calcification were found within these radiolucent areas of metaphysis. The growth plates were wide and irregular. The epiphyses and the diaphyses were normal in appearance.

At the age of twelve these radiolucent lesions seemed to be healing except in the hands, where the metaphyses were so enlarged that the ends of the affected bones appeared to be more clubbed (Fig. 3). Similar changes were found in the bones of the forearms.

By the age of nineteen the various abnormal findings had nearly disappeared and the irregular metaphyses had developed into a normal bone structure with some coarsening of the trabeculae pattern (Fig. 4). Both ends of long tubular bones were expanded, giving a dumb-bell-like shape. However, in the short tubular bones of the hands, the radiolucent lesions still remained, with an appearance similar to enchondromatosis (Fig. 3).
FIG. 4
Photograph of feet at age 19, and radiographs at 12 and 19 years. The metaphyseal areas show changes similar to those in the hands.

FIG. 5
Radiographs of pelvis and hips taken at 5 and 19 years. Note the symmetrical involvement of the metaphyses of the femora.

FIG. 6
Radiographs of the left foot taken at the age of 5 and 19. The irregularity of bony structure of the calcaneus had resolved by the end of growth.
Flat bones—The characteristic changes were most pronounced in the pelvis (Fig. 5). There was markedly irregular ossification of the iliac crests and irregular cystic changes with calcified streaks at the margins of the acetabulae. The pubic symphysis and ischio-pubic junctions were widened and irregularly outlined. The sacro-iliac joints appeared to be wider than normal. In the shoulder region the glenoid area was most affected; the normal epiphysis of the humerus was seen between the affected glenoid and the humeral metaphysis with the widened growth plate. The ribs and clavicles were short. The sternal ends of the clavicles were expanded and the costochondral junctions were cupped, with characteristic beading.

At the age of twelve similar changes were still found in the ribs and clavicles, but by the age of nineteen those changes had resolved leaving no marked deformities. Cuboid bones—None of the examinations at the age of five, twelve and nineteen years showed involvement of the carpus and tarsus except for irregularity of the posterior outline of the calcaneus at the age of five, and by the age of nineteen all these bones showed normal structure (Fig. 6). There was no retardation of skeletal age. The vertebral bodies and discs were normal in size and shape.

Cranium—Examinations at five and nineteen years showed normal ossification with slight platybasia and brachycephaly because of underdevelopment of the base.

Investigations—Laboratory findings at twelve and nineteen years were obtained. All tests showed normal values, including renal function tests (phenolsulphphthalein excretion, creatinine clearance, and Fishberg concentration test). Serum inorganic phosphorus was 4.7 and 3.3 milligrams/100 cubic centimetres; serum calcium, 5.5 and 5.1 mEq/l; serum alkaline phosphatase, 15 and 9 King-Armstrong units respectively. The examination of a bone marrow smear gave normal values. The twenty-four-hour excretion of 17-ketosteroids and 17-hydroxycorticosteroids was normal for age.

Histological examination—A biopsy of the lower end of radius was performed at the age of twelve. The epiphysis and metaphysis appeared to be normal, though the growth plate was abnormally wide. For histological study the specimen was cut longitudinally. A characteristic change was found at the junctional area between growth plate and metaphysis (Fig. 7, B). The growth plate was abnormally rich in cartilage matrix but poor in cells, which were arranged in a disorderly manner at the junctional area (Fig. 9). In the cartilage matrix scattered clusters of a few cartilage cells with fusiform or elliptical cytoplasm and small round or elliptical nuclei were seen. These clusters were located in the half of the growth plate towards the epiphysis (Fig. 8). This area was, on the whole, avascular. The nearer to the metaphysis the more hypertrophied were the chondrocytes, here showing vacuolated cytoplasm and flattened nuclei and tending to form irregular columns separated by a great deal of matrix (Fig. 9). Although ossification was found towards the metaphysis, the new bone and cartilage matrix showed a disorderly arrangement and pillars were not formed. There were no clusters of cartilage cells in the epiphysis or the diaphysis.

These radiological, biochemical and histological findings made us think that this case could be diagnosed as an example of the Jansen type of metaphyseal dysostosis.

DISCUSSION

Metaphyseal dysostosis is characterised by a disturbance of enchondral ossification confined to the metaphyses. When the diagnosis is made, especially of the Jansen type, other diseases affecting the metaphyses should be eliminated, especially achondroplasia, multiple enchondromatosis, various types of rickets, and hypophosphatasia.

In achondroplasia the abnormalities are generally noticed soon after birth, but in metaphyseal dysostosis they are found only after the patient starts to walk, perhaps at the age of four or five years. The facies of achondroplasia is quite characteristic; furthermore the proximal segments of the limbs are short compared with the distal segments, a disproportion opposite to that of metaphyseal dysostosis.

Ollier's disease can be easily distinguished by the
asymmetrical involvement. Cases of multiple enchondromatosis in which the bones are involved almost symmetrically can be differentiated by the fact that the bone changes are found throughout life (Weil 1957) and by the histological findings. In multiple enchondromatosis the growth plates do not appear to be radiographically abnormal because they contribute relatively little to the accumulation of cartilage. On the other hand in metaphysial dysostosis the abnormal proliferation of cartilage is closely related to active enchondral ossification, and so the growth plates themselves are found to be abnormal. Furthermore the cartilage in multiple enchondromatosis is much more cellular (Jaffe 1972). Various types of rickets and hypophosphatasia can be differentiated by the biochemical findings.

There are few reports on the pathological findings in metaphysial dysostosis. According to the descriptions of Jansen (distal tibia), Cameron et al. (distal femur), and Gram et al. (distal femur), a wide irregular mass of cartilage protrudes into the diaphysis and the growth plate almost disappears. Consequently the clusters of chondrocytes are scattered in disorder and the normal regular columns are not formed. Moreover, no excess of osteoid tissue is present and enchondral ossification is scarcely found.

In our case the characteristic change was found in the growth plate or physis, especially in the zone of "resting" cartilage. Here the chondrocytes are not resting but are actively participating in forming matrix (Trueta and Little 1960). The pathological findings in our case suggest that cellular function in this zone is disturbed by some unknown mechanism. Further studies are needed to clarify the pathogenesis.

Although the radiological changes are found in both physis and metaphysis, the histological appearances suggest that the disease process originates in the physis and extends to the metaphysis. Therefore the term "physial" dysostosis may be preferable to "metaphysial" dysostosis.

REFERENCES