9. CHONDRO-OSTEO-DYSTROPHY

Morquio-Brailsford Type

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This disorder is characterised by dwarfism with shallowness of the vertebral bodies, marked kyphosis, sometimes angular increase of the spinal curve at the dorsi-lumbar junction, and progressive changes in the femoral head and acetabulum in a child of normal intelligence. It lacks the special features that are characteristic of the other type of chondro-osteo-dystrophy known as gargoylism. To a varying extent the whole skeleton is affected, with the exception of the bones of the skull and face which are usually normal.

The condition is generally associated with the names of Morquio and Brailsford. Cases that we should now place in this group were undoubtedly published under various titles before 1929, but in that year Morquio described "A Form of Familial Osseous Dystrophy" seen in four members of a family of five; and Brailsford suggested chondro-osteo-dystrophy as a suitable title for the condition he found in one patient, the radiographic changes of which were described in detail. In 1920, Wheeldon reported two patients with "achondroplasia" but with the unusual feature of a wedge-shaped vertebra which is so often a characteristic feature of both types of chondro-osteo-dystrophy; and one of these patients was later followed up and reported by Pohl (1939) as an example of Morquio's disease. In 1925, at the Royal Society of Medicine, Thursfield showed "A Case of General Enlargement of Joints" which this author had seen with him, and which he published with illustrations in 1927; this case we should now place in the group under discussion. Many others have since been reported.

Hereditary and familial influences—Hereditary influences are seldom apparent, whereas familial influences are common. Statistics vary because of differences of opinion whether or not individual cases should be included. Of the sixty cases known to this author, which he believes should be classified in the group, it was found that another member of the family was affected in about one-third. Jacobsen (1939) reported twenty members in five generations of one family affected by a condition which, though not typical, appears to be allied closely with the Morquio-Brailsford syndrome.

Sex—Both sexes are affected, males slightly more often than females.

Age—Some abnormality may be present at birth (Hirsch 1937) but the developmental error is seldom apparent until the child begins to walk and appreciable changes are often first recognised at about the age of 4 years or even later. Only six patients in the series studied by this author were seen under the age of 4 years, but thirty-six (60 per cent.) were under 10 years of age.

Etiology—The possible causes have been discussed by many authors but without any convincing evidence, and it must be acknowledged that the cause is unknown. Ashby, Stewart and Watkin (1937) suggested that the disorder will eventually be included with gargoylism in the group of lipoidoses.

Clinical characteristics—At about the age of 4 years it may be noted that there is curvature of the spine, failure to gain normal height, and the development of symmetrical deformities which increase, with progressive crippling, until the child is unable to walk without aid. The typical appearances are those of a round-backed, knock-kneed, flat-footed child who stands with the hips and knees flexed in a crouching position, with the head thrust forward and sunk between high shoulders, looking not unlike a case of cervical caries, and walking in the waddling manner of a duck (Morquio 1929). The face is intelligent but perhaps inclined to conform to an almost characteristic type. The bridge of the nose may be depressed and the eyes widely separated; the head may be large but it is usually normal in size and

shape; the neck is short. There is marked kyphosis of the spine with a short lordotic curve below. In about one-third of the patients there is angular accentuation of the kyphosis in the dorsi-lumbar region which may suggest caries of the spine, but pain in the back is most unusual. There is always limitation of movement, particularly of extension of the spine, and there may be scoliosis. The chest is narrow and the antero-posterior measurement is increased, the sternum being thrust forwards (pectus carinatum). Muscle weakness without changes in the electrical reactions has been noted. The spleen and liver may be felt rather easily but they are not enlarged.

Though the child is dwarfed generally, it is shortness of the spine that is chiefly responsible for the lack of height. The limbs are relatively long. It has often been recorded that in the standing position the hands reach almost to the level of the knees. Dwarfing of the proximal segments of the upper limbs, which is so marked a feature of achondroplasia, was noted in only one of the sixty cases. Some authors have said that there is congenital elevation of the scapula (Sprengel's shoulder) but their description of the mobility of the scapulae hardly agrees with the usual finding in this deformity.

The epiphyses are often but not always enlarged. In some joints there is limitation of movement whereas others show hypermobility, this variable feature being evident sometimes in different joints of the same patient. As would be expected from the radiographic appearances there is often stiffness of the hip joints and less frequently of the shoulders, knees, ankles, elbows, wrists, fingers and toes. General stiffness involving many joints was a feature in seven patients. Laxity of ligaments with hypermobility is seen most often in the wrists, fingers, feet and toes, and less often in the knees and ankles. It may be possible to dorsiflex the wrists until the fingers touch the back of the forearm. In one unpublished case of a boy aged 4 years, with widespread laxity of ligaments, several joints could easily be dislocated, and both patellae dislocated whenever the knee joints were flexed. Knock-knee and other deformities occur at the joint level, or close to it, and are not the result of bending of the shafts of the bones; they tend to become gradually worse.

The fingers are usually broad and blunt. Enlargement of the interphalangeal joints of the fingers was a striking feature in four patients, and to a less extent in a fifth, the swelling suggesting polyarthritis; but the enlargement was due to thickening of the bones and not to swelling of the joints. Widespread stiffness involving many joints was a feature of these cases (Thursfield 1925, Scott 1929, Ellman 1932, Hardwick 1938).

Pain is unusual, but as bone changes in the hip joints increase there is sometimes pain in this region which may be the first symptom responsible for the child being taken to hospital. *Blood examination* reveals nothing of importance. The serum calcium may be raised, lowered or normal.

Radiographic appearances—General porosis of the skeleton has often been noted. This is of no diagnostic importance and it is almost certainly no more than the result of limited activity due to crippling. The spine shows flattening of the vertebral bodies which may be more obvious in the dorsal than in the lumbar region. There is platyspondyly with increase in the transverse diameters, and particularly in the antero-posterior diameters, of the bodies. In lateral radiographs the bodies have a characteristic shape by which they can be distinguished readily from the typical vertebral bodies of gargoylism. The upper and lower surfaces are irregular, ill-defined and defective, with a tendency to approximate towards each other in front, thus accounting for a wedge-shaped appearance which is accentuated by a central prolongation, or tongue. Later on, multiple centres appear by which the defects are repaired and the epiphysal rings formed (Brailsford 1944). In the lumbar bodies, a layer of less dense bone has been seen above and below, with a more dense layer between (Guérin and Lachapèle 1938). The typical shape is most obvious in the lower dorsal and upper lumbar regions, the lower lumbar vertebrae tending to be more normal in shape. When there is an angular kink in the spine, lateral radiographs show that one vertebral body

at the dorsi-lumbar junction is smaller than the others and is displaced a little backwards, as if it had been squeezed out of position by the bodies above and below. This mal-alignment is always more obvious immediately above the small body than below it; in fact the appearance suggests that the spine above has slipped forwards on the small wedge-shaped body. The first lumbar vertebra is most often affected in this way but the anomaly may be seen in the twelfth dorsal, and occasionally in the eleventh dorsal vertebra. The second lumbar vertebra was the centre of a kink in one patient and the third lumbar vertebra in another. The body next below the displaced one was also rather small in three cases (Summerfeldt and Brown 1936, Pohl 1939): the body next above was reduced in size in only a single, unpublished case. As a rule, the intervertebral discs are relatively deep, but occasionally they are reduced in depth. The pelvis may be narrow or shaped as in the ape. The ribs are more horizontal than usual and they are expanded at both extremities.

There is usually irregularity in outline of at least some epiphyses. The hips are always affected, the changes becoming progressively more marked as the child grows. The acetabula are enlarged and irregular. The femoral heads are irregular, flattened and fragmented. Sooner or later the femoral necks appear short, thick and spread, with coxa vara. Examination of radiographs taken at intervals of three to six years in four cases in the author's collection shows not only that changes are definitely progressive but that the femoral heads may be normal to begin with and only later show signs of faulty development or degeneration. There may be incomplete or complete dislocation of the hip joints on one or both sides. In one patient there was no displacement of the femora at the age of 9 years and yet both hip joints were dislocated when re-examined at the age of 15 years. Other epiphyses that sometimes show degenerative changes are those at the lower end of the femur, upper end of the tibia (Ruggles 1931) and upper end of the humerus; but it is only the changes in the hip joints that are important from the diagnostic point of view. "Several" or "many" epiphyses were said to have been affected in seven cases. It is also said that irregularity and fragmentation of the epiphyses may disappear later. Delay or irregularity in ossification may be seen in the patella.

The joint spaces appear to be unusually wide in younger children. The shafts of the major long bones are usually normal but, occasionally, they are short and thick. There was symmetrical thickening of the cortex on the outer side of the upper femoral shafts in one patient—a curious feature that has been seen in only two other patients, both suffering from gargoylism. The metaphyses may be splayed to accommodate the enlarged epiphyses especially in the radius and ulna where the epiphysal lines at the lower ends are tilted towards each other. The ulna, as in so many developmental errors, may be short. The fibula may also be short, whereas in achondroplasia it is usually long.

The metacarpals and phalanges are stubby, with expanded ends. The bases of some metacarpals, especially the third and fourth, and the distal extremities of the phalanges, tend to be pointed. There may be multiple centres of ossification for the epiphyses of the hands and feet. Ossification of the carpus may be delayed and when the bones are ossified they may be irregular in outline. There may also be irregularity in shape of the tarsal bones. In one case, included with confidence in this group because of other skeletal changes, the great toes were abnormally long and large, the first metatarsals sharing enlargement with the phalanges (Thursfield 1925).

Changes in the skull are usually minimal and unimportant. The pituitary fossa is usually normal; it has sometimes been found small and sometimes enlarged. Digital markings in the skull were seen in two brothers in a family of eight children in which a third member showed signs of the Morquio-Brailsford affection.

Progress—As a rule radiographic changes in the bones advance, and deformities progress, with increasing disability, until walking becomes impossible without assistance.

Pathology—The pathology is unknown. Shelling (1945) examined biopsy specimens from the lower femoral epiphysis and diaphysis in one case: the epiphysal line was irregular;

there were cartilaginous nests within the bony trabeculae; and the matrix in these nests was striated and stained in an irregular manner. Harris and Russell (1933) believed that mucoid degeneration of cartilage in place of normal calcification was the fundamental change in dwarfism including achondroplasia.

Differential diagnosis—Many examples of Morquio-Brailsford chondro-osteo-dystrophy have been reported as cases of achondroplasia, with or without the prefix "atypical"; but as a rule the appearances of the head and face in chondro-osteo-dystrophy are quite unlike those of achondroplasia. In achondroplasia there is apparent lordosis with prominence of the buttocks, less secondary kyphosis, normal length of the spine, shortening of the limbs and particularly of the proximal segments, and usually bowing of the legs rather than genu valgum.* There is seldom coxa vara in achondroplasia and there are never the gross epiphysal and articular changes seen in the Morquio-Brailsford affection. The achondroplasiac patient is sturdy and strong; he is not feeble as are the patients discussed in this chapter.

The special features of gargoylism, the other type of chondro-osteo-dystrophy, are the heavy facies, mental deficiency, cloudy corneae, and enlargement of the liver and spleen. In gargoylism the spine may also show a kink in the dorsi-lumbar region with one vertebral body small and displaced backwards, but the shape of the bodies differs markedly from that seen in the Morquio-Brailsford type. Very seldom is there difficulty in deciding to which group a case belongs after examination of radiographs of the spine, but the one described by Snoke (1933) is an exception.

When many epiphyses are involved the condition must be distinguished from dysplasia epiphysialis multiplex in which the spine is usually normal and the acetabulum is not altered in the way that it almost invariably is in the Morquio-Brailsford syndrome. Only one example of multiple epiphysal dysplasia with flattening of the vertebral bodies is known to the author. When the patient complains only of the hip joints, local radiographic changes might suggest the diagnosis of pseudo-coxalgia were it not for the striking deformities of the trunk.

Deformity in the dorsi-lumbar region due to wedging of a vertebral body may be seen occasionally in cretins, even in foetal life. (Annual Report of the Institute of Social Medicine, Oxford 1946.) The appearances in one patient, seen by the author, would suggest that the abnormality in shape of the vertebral bodies in cretins is of the type seen in gargoylism rather than that of chondro-osteo-dystrophy. A similar local deformity of the spine has been seen in a child who appeared to be entirely free from other skeletal abnormalities.

The distinction from spinal caries of the dorsi-lumbar region should be made without difficulty after examination of lateral radiographs of the spine. It must be recognised, however, that a degree of dwarfism is a feature of several conditions, and atypical cases occur which, for the moment, it is difficult to classify with any degree of conviction.

* It is true that in two unquestionable cases of achondroplasia there was an angular kyphosis at the dorsi-lumbar junction. In one of these a vertebral body at the angle was smaller than the others. But in neither were the vertebrae flattened and spread.

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CASE 10—CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford Type)

(Figs. 22–26.) Boy aged four and a half years. Enlargement of joints and other deformities first noticed after an attack of bronchitis when six months old. Did not walk until the age of three and a half years. Family history negative. Clinical features—kypho-scoliosis with

FIG. 22

Case 10. Photographs of the child, aged four and a half years, showing thickening of the ends of the bones and lengthening of the great toes. Note the kyphotic curve, and the typical standing attitude with the hips and knees flexed.

enormous enlargement of the epiphyses and lengthening of the great toes (an exceptional feature); some limitation of rotation movement at the shoulder joints and of pronation and supination of the forearm. Fingers thick and stumpy; nails unusually short; unable to flex the fingers properly, especially at the metacarpo-phalangeal joints. Backward child. Head rather large. (Under the late Dr Hugh Thursfield. Reported Thursfield 1925, Fairbank 1927.)

FIG. 23

Case 10. Upper limb, showing the stout bones with enlarged ends and some irregularity of ossification of the epiphyses.

FIG. 24

Case 10. Lateral radiograph showing increased antero-posterior measurement of the bodies; disc spaces not unduly wide; no abrupt kyphosis at the dorsi-lumbar junction.

FIG. 25

Case 10. Enlargement of the great toes with irregular ossification at both ends of the first metatarsals and the proximal phalanges.

FIG. 26

Case 10. Showing ape-like shape of the pelvis, poorly developed acetabula and marked coxa vara with delayed and irregular ossification of the femoral heads.

CASE 11. CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford Type)

(Figs. 27-29.) Girl aged six years. Sent to hospital for deformity of the wrists and spine. Family history negative. Head big; skull of normal shape; premature closure of sutures. Rigidity localised to the dorsi-lumbar junction. Femoral heads prominent; abduction of the hips not limited. Genu valgum. Abduction of the shoulder joints limited to 80 degrees. Extension of the elbow joints slightly limited. Forearms short, especially the ulnae; supination excessive. Marked hypermobility of the wrist joints in all directions; the fingers can easily touch the flexor aspect of forearms. Fingers and thumbs blunt. (Under Mr H. L.-C. Wood.)

FIG. 27

Case 11. Spine, showing typical shape of the bodies with the central "tongue" in front. The second lumbar body is small and displaced backwards. The discs are unusually deep.

FIG. 28

Case 11. All the long bones are rather short and stout. Note shortness of the ulna and tilting of the lower epiphyses of both forearm bones. "Pointing" of the bases of the metacarpals is not striking in this case.

FIG. 29

Case 11. Pelvis and hip joints, showing ape-like shape of the pelvis, large acetabula and only slight irregularity in the ossification of the femoral heads.

CASE 12. CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford type)

(Figs. 30-34.) Boy, aged nine and three-quarter years. Deformity of the left hand, suggestive of rheumatoid arthritis, since birth. Other deformities not noticed until the age of three or four years. One sister was said to have deformities of the spine and hip joints; three other sisters normal. Dwarfed. Flat depressed nose, forehead prominent. Teeth hypoplastic. All epiphyses enlarged and joint movements restricted. Complains of lumbar pain when the hip joints are flexed beyond 70 degrees. General muscular weakness. Blood investigations negative, but said to have had negative calcium balance treated successfully with calcium gluconate and vitamin D. Marked kyphotic curve with angular accentuation at the dorsi-lumbar junction, the twelfth dorsal body being small and displaced backwards. Marked changes in the head and neck of both femora: no subluxation. Irregular ossification in the epiphyses of the upper end of the tibia, lower end of the humerus (capitellum and medial epicondyle), lower end of the ulna and upper end of both humeri. (Under the late Dr Gordon Pugh.)

When examined at the age of fifteen years there was marked kyphosis with a short lordosis below which had improved his general posture; genu valgum; feet flat; general laxity of the knees, ankles, fingers, and particularly the wrists; feet blue and cold. Skull broad; forehead prominent. Teeth good. The outline of the vertebral bodies is now much more irregular in both antero-posterior and lateral films, and there is further destructive change in both femoral heads which are now subluxated. (Under the late Sir Henry Gauvain.)

FIG. 30

Case 12, at the age of nine years. Radiograph of the spine shows typical "tongued" vertebral bodies. The twelfth dorsal vertebra is reduced in size and is the apex of an angular kyphosis. The second lumbar body approximates more closely in shape to the twelfth dorsal than do the others: the eleventh dorsal body is slightly smaller than the bodies above it. The discs are deep.

FIG. 31

Case 12, at 9 years, showing mottling and fragmentation of the capitellum and internal epicondyle of the humerus.

FIG. 32

Case 12, at 9 years, showing irregular ossification of the outer part of the tibial epiphysis.

FIG. 33

Case 12. At the age of nine years. Radiographs of the pelvis and hip joints show that the pelvis is narrow, and there is fragmentation and destruction of the femoral heads with thickening of the femoral necks. The acetabula are large and poorly formed.

FIG. 34

Case 12, at the age of fifteen years. The pelvis and femora show further changes in the femoral heads, now with definite subluxation of both hip joints which was not present at the age of nine years (Fig. 33).

CASE 13. CHONDRO-OSTEO-DYSTROPHY (Morquio-Brailsford type)

(Figs. 35-38.) Girl, aged five years. Unwilling to walk far; cried with pain. Enlarged joints and round shoulders since infancy. Father's mother and sister both of short stature (both dead). Stiffness of the shoulder, elbow, wrist, hip and knee joints; some limitation of pronation and supination of the forearms. Valgus deformity of feet. Blood examination showed nothing of significance. General dwarfism, limbs more affected than trunk. Moderate kyphosis. Little movement in the spine except in the cervical region. Bridge of the nose sunken. Forehead prominent. Long bones stout, with splayed ends. When the child is standing the finger tips reach just below the greater trochanters.

FIG. 35

FIG. 36

Case 13. Fig. 35 shows the condition of the spine at the age of two years; note the shape of the vertebral bodies, the deep disc spaces, and the enlargement of the anterior ends of the ribs. Fig. 36 shows the condition at the age of five years; there is irregularity in outline of vertebral bodies; in the lumbar region the appearance suggests that less dense bone has been added above and below the rather less dense bodies previously present.

FIG. 37

Case 13, at the age of two years. Radiograph of the pelvis and hip joints shows rather large acetabula and, for this age, normally ossified though rather small centres for the femoral heads.

FIG. 38

Case 13, at the age of five years. The pelvis and hip joints show progressive changes that were not present at the age of two years (Fig. 37). Thickening of the cortex now seen on the lateral aspect of both femoral shafts is not believed to be significant.