10. GARGOYLISM

Synonyms—Hurler’s syndrome, Dysostosis multiplex

This type of chondro-oste-o-dystrophy is characterised not only by dwarfism but also by a heavy, ugly facies, corneal opacity, mental deficiency, kyphosis, distension of the abdomen, and enlargement of the liver and spleen. The first two cases were reported by C. Hunter in 1917; the patients were brothers; neither had the corneal opacities that are so often a striking feature. It is to Hurler that priority of description is often given. She published two cases in 1919, both boys; one was investigated later by Tuthill (1934) who first published a detailed account of the neuropathology. In 1933 Binswanger and Ullrich reported two cases and suggested the name “dysostosis multiplex.” In 1936 Ellis, Sheldon and Capon, in a valuable contribution, reported seven cases and reviewed eight others previously published; they proposed the title “gargoylism” and suggested the possibility that a metabolic error might be responsible. Many other cases have since been reported. For this review fifty reported cases have been selected. Hereditary and familial influences—There is little evidence that heredity plays any part but familial influences are common. Familial incidence was a feature in thirty-two of sixty-two cases collected by Henderson (1940).

Sex—Both sexes are affected, males more often than females in the proportion of four to three.

Age—Only three of the cases studied were under twelve months of age, the youngest being eight months; but 87 per cent. were under ten years. Few lived until growth was complete.

Etiology—It is now agreed, fairly generally, that this condition must be classified with the lipoidoses, although endocrine dysfunction has also been suggested as an explanation of the somewhat complicated pathology which is characterised by changes in so many different tissues. Henderson (1940) remarked that “hypothalamic disturbances are probably connected with the changes seen in the pituitary and thyroid glands, and these in turn with some of the clinical features of the disease such as chondrodystrophy and dwarfism.” He agreed with Ellis (1937) that it is “yet too early” to assess the part played by the thyro-pituitary mechanism. It is difficult to see how metabolic or endocrine error could account for the curious shape of vertebral bodies, and still less for local deformity of the spine. Engel (1940) attributed the hypophysial dysfunction to “blebs” caused by escape of cerebrospinal fluid into the adjacent tissues in early embryonic life. He included in the “bleb diseases” a group of ten different syndromes. It seems probable that the fault exists at birth but we have found only three reported cases that were recognised in the first year of life.

Clinical signs—At birth, the size and weight of the child is often above the average but, after the first year, growth is restricted and there is usually, though not invariably, increasing evidence of dwarfism. There is some degree of micromelia. In a well-marked case the head is large; the eyes are wide apart, sometimes suggesting hypertelorism; the bridge of the nose is depressed and the general facies is heavy and ugly. There may be prominence of the supraorbital ridges, bulging of the temporal regions, and ridges along the sutures and around the anterior fontanelles. Scaphocephaly, acrocephaly, oxycephaly and brachycephaly have all been noted (Ellis et al. 1936). Hydrocephalus occurs in more than one-third of cases. The lips are everted, the mouth open and the tongue enlarged, so that many are suspected of cretinism. In one patient there were fissures of the tongue and prominent papillae as in a mongol (Ashby et al. 1937). The mandible is often large. The eyebrows are coarse, dark and bushy, but the hair is usually fine and silky. The ears are set low on the head. Nasal discharge is frequent. Dentition may be irregular and delayed. Cloudiness of the cornea is a striking feature and, from the diagnostic point of view, important; it is caused by multiple opacities in the deeper layers of the cornea. There may be lateral nystagmus (Slot and Burgess 1938). Buphthalmos has sometimes been reported. Optic atrophy occurred in two siblings reported by Davis and Currier (1934) and there is sometimes deafness.
There is often, but not always, mental deficiency. In some patients it has been noted that there was gradual mental deterioration in the course of a number of years. One girl, aged eighteen years, showed a very marked degree of statural, mental and sexual infantilism (Ellis et al. 1936). The neck appears to be short and the shoulders are high. Sometimes the deformity of the shoulders almost warrants the title of "congenital elevation of the scapula" (commonly, but quite unjustifiably, known as "Sprengel's shoulder"). The clavicles may be thick. As a rule there is marked kyphosis, angular in shape, in the dorsi-lumbar region. There is seldom scoliosis or pigeon-breast. The abdomen is distended to an even greater extent than could be accounted for by enlargement of the liver and spleen which is an important feature in most cases. The liver is more often enlarged than the spleen, both being smooth and firm on palpation. Quite often there are umbilical and inguinal herniae.

There is often limitation of movement of some joints, and occasionally of all joints (Davis and Currier 1934, Ellis et al. 1936). The upper limbs are more often affected than the lower limbs and in the shoulders, elbows, and particularly the fingers, there is not only limitation of movement but also flexion contracture. Claw hand was regarded as an important feature by Ashby et al. (1937). The fingers may be short, and the ring and little fingers incurved. There may be limitation of extension of the knee joint, genu valgum, genu varum, or flat-foot. The epiphyses are not enlarged as they so often are in the Morquio-Brailsford group. Sometimes, even in members of the same family, one patient may show all features of the syndrome while another shows only bone changes (Ellis et al. 1936).

Blood examination reveals nothing of importance. Biochemical studies have shown no constant abnormality.

Radiographic appearances—The radiographic appearances in gargoylism show general resemblance to the changes that are seen in Morquio-Brailsford disease, but there are distinct differences in the skull, the vertebral and the hip joints.

The skull—Most cases of gargoylism show enlargement of the sella turcica, even to twice the normal size, with or without hydrocephalus. There is no evidence of erosion and it has been suggested that this enlargement is due to malformation of the sphenoid rather than to abnormality of the pituitary gland or increased intra-cranial pressure (Ellis et al. 1936).

The spine—In the spine, the upper and lower surfaces of the vertebral bodies are convex, so that they present a circular rather than a quadrilateral outline; the discs are biconcave and deeper than normal. It is often said that the bodies are spread and flat, as in the Morquio-Brailsford type, but this is not accurate. When there is angular kyphosis—and this occurs with far greater frequency than in the Morquio-Brailsford type—one body is usually smaller than the others and is displaced backwards as if squeezed out of line. The mal-alignment is always more obvious above the small body than below it: the vertebrae above appear to have slipped forwards on the small deformed body. This deformity is seen in both types of chondro-oste-o-dystrophy but there is no other resemblance. The displaced vertebral body is concave on its anterior surface, the upper part being deficient and the lower part projecting forwards in the form of a beak. This beak is quite different, both in shape and position, from the central "tongue" seen in the Morquio-Brailsford type. The typical shape and displacement is seen most often in the second lumbar vertebra and, next in frequency, in the first lumbar vertebra: in only one case was the twelfth dorsal as well as the first lumbar vertebra small, beaked, and displaced. A similarly peculiar shape is often seen in the vertebral body next below the one displaced and occasionally in the one above it. This distortion, which is a diagnostic feature, is usually seen only in two or three of the upper lumbar bodies; but in two patients the first four lumbar bodies were all affected. In one patient the fifth lumbar vertebra showed typical deformity: in this case the first and second bodies and possibly the fourth were also affected, but the third lumbar vertebra was normal. Only one case has been found in which the shape of the bodies as seen in lateral radiographs failed to indicate clearly to which group of chondro-oste-o-dystrophy the case belonged (Snoke 1933). If lateral
radiographs are taken when the spine is flexed it will be seen that much more movement takes place at the level of the disc above the small body than in the disc below.

Angular kyphosis may be present without any vertebral body being small or displaced. The ribs may be thicker than normal, particularly anteriorly. In one case the lower ribs were said to be like Indian clubs (Slot and Burgess 1938). The long bones are often thick and of uniform density. On the whole, the bones of the upper limb show greater change than those of the lower limb (Caffey 1945).

Hip joints—The hip joints show peculiarities that are quite different from those seen in the Morquio-Brailsford type. The roof of the acetabulum is usually shelving but there is no gross enlargement or irregularity such as is seen in the other type. There is coxa valga and the femoral necks are long. The epiphysis for the femoral head may be deformed and irregular, particularly on the inner side, but it does not show the gross changes that are so characteristic a feature of the Morquio-Brailsford type. The femoral heads may be displaced a little upwards but there is seldom true subluxation. There may be irregularity of ossification of other epiphyses, particularly of the head of the humerus, and of the glenoid which is flat. Ossification may be delayed and there may be delayed fusion with the shaft. There is often delay in ossification of the carpus and the patella. The lower ends of the radius and ulna may be deformed as in the Morquio-Brailsford type. The long bones of the hands may be short, thick and honeycombed, with the bases of the metacarpals pointed. Symmetrical thickening of the lateral aspect of the upper femoral shafts was seen in two cases, but precisely similar thickening was seen in one case of the Morquio-Brailsford type of chondro-osteo-dystrophy.

Progress—Sometimes the condition remains stationary but as a rule there is gradual deterioration and the child dies before growth is complete. Five patients, ranging in age from one to three and a half years, all died before reaching the age of eight years.

Pathology—Tuthill (1934) first recorded the finding of lipoid in the brain with changes corresponding to those of juvenile amaurotic idiocy. Ashby et al. (1937) reported autopsy findings in two cases and confirmed these observations: they did not find evidence of lipoid deposit outside the nervous system but thought nevertheless that the condition must belong to the lipoidoses; they suggested that the lipoid was not in pure form but was combined with protein; and they found changes in the thyroid gland and were convinced that in both cases there must have been hypothyroidism. Kressler and Aegerter (1938) are credited with the first demonstration of extracerebral lipoids in the liver, spleen, cornea and pituitary, but not in the bones.

Diagnosis—The distinctions between gargoylism and the Morquio-Brailsford type of chondro-osteo-dystrophy have already been discussed. Differentiation from cretinism, which has often been the first diagnosis, is made more difficult by the fact that angular kyphosis with diminution in the size of one vertebral body may sometimes be observed in a true cretin. On two occasions we have seen a similar spinal deformity in patients with all the signs of achondroplasia but without the other features of gargoylism. Congenital syphilis can be excluded by the Wassermann reaction and by the entirely different appearance of the bones (Ellis et al. 1936). In one case reported by Ellis et al. there was a suspicion of acromegaly because the faces was suggestive and the pituitary fossa was large, but such differentiation should soon be made easy when it is recognised that in chondro-osteo-dystrophy growth is retarded and not accelerated.

REFERENCES

Henderson, J. L. (1940): Archives of Disease in Childhood, 15, 201.
CASE 14—GARGOYLISM

(Figs. 39–43.) Male, aged two and a half years. Deformity of chest noticed at nine months; becoming worse. Kyphosis present at eleven months. Head large; facies heavy. Backward but no gross mental deficiency; squints. Limitation of movement of some joints, especially the shoulders. Hands spade-like; fingers curved. Stands with hips and knees flexed. Knock-knee. No corneal opacities. Liver and spleen not enlarged. Umbilical and left inguinal herniae. Radiographs: sella enlarged; spine typical of gargoilism with lumbar kyphosis; clubbing of lower ribs; bilateral coxa valga; metacarpals of typical shape. Two other children both normal. (Under Mr Eric Lloyd.)

Case 14. Photographs showing the large head and typical heavy features. Note the typical attitude on standing with the hips and knees flexed, and the lumbar kyphosis.

Case 14. Showing enlargement of the sella turcica (Fig. 40) and enlarged acetabula, poorly formed roofs, and a mild degree of coxa valga (Fig. 41).
Case 14. Lateral radiograph of the spine (Fig. 42) showing the apex of the kyphosis formed by the second lumbar body which is small (L12 is without corresponding ribs). The bodies of the second and third lumbar vertebrae show a beaked shape. There is some enlargement of the anterior parts of the ribs. Lateral radiographs of the spine taken in flexion (Fig. 43) show that there is much greater forward movement of the first lumbar vertebra, occurring at the intervertebral joint between it and the small displaced second lumbar body, than at any other level of the spine.
CASE 15—GARGOYLISM

(Figs. 44-47.) Male, aged three years. Mentally backward. Corneae cloudy. Facies coarse and heavy. Head large; bossing above ears; eyes widely separated; bridge of nose broad; teeth spaced; hair coarse, eyebrows thick. Liver and spleen enlarged. Nasal discharge. Unable to sit up. Well-defined angular kyphosis in upper lumbar region. Some scoliosis. Limitation of movement of the elbows. Radiographs: coxa valga; femoral necks long; acetabular roofs sloping; skull large; pituitary fossa enlarged antero-posteriorly; no sign of erosion; second lumbar body rather small, of typical shape, and slightly displaced backwards; other bodies biconvex. Biochemical investigations revealed nothing of importance. (Under Dr Wilfred Sheldon.)

Case 15. Lateral radiograph of the skull (Fig. 44) shows the abnormal size of the sella turcica, which has a smooth, sharply defined outline. Radiograph of the hand (Fig. 45) shows the abnormal shape and texture of the bones. The bases of the metacarpals are somewhat pointed. The radius and ulna are thick and the lower ends of their shafts deformed.

Case 15. The roof of the acetabulum is poorly formed on both sides and the femoral heads lie a little high (Fig. 46). There is bilateral coxa valga and the femoral necks are of unusual length. Radiograph of the spine (Fig. 47) shows an angular deformity with the apex at the second lumbar vertebra, the body of which is small, beaked and displaced a little backward. The other vertebral bodies are biconvex and not flattened.
CASE 16—GARGOYLISM

(Figs. 48-51.) Male, aged nine years. Mentally backward but talkative and observant. Walked at the age of one year. Noticed to be clumsy with his hands at the age of two years. Definitely dwarfed. Head not unduly large. One eye removed for glioma of retina. Spleen just palpable; liver not enlarged. Some limitation of movement of the shoulder, elbow, hip and knee joints. Fingers short and stubby; joints thick; extension limited. The three inner fingers curve towards the first. Bones of the arms, forearms, and wrists feel thicker than normal. Radiographs: sella small; long bones thickened; coxa valga; acetabula of better shape than usual; spine typical. Blood examination: nothing of significance. He is the seventh of a family of seven, the eldest being twenty-eight. (Under Dr E. A. Cockayne.)

Figs. 48-49
Case 16. Photograph of the child at the age of nine years (Fig. 48) shows that the face is by no means typical. The arms are rather short. Radiographs of the skull showed a small sella turcica and no signs of frontal sinuses which should be visible at this age. The spine (Fig. 49) shows biconvex bodies, the second lumbar being rather small and of typical beaked shape; a suspicion of a similar shape is seen in the third and fourth lumbar bodies.

Figs. 50-51
Case 16. The right forearm (Fig. 50) shows stout bones, impaired ossification of the lower radial and ulnar epiphyses and of the carpus, and abnormal shape and texture of the bones of the hand. Note the tilting of the lower ends of the radius and ulna. The femora show unusual thickness (Fig. 51). The symmetrical thickening of the lateral cortex is curious but is not regarded as significant; similar thickening has been seen in a case of chondro-osteodystrophy of the Morquio-Brailsford type.