DYSOSTOSIS MULTIPLEX :

PFAUNDLER-HURLER SYNDROME

REPORT OF TWO CASES

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Pfaundler reported two cases to the Medical Society in Munich which were described in detail in 1919 by his assistant Hurler. They displayed the following unusual combination of congenital anomalies : clouding of the corneae, a deformity of the skull (oxycephaly), a disproportionate dwarfism strongly resembling that of hypothyroidism and associated with some of the usual signs of that condition (saddle nose, mental defect, dry skin, inguinal and umbilical herniae, crura valga, pedes valgi), a contraction of the fingers, limitation of movement in other joints (shoulders, elbows, knees) and defective hearing, to mention only the most striking features. Pfaundler at once suspected that he was dealing with a new syndrome. His assumption proved to be correct, as since his publication, twenty more cases have been recorded in Britain, America and Germany, showing the same combination of anomalies.

I recently had the opportunity of observing two similar cases in China. The publication of these seems to me to be justified, not only on account of their rarity, but also because the patients were brothers, because they are the first of their kind observed in China, and because they both presented in addition to the anomalies described by the other authors, a bilateral Sprengel's deformity (congenital elevation of the scapula) which was present, but overlooked in some of the previous cases. The name dysostosis multiplex was recently proposed for the syndrome. I consider it more suitable than the name gargoylism, proposed by Ellis and his associates.

Case reports

History.—The mother is Chinese, and forty-five years of age. She has never been seriously ill. She had one miscarriage at the sixth month and six full-term pregnancies. Two of the children died from infectious diseases at the ages of ten and twenty-one years respectively. Two daughters, who have both been examined, are normally developed, anaemic, generally weak, but not otherwise abnormal. The father of the patients died from haemoptysis at the age of thirty-four. The maternal grandmother is sixty-four and had seven children ; one of them died two days after birth. The mother of the two patients here described was her second child. The third child died at the age of seven months, the fourth at the age of nine, the fifth at one year. The sixth child is alive and

healthy. The seventh child died at the age of sixteen years from heart disease. No deformities were noticed in the seven children nor in the ancestry. The paternal grandmother had six children, one of whom died from diabetes. The paternal grandfather died from syphilis. The present two patients were full-term children. The older will be called hereafter 'A', the younger one 'B.' During the fourth month of pregnancy of 'B' the mother took some Chinese drugs to induce abortion; they caused haemorrhage. At birth 'A' and 'B' were of normal size; each had an umbilical and bilateral scrotal hernia. The corneae of 'A' were clear; those of 'B' were cloudy. Both were breast fed. They only started walking and talking at the age of five years. The mother noticed in 'A' after one year, in 'B' after six months, that growth was retarded.

FIG. 1.

They seemed to her of normal size at birth. 'A' started to stand at the age of one year; he could speak a few words, but his mental development subsequently stopped; the mother thought this due to continuous intercurrent diseases (colds and coughs). 'A' always suffered from difficult, asthma-like respiration. 'B' suffered only from colds.

Examination of 'A'.—The patient was twelve years old; his growth was stunted, and he had the appearance of a malproportioned dwarf. His height was 1.155 metres on February 27, 1935. On April 14, 1935 (after thyroid therapy), and again on June 16, 1935, he measured 1.177 metres.

The expression of his face was idiotic; the face was puffy and the lips thick. He spoke only a few words, and could not answer simple questions, but

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he recognized people and was aware of his surroundings. He was of passive character. He did not attend school, and could not read or write. His gait was heavy.

The skin was dry and scaly, and covered with fine lanugo ; he frequently scratched himself. The skull was larger than normal and was out of proportion to the rest of the body ; its circumference was 54 cm., the occipito-frontal diameter was 18.3 cm., the biparietal diameter 14.5 cm. ; the occipital region was pointed, the forehead well arched ; the occiput fell abruptly from the vertex ; it was flat and ran parallel to the plane of the face. The fontanelles were closed ; the sutures could not be felt. The ears stood out abnormally and were rather low set. The root of the nose was flatter than that of a normal Chinese. There

FIG. 2.

was a constant dribbling of saliva from the open mouth ; the teeth were irregularly set, partly in two rows. There were twelve teeth in the maxilla and ten in the lower jaw. The jaws were massive. The right cheek was pushed forward by a tumour the size of a walnut which was localized in the horizontal part of the mandible, corresponding in position to the first molar tooth ; it was bony hard, well defined, and felt like an exostosis of the mandible. The tonsils were large. The neck was short ; neither the thyroid nor the cervical lymphatic glands could be palpated.

The distribution of the subcutaneous fat in the body was normal, with possibly a slightly increased adiposity above and around the hips. The thorax was rather emphysematous ; no rosary of the ribs was palpable. Posteriorly,

there was a remarkable elevation of both scapulae, which were raised to the level of the upper margin of the shoulders. They were converging towards the head ; the inner border stood away from the thorax. The distance of the right angulus scapulae from the middle line was 6 cm., and that of the left 7 cm. The movements of both shoulder joints were considerably restricted ; active flexion and abduction of both arms was possible only up to the horizontal. During abduction the two shoulder blades stood out like wings, and the distance of the angulus from the mid-line was 10 cm. During forward elevation the angulus slipped as far as to the mid-axillary line (13 cm. from the middle line). The rotation in both shoulder joints was normal. No defect of any muscle could be detected either from configuration or function. The active movements of the body were normal. There was no deformity of the spine, and no cutis laxa. There was limitation of extension of both elbows of approximately 20°. There was clinodactyly of the fourth and fifth fingers (with convergence towards the radial side). The end of the fifth finger only reached the middle of the middle phalanx of the fourth finger. No obvious limitation of extension of the fingers was noticed, except that there was a tendency to hold the two thumbs in a flexed position.

A reducible umbilical hernia and bilateral indirect inguinal herniae were present ; all three were of the size of a man's fist. The penis was small and retracted into the hernial sac. The testicles were of the size of olives.

There was bilateral genu valgum of moderate degree, and limitation of extension of both knees, the maximal passive extension being 165°. This limitation was not due to the deformity of the knee.

The pulse was 96, regular and soft. The heart was enlarged towards the right side. There was a blowing systolic murmur in the mitral area. There were signs of bronchitis over both lungs. The abdomen was soft, with considerable divarication of the recti. The liver was enlarged, the upper border reaching the nipple line, the lower border being 5 cm. below the costal margin. The spleen was of normal size on percussion, and was not palpable.

OPHTHALMIC REPORT (Dr. Meyerbach).—Vision in both eyes approximately 0.2, binocular approximately 0.25. There was a diffuse dense clouding with turbid patches of both corneae strongly resembling keratitis parenchymatosa. The disc was pale on both sides, but not light enough to justify the diagnosis of optic atrophy. The pupillary reaction to light and accommodation was retarded ; one hour after application of homatropine they only dilated to a moderate degree and were normal.

The neurological findings were normal.

The urine was acid ; calcium oxalate was present ; there was no albumin and no sugar. The stool was normal.

Blood count : white blood cells 7,600 per c.mm., neutrophils 79 per cent., lymphocytes 16 per cent., mononuclears 5 per cent., eosinophils 0, basophils 0, no pathological forms. Haemoglobin 80 per cent.

Blood sugar : 130 mgm. per 100 c.c. blood. Chlorides : 511 mgm. per 100 c.c. blood.

Cerebrospinal fluid : clear, 5 cells per c.mm. Wassermann negative, Kahn negative, Nonne-Appelt negative, Pandy negative.

Basal metabolism : 16.3 per cent., at 37° C. temperature ; pulse 100 ; respiration 24.

For the purpose of testing the function of the hypophysis the water excretion was measured by Hoff's method under the following conditions : first without interference, secondly applying diathermy to the head (two poles bitemporal) for 15 minutes, immediately after the intake of fluid, and thirdly after an injection of pituitan. The result of the three experiments, carried out by Dr. F. Halpern on three successive days, showed that pituitary extract did not decrease,

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and diathermy of the base of the skull did not increase, the diuresis, as it does under normal conditions. From this finding, dysfunction of the hypophysis was considered probable.

Water excretion of the kidneys :

8 A.M.				INTAKE	1000 C.C.	SPECIFIC GRAVITY 1000
9 a.m.	..	..	..	output	180 cc..	
10 a.m.	..	..	..	„	100 c.c.	
11 a.m.	..	..	..	„	250 c.c.	1001
12 noon	..	..	..	„	60 c.c.	1001
2 p.m.	..	..	..	„	40 c.c.	1010
4 p.m.	..	..	..	„	33 c.c.	1013
				Total	660 c.c.	

Examination of ‘B’.—The patient was nine years old and was much smaller than the average child of his age. He resembled his older brother in every respect, so much so that I shall emphasize the differences between the two to avoid repetition. His height was 1·072 metres on February 27, 1939. On March 14, 1935 (after thyroid therapy) it was 1·076 metres ; on June 16, 1935, it was 1·08 metres, and on October 30, 1935, 1·095 metres.

The expression of the child was similar to that of ‘A’ though he was a little more intelligent. He took more interest in his surroundings, spoke more coherently, and had a bigger vocabulary. He was more cheerful and happy than ‘A’ ; he looked around the room, enjoyed playing, understood jokes, but did not read or write. His smile was like the risus sardonicus. The face was puffy and the skin similar to that of ‘A.’ In general he was the alter ego of his older brother. The circumference of the head was 52·5 cm., the fronto-occipital diameter 17·5 cm., the bitemporal diameter 12·5 cm. The skull was a little tower shaped ; the two temples were protruding ; the fontanelles were closed ; no ridges or sutures were palpable. The bridge of the nose was flat. There were twelve teeth in the upper and ten in the lower jaw ; none were of Hutchinson type. The tumour described in ‘A’ was missing.

The neck was short ; the thyroid gland could not be palpated. The thorax was narrow and flat in the upper region, and wide and barrel-shaped in the lower. The spine was deformed : there was a dextroconvex dorsal, and a sinistroconvex lumbar scoliosis with considerable torsion. The scoliosis was of a fixed type. The two scapulae were highly placed (see x-ray picture) ; they stood away from the thorax and their lower angles were divergent. The length of the scapula was 11 cm. (in the sagittal line), the greatest width 12 cm. ; they were mobile, and no bony strings were palpable around them. Both active and passive movement in the shoulders was much restricted : the lateral elevation on the left side amounted to 70°, on the right side to 80° ; elevation in front was 80° on both sides. The distance of each angulus scapulae from the middle line was 7·5 cm. during frontal elevation, and 13·5 cm. during lateral elevation. There was no paralysis of the shoulder muscles ; the patient could be lifted up by the elbows with adducted arms. All the muscles were present and their function was normal.

The movements of the two elbows were restricted ; active and passive extension could only be effected to an angle of 175°. The two thumbs showed flexor contraction and otherwise were of the same shape as those of ‘A’ (see x-ray picture). The other fingers were also similar to those of ‘A.’ There was no sign of rickets in the bones.

The knees could only be extended to 160° . There was a marked degree of genua valga and pedes plano-valgi. An umbilical hernia the size of an apple, and a right indirect reducible inguinal hernia the size of a child's head, reaching nearly down to the knees, were present.

The temperature was normal; pulse 87, regular and feeble. There was nothing abnormal in the heart; in the lungs there were signs of a mild bronchitis. The liver and spleen were of normal size; considerable divarication of the recti was present.

The right angulus was at the level of the fifth rib, the left at the level of the seventh; both were laterally dislocated. The left clavicle was horizontal, the right directed upwards corresponding to the higher scapula. The humeri and the rest of the visible skeleton appeared normal.

LABORATORY INVESTIGATIONS

Urine: albumin 0, sugar 0.

Blood count: leucocytes 7,900 per c.mm., haemoglobin 80 per cent., neutrophils 44 per cent., lymphocytes 50 per cent., normoblasts 6 per cent.

The Wassermann reaction of the blood was negative.

Cerebrospinal fluid: clear, 18 cells per c.mm., Nonne-Appelt + + +, Pandy + + +, Wassermann + + +, Kahn +.

Blood sugar: 131 mgm. per 100 c.c. blood.

Blood chloride: 478 mgm. per 100 c.c. blood.

The water excretion test of Hoff gave a similar result to that in case 'A.'

OPHTHALMIC REPORT.—Palpebral fissure—Right 25 mm., Left 25 mm.

Vertical diameter of the corneae—Right 11.5 mm., Left 11.5 mm.

Horizontal diameter of the corneae—Right 12 mm., Left 12 mm.

Radius—Right 9.1 mm., Left 9.1 mm.

Refraction—Right 37 dioptries, Left 37 dioptries.

There was a marked diffuse clouding of the corneae which made the pupils so dim that an examination of the fundi was impossible. The reaction of the pupils was sluggish; half an hour after homatropine application they were only semi-dilated.

Fig. 3 of patient 'A' shows the high position of the scapulae.

FIG. 3.

FIG. 4.

RADIOLOGICAL EXAMINATION.—Skull of 'A' (reported on by Mr. Norman Dott). Large slightly hydrocephalic type skull, a little thinner than the average. Thickness of vault remarkably even. Slight fullness in temples suggests increased pressure in later childhood (cf. oxycephaly). Sutures abnormally fused—even the coronal difficult to make out—yet sparse diploic venous channels clear enough. Frontal and mastoid cells practically absent. Sphenoidal cells absent. Sphenoid solid cancellous bone. Sella turcica small, rounded

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cavity surmounted by short, thick dorsum sellae and indefinite decalcified posterior clinoid processes. Region of tuberculum sellae and anterior clinoids relatively low level, continuing straight back on level of olfactory plate instead of rising up ; also rather decalcified. 'Middle clinoid process' (completing carotid canal under anterior clinoid) ossified on one side. The whole picture suggests moderate hydrocephalus—not now actively progressive, and abnormal obliteration of suture lines.

Skull of 'B' : Similar features generally, but a younger skull ; it is not so

FIG. 5.

FIG. 6.

large and is less hydrocephalic ; suture lines of coronal and lambdoid visible though inconspicuous. Large, relatively symmetrical frontal diploic venous system. No sphenoidal air sinus. Floor of the anterior fossa continues back in low level, dipping gently into average-sized sella without any eminence of tuberculum sellae. Anterior clinoids are low set, not otherwise abnormal unless slightly decalcified. Dorsum sellae thick cancellous bone, average height. Poorly formed posterior clinoids (normal for age ?).

In addition to the retarded pneumatization of the sinuses, the extremely bulging temples and the unusually shaped massive, broad mandibular bone should be noted.

The x-ray pictures of 'A' and 'B' show no signs of rickets. The meta-

FIG. 7.

carpal bones are all present ; there is no retardation in their development. The terminal phalanx of both thumbs is in flexor position, the bones of both are cone shaped. The fifth finger of 'A' and the fourth and fifth fingers of 'B' show a strong inclination towards the radial side. The first phalangeal bones of 'B' are very large and clumsy. The middle phalanx of the fifth finger of 'A' is shortened, the diaphysis and epiphysis being nearly equal in length. Both hands show a certain webbing of the fingers.

To recapitulate briefly the findings in these two patients, the first point of interest is that they display a combination of exactly the same symptoms. The only difference between the two was that 'A' had a tumour-like swelling of the mandible, which was absent in 'B,' and that 'B' showed a scoliosis missing in 'A.' The cephalic signs were as follows : a deformity of the skull simulating oxycephaly, a massive broad jaw, delayed dentition, low-set ears, defective hearing, and congenital clouding of the corneae.

A second series of anomalies could be grouped under the heading endocrine disturbances, somewhat resembling myxoedema and consisting of dwarfism, diminished intelligence, broad saddle nose, dry puffy skin, congenital umbilical and congenital bilateral inguinal herniae, reduced basal metabolism, diminished water excretion, crura valga, and pedes plano-valgi.

The third group of signs concerns the osseous system (excluding the skull).

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In both patients there was a bilateral elevation of the scapulae (Sprengel's deformity), restricted movement of the shoulder, elbow and knee joints, and flexion-contraction of the fingers with minor deformities of the phalanges.

Discussion

The following is a summary of the cases published hitherto and a discussion of the author's two cases in relation to the others. Since Pfaundler described two cases in 1919, twenty further cases have been recorded, the total number being now twenty-four. There is reason to assume that dysostosis multiplex is not as rare as this low figure suggests. Helmholtz and Harrington (1931) reported four cases and had knowledge of two others in the United States. Jewesbury and Spence (1927) observed one, Ellis and his associates (1936) seven cases in England, Putnam and Pelkan (1925) another case in U.S.A. Pfaundler's original two cases came from Germany, and mine come from China, a wide geographical distribution. In addition, single cases have been described by Liebenam, Binswanger and Ullrich, Slot, Ellis (1937, 1938) and Ashby et al.

Sex.—Out of twenty-four cases thirteen were boys, eleven girls. The two cases known to Helmholtz and Harrington were boys; both sexes seem to be equally affected.

Age.—All patients previously recorded were children between the second and seventh year, except one girl of eighteen years (Ellis), another of fifteen (Liebenam), and a boy of nineteen years (Ashby); the author's two cases were nine and twelve years old. A lowered resistance seems to prevent survival for long. The general inclination to colds is probably due to their narrow air passages. In the author's cases cardiac function was bad.

The syndrome is definitely hereditary, in spite of Hurler and Putnam, who claim otherwise. Of the twenty-four cases recorded the two cases of Helmholtz and Harrington were brothers, two were brother and sister and my two were brothers. A sister of the case I of Ellis had the same condition (case 2 Ashby). Jewesbury and Spence mention that a child of a paternal uncle had claw fingers, and resembled their case in appearance.

The deformities and anomalies are all congenital, that is to say that patients are born either with some anomalies or with the potentialities for their development. The signs and symptoms are discussed in three groups; first the anomalies of the head, second anomalies due to endocrine disturbances, third anomalies of the skeletal system apart from the skull.

Head.—The study of the skull in dysostosis multiplex is much less complete than that of such related conditions as oxycephaly. The reasons for this are that there have been only three post mortem records of dysostosis multiplex, and a thorough study of the skull in the living individual is bound to be incomplete and the majority of cases were in children in their first years when the skull is not yet definitely formed. The available reports and the x-ray pictures show that not one skull amongst the twenty-four was normal. They are described as scapho-, oxy-, trigono- and brachy-cephalic, and usually present

signs of early hydrocephalus, and a premature fusion of the sutures. The striking similarity between the oxycephalic skulls and those of dysostosis multiplex will be discussed later.

The sella is usually abnormal in size and shape, in some cases enlarged, in others small. In four cases of Ellis, in one case of Jewesbury and Spence, in one case of Helmholz and Harrington and in two cases of Ashby and in that of Slot the sella was very elongated, but without evidence of bone erosion. The clinoid processes were often described as abnormal. In the autopsy of Hurler's case there was bowl formation of the sphenoid and the lamina cribrosa. In the middle fossa there were several bone defects of the size of a lentil, bridged by a fibrous membrane. There were exostoses on the base of the skull, but no sphenoidal sinus and no diploë present.

The signs of early hydrocephalus are of interest in the etiology of the condition ; they will be discussed elsewhere.

Clouding of the corneae was present in all the twenty-four cases, was congenital, and was usually so diffuse that it made examination of the fundi impossible. In some cases there were multiple punctate opacities, chiefly in the deeper layer of the cornea. The anomaly is considered in the literature to be due to an arrested development of the corneae. The author at first took its occurrence in his two cases for a syphilitic keratitis parenchymatosa, owing to the history of syphilis in the family and the positive Wassermann reaction in the cerebrospinal fluid in one of the brothers. But syphilis in China is so common that the post hoc ergo propter hoc is certainly not justified, especially as in all other cases there was no sign of syphilis. The Wassermann reaction was always negative. The blood Wassermann reaction of the mother in my two cases was negative, and there were no other signs of a syphilitic nature, either in the two patients or in their two sisters. Whilst the real nature of this anomaly is unknown, it is certainly not syphilitic.

In Helmholz and Harrington's second case puffiness of the eyelids and narrowing of the palpebral fissure were noticed—signs to which the author attaches much significance. Internal strabismus was noticed in the case of Putnam and Pelkan.

In all cases where the ears were mentioned they were set very low, as may be seen in the picture of my two children. Defective hearing, also present in the author's two cases, is mentioned by Pfaundler and Helmholz, and Liebenam and Binswanger. As a thorough examination of the ears was not obtained it is difficult to say whether the defective hearing was due to a retarded perception and slow reaction of unintelligent children or whether there was a real organic central or peripheral lesion. More stress should be laid on this point in future.

The tongue when mentioned in the reports was described as very large and often protruding from the mouth.

Endocrine disturbances.—Under this heading are summarized, rightly or wrongly, a group of signs which also occur in some known endocrine dysfunctions, although it may be said from the outset that they did not react to endocrine therapy. These signs are : (1) a characteristic facies ; (2) diminished intelligence and torpidity ; (3) dwarfism ; (4) dry pasty skin ; (5) con-

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genital herniae ; (6) low basal metabolism ; (7) water retention ; (8) a dysfunction of the hypophysis in some cases with enlargement of the sella.

Concerning the facies, reference to the photograph (fig. 1) shows the similarity of the cases, a similarity so striking, that Pfaundler's first case, in spite of being a German child, resembles my Chinese children as much as if they were brothers. This striking resemblance, like that amongst acromegalic and cretinous individuals, is to be expected in an endocrine disturbance.

The intelligence was normal only in Liebenam's case. Helmholtz and Harrington described one case as mentally alert, but this statement about a child of seventeen months has to be accepted with reservation. All the other children were mentally retarded, more or less. There was difficulty in speaking, a symptom mentioned by nearly all authors, and torpor very similar to that of cretinism. The mental capacity did not improve on administration of thyroid in any case.

The dwarfism was disproportionate owing to the size of the head. The limbs were not strikingly out of proportion to the body. The shortness of the neck was due to the undescended scapulae. The degree of retardation of growth and the presence of hypogenitalism are difficult to judge, because only three patients reached adolescence. The retardation in growth was noticed in the author's cases at the age of six and twelve months respectively, a retardation attributed in other cases by the mothers to an intercurrent disease. Dwarfism was observed in twelve out of the twenty-four cases; in the others it was not noticeable, probably on account of the early age. It is significant that thyroid and pituitary extract medication did not influence growth appreciably. In the two females that reached puberty (Ellis and Liebenam) hypogenitalism was recorded with delayed menarche.

The dry, scaly skin, present in both the author's cases, is mentioned by Pfaundler and others. The puffiness of the face is described in several cases. Contrary to expectation in all the cases in which mention was made of the skin, a hypertrichosis was present : the body was covered, at least in parts, with a kind of lanugo, and the eyebrows were very well developed and dense, reaching to the mid line.

Large umbilical and bilateral inguinal herniae were present in both the author's cases, and a congenital inguinal hernia with or without a congenital umbilical hernia was recorded fifteen times out of twenty-four.

The basal metabolism and water excretion, not tested by the others, were considerably decreased in the author's cases ; Hoff's functional test of water excretion indicated a dysfunction of the hypothalamus or hypophysis.

The sella turcica has been described in detail ; and although it may appear at first sight to be enlarged, on account of the widening of the introitus to the sella and the flat enlargement of the sulcus chiasmatis, there is no indication of an enlarged hypophysis. The abnormal configuration of the base of the skull is rather the result of an early hydrocephalus. The hypophysis was normal at autopsy of Hurler's case, but much enlarged in Ashby's two cases.

All the symptoms just enumerated fit into the picture of a hypothyroidism, including dysfunction of the hypophysis, which is very often, though not always,

associated with hypothyroidism. Against the assumption of myxoedema are the normal ossification of the carpal bones (fig. 7), instead of retardation : the frequency of hypertrichosis, uncommon in myxoedema : and the failure of thyroid treatment to improve the mental state, promote growth or alter the facies and skin of the patients. There is no satisfactory explanation of these discrepancies. Ashby found on histological examination a foetal character of the parenchyma of the thyroid in one case and atrophy with secondary fibrosis in the other.

Osteoarticular anomalies.—There was great variation in the intensity and localization of the signs in the twenty-four cases under review. The upper extremities were usually more affected. The long bones had often a heavy square appearance. The pathological changes increased towards the distal ends. There was no evidence of rickets, except in two cases of Helmholtz. The fossa glenoidalis and the acetabulum were often described as shallow, the head of the femur and humerus as flat. A coxa valga was recorded twice by Ellis and once by Slot. The genua valga and pedes plano-valgi, present in the present two cases, were described also by several other authors. The case of Helmholtz displayed crura vara, one of Ellis' bilateral pes equinovarus, that of Slot a pes cavus, with an enlarged big toe. Minor deformities of the bones of the hand were present in several cases, and are to be seen also in fig. 7.

One of the most characteristic features is the restricted extension of the shoulders, elbows, fingers and knee joints. The most marked contractions were seen in the fingers ; described sometimes as 'claw fingers.' Flexion was always free. The limitation of the shoulder movements was due in my two cases, and in at least five others, to bilateral undescended scapulae.

Hurler noticed in one case a subluxation of the capitulum of the proximal phalanges towards the vola manus. The distal end of the radius and ulna were found irregular in the cases of Helmholtz and Slot. A broadening and thickening of the long bones are a common sign.

In one case mention is made of 'an unusual angulation of the collum humeri' by Hurler.

Deformity of the spine was present in all the cases recorded, except Putnam's, eighteen times in the form of a kyphosis, once (case 'B') as an S-scoliosis, twice as a kypho-scoliosis. Ellis and associates attribute the spinal deformities to a peculiar malformation of the vertebral bodies, which are irregular, flattened or wedge-shaped in outline, and may be considerably reduced in size. The vertebral body has often an anterior hook-like process. Ellis had an opportunity of comparing the radiological changes of the vertebral bones in Morquio's disease and in dysostosis multiplex, and says that 'too much emphasis cannot be placed on minor differences, unless these are found to be constant in a large number of cases, and at first sight one would be struck by the similarity rather than dissimilarity of the two types.' The peculiar wedge-shaped vertebrae are certainly of congenital nature, similarly to the deformities of the other bones. In my two cases there was no x-ray evidence of vertebral deformities. (No picture was, however, taken of the lumbar spine.)

One of the most conspicuous features of the present two cases was the

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bilateral elevation of the scapulae (Sprengel's deformity). It is of interest not only because of the relative rarity of the bilateral form of this anomaly, but also because it supports the view as to the etiology of this intricate syndrome. Incidentally it indicates that a considerable number, if not all, cases of Sprengel's deformity are of hereditary origin, a view not yet generally recognized.

It is not surprising that the presence of this deformity has not been mentioned by any of the former authors, though its symptoms have been correctly described by some of them, and shown very conspicuously in a picture by Putnam, and the x-rays of Liebenam. A bilateral Sprengel escapes attention more readily than a unilateral one. If there are restrictions of other joints, the otherwise pathognomonic restriction of movement in the shoulders is easily misinterpreted as being in line with the contractions of the other joints (and dealt with summarily) and dismissed.

Hurler described in her first case the shoulder symptoms as follows: 'Die Hebung der Arme im Schultergelenk ist eingeschränkt. Heben gelingt nur bis zur Schulterhoehe durch starke Mitbewegung des Schulterblattes. Die Rotationsbewegungen bei fixierter Scapula nach vorn und rueckwaerts in geringem Umfang moeglich'—a typical description of the symptoms met with in cases of Sprengel's deformity. The malformation of the scapula in her second case is also characteristic of the same disease. She says 'The substance of the shoulderblades appears very compact, the acromion much enlarged, the articular surface shallow and small.' Putnam says: 'The scapula, which appeared rather small and far apart, rotated strikingly as the arms were elevated, so that the outer borders and angles protruded several centimetres on each side of the body.' His picture is a typical example of an elevation of the scapula. In the x-ray of Liebenam's case the right scapula is at the level of the first, and the left scapula at the level of the second rib.

From these descriptions one can clearly recognize the presence of Sprengel's deformity in five cases. Helmholtz mentions in the history of case 1 that one maternal uncle of his patient had a large head and another 'a prominent shoulder girdle.' He mentions in two of his cases 'a short and thick neck,' also recorded by others, and in another, limitation of the shoulder movements. These signs may well have been due to elevation of the scapulae.

From this evidence it seems to be justifiable to include Sprengel's deformity as one sign of dysostosis multiplex. Elevation of the scapulae is rarely bilateral. Hayashi and Matsuoka collected from the literature up to 1912 only fifteen bilateral as against a hundred and ten unilateral cases. Out of the ninety-two cases collected by Horwitz, sixty-seven per cent. were associated with some other defect in another part of the body, a fact in line with experience of dysostosis multiplex, and pointing to its hereditary origin.

The discussion of the individual signs of dysostosis multiplex and their occurrence in the published cases shows that, in spite of their large number, there is a surprising constancy in their combination, with only minor variations in their degree. There is justification for considering the peculiar combination of these signs as a constant syndrome. How far this syndrome should be demarcated from others, will be discussed elsewhere.

Summary

Two cases of dysostosis multiplex of the Pfaundler-Hurler type (gargoylism), occurring in two Chinese brothers, are described in detail. In addition to the usual signs, both patients showed bilateral undescended scapulae (Sprengel's deformity), a sign that was present but overlooked in some of the cases previously described. It seems to be a part of the whole syndrome. The etiology will be discussed elsewhere.

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