AMYOPLASIA CONGENITA ASSOCIATED WITH MONGOLISM

BY

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The rare condition known variously as multiple congenital articular rigidity, arthrogryposis multiplex congenita and amyoplasia congenita has been made known in this country mainly by the work of W. Sheldon⁹, who introduced the name used in this paper. A further title has been applied by D. S. Middleton¹, who uses the term myodystrophia foetalis deformans, as being more accurately descriptive of its probable pathogenesis. The present case is particularly interesting on account of its association with mongolism and because of certain similarities between the two conditions. The presence of deformities of the bones in the affected joints is also noteworthy.

Case report.

The patient, a girl, aged seven-and-a-half years, was admitted to the Fountain Hospital for mental defectives on November 8, 1933.

Family history. The parents are unrelated and were both twenty-nine years old when the patient was born. The father, a mechanic, is stated to be normally intelligent and in good health. The mother is of fair education and intelligence, but 'highly-strung.' The patient was the last of three pregnancies; the first child, now a boy of fourteen years, is said to be normal in every way and to be doing well at school, and the second was a three months' miscarriage. No abnormalities or further points of interest in the family history can be discovered.

Gestation and birth. Except for 'some haemorrhage after a long omnibus ride which passed off after a night's rest' in the third month of pregnancy, the mother enjoyed good health until the sixth month, when she suffered from a considerable amount of vomiting, especially at night. She experienced no severe shocks, falls or accidents of any kind nor had she been irradiated by x-rays or radium. The child was born at full term and delivery was rapid (first stage—3 hours; second stage—10 minutes; third stage—5 minutes). Birth occurred in an unreduced right occipito-posterior position with extended legs, the face and brow presenting themselves first. The amount of amniotic fluid was normal and there was no premature rupture of the membranes. The placenta was cyanotic in appearance. Birth weight was 6 lb. (I am indebted to the British Hospital for Mothers and Babies, Woolwich, for this information as regards labour). The mother reports that the baby's weight soon went down to 3 lb. and that she was so flaccid that her head 'flopped back to touch the middle of her back.' Her legs were deformed from birth and appeared to be 'back to front.'

Early childhood. At the age of eight weeks she attended the Royal National Orthopaedic Hospital, and to the authorities there my thanks are due for the following information. She was found to be suffering from congenital genu recurvatum, severe bilateral congenital equino-varus and cervical opisthotonus. Her musculature was very poor. She was treated by stretching and splinting and later by tenotomy of the tibiales tendons. At the age of two years she was admitted to the Hospital's country branch, where daily manipulations, stretching and treatment by means of the mercury vapour lamp effected some improvement. Whilst there she suffered from paroxysmal tachycardia.

State on admission. She was a fairly well-nourished girl of seven-and-a-half years, suffering from a severe degree of mental deficiency and a remarkable deformity of the lower limbs. She was considerably below average height and weight and showed many mongol characteristics, her general appearance, skin, hands, palate, ears, epicanthus, flabbiness and hypotonia and especially her articulation, mannerisms and general personality being typical of this condition.

Physical characters. Her head circumference was nineteen-and-three-quarter inches (50 cm.) and her cephalic index 71, denoting a rather more dolicocephalic configuration than is usually associated with mongols. Another trait uncommon in mongolism was shown in her possession of curly hair. Her eyes appeared to be widely separated and the palpebral fissures small, because of a well-marked bilateral epicanthus. The space between the eyes was 36 mm. Pupil reactions, vision and fundi were normal. The ears were small and lobeless. The hard palate was high and narrow-arched, with a long overhanging soft palate; the tonsils were large and unhealthy; the buccal mucous membrane was hyperaemic and always liable to inflammation and ulceration and the gums were spongy. Her hands were short and podgy and her skin scaly and dry.

Speech was monosyllabic, explosive, very indistinct and typically mongol in character. Her words were usually accompanied by simple gestures and she made no attempt to string together even elementary phrases. Lalling was exhibited in her substitution of T for hard C or K. Her contours were rounded owing to subcutaneous fat, but her muscles were flabby and toneless and her ligaments very lax. Abnormal mobility was present at all joints except the knees and ankles, where deformity was present. The extreme range of movement at the hip joint can be seen in fig. 1 and her ability to entwine neighbouring toes was remarkable.

Cardiovascular system. No obvious heart lesion was present, but her peripheral circulation was poor and she was subject to frequent chilblains. This picture of peripheral stagnation is, of course, not confined to mongols, but outside mongolism it is mainly found in anergic aments of low grade.

Central nervous system. Knee and ankle jerks were impossible to obtain owing to her deformities. Tendon reflexes were sluggish, but equal. Plantar reflexes were flexor and abdominals present and equal.

Other systems were normal. Serum Wassermann and Meinicke macroklarung reactions were negative.

Deformities. There was a bilaterally symmetrical genu recurvatum of such a degree that the knees appeared to be facing backwards (fig. 2). The legs were usually held in a position of hyperextension, and flexion beyond 180 degrees either by active or passive movement was impossible. The whole range of movement at the knee joint was approximately thirty degrees.

FIG. 1.—General appearance. Note hyper-mobility at hip-joint.

FIG. 2.—Walking position.

The patellae were not palpable. The feet were fixed in an extreme varus position with some degree of equinus (fig. 3). Practically no movement could be elicited at the ankle joints.

Gait. She was unable to walk or even assume an upright posture, but was able to get about very actively on all fours, progressing in a typically simian manner. Her weight was borne mainly on her palms and on the dorsal surfaces of her feet, her legs being hyperextended and her buttocks sticking out prominently in a backward and upward direction (fig. 2). She was wont to end her journeys with a rapid turn into a sitting position and an exceptionally beaming smile.

X-ray examination. Skiagrams showed no bony abnormalities except in the region of the knee joint. Here gross deformity and posterior subluxation of the lower end of the femur was apparent. The patellae could be faintly seen well above their usual site and were obviously undeveloped (fig. 4). The hip joints showed no sign of dislocation. Dr. Peter Kerley was kind enough to examine the films and reported that the structure of the bones and epiphyses was normal and that there was no sign of developmental or acquired lesion. The muscles showed no radiological abnormalities. Soft x-rays were not taken.

Mental state. INTELLIGENCE. Her mental age was approximately two years. She could point to her nose and was able to pick out, but not name, common objects, such as a penny, key, pencil or scissors. She could obey simple orders, but was unable to execute two consecutive commissions. She failed to give her name or sex, but was able to recognize a paper-wrapped sweet and would undo it before putting it into her mouth. Her attention was difficult to hold and she did not try to co-operate in any way. She was unable to use a spoon and made no effort to help in dressing or undressing herself. Her habits were faulty and she required every personal attention.

BEHAVIOUR. She was a lively and mischievous child, inclined to be aimlessly destructive with toys and other objects. The simplest kind of constructive playing was quite beyond her powers. Her nature was cheerful and contented and she seldom cried. She liked plenty of attention and appeared to take considerable pleasure and pride in strutting round in front of other children or visitors. Her smile, her mannerisms and her whole nature were typical of the mongol.

Progress. She soon settled down happily, showing interest in her surroundings and neighbours and becoming a general favourite. Her physical condition, like her character and conduct, conformed to mongol expectations and she soon showed herself to be delicate and to have little resistance against infection. In January, 1934, she suffered from cellulitis of the right leg and thigh, in February from Vincent's angina, which cleared up rapidly after two arsenical injections, and in March from a feverish cold and cough. During June she became much more subdued and lacking in energy. No physical signs to account for this were present, but she went off her food and was obviously unwell. She recovered, however, and was quite at her best until she contracted scarlet fever in September. On January 7, 1935, she was put to bed with an ordinary afebrile cough and cold. No physical signs developed, but, as in June, she was very listless and 'floppy.' Three days later she died suddenly, shortly after sitting up in bed quite happily and comfortably.

FIG. 3.—Showing the deformity of the feet. Note wide space between first and second toes.

FIG. 4.—X-ray of knee-joint,

Pathological examination. A substantial layer of subcutaneous fat was present, but the muscles were pale and exiguous. The heart was exceptionally large and heavy, weighing 184 gm. There was general muscular hypertrophy, but no dilatation. The right side was filled with dark coloured clot. There were no congenital anomalies. The liver was pale and greasy and weighed 539 gm. Sections showed a state of extreme fatty degeneration with moderate venous engorgement. The nuclei were well preserved, but the cytoplasm was almost entirely replaced by fat, especially in the neighbourhood of the hepatic veins. The thyroid approximated to the foetal type. The acini were small and the colloid scanty. There was proliferation both of the epithelial cells and of the inter-acinous fibrous tissue. The brain weighed 1,134 gm. and, as the shape of the skull suggested, was not as rounded as is usual in mongolism. A small tumour about the size of a large pea was found attached to the wall of the right lateral ventricle. Sections showed it to consist of choroid plexus tissue. The lungs, kidneys, spleen, pancreas, suprarenals, ovaries, thymus and pituitary body showed no naked-eye or microscopical abnormalities.

FIG. 5.—Knee-joint.

KNEE JOINT (fig. 5). The tibia was subluxated forwards on the femur, apparently owing to the anterior part of the femoral condyle having failed to develop. Not more than 30° of movement was possible and the joint became locked at 180° . The existence of the semilunar cartilages and of the cruciate ligaments could not be definitely determined. If the latter were present, they must have been greatly stretched out. The muscle tissue, normally to be found around the joint, was for the most part replaced by fibrous tissue and fat, embedded in which were areas of calcification. Apart from this the muscle was of normal appearance.

Discussion.

The present case differs from other published cases of amyoplasia congenita in several ways. In the first place normal intelligence has been definitely recorded in the majority of cases and mental deficiency has only once been noted (Middleton). Secondly, the distribution and position of the deformities do not fall in with any of Rocher's three main clinical

types⁵, although these types are by no means all embracing. Of greater interest is the occurrence of actual hyper-extension at the knees with complete flexion-inability beyond 180°. Although extension deformity at the knee joints, usually in combination with abnormalities of other joints, has been commonly described in this condition (Rocher^{5, 6}, Rocher and Ouray⁷, Sheldon⁹, Middleton¹, Schapira⁸), no record of the deformity reaching such a degree of genu recurvatum has been discovered by the writer. Thirdly, x-ray examination has shown in most cases that a normal bony disposition is a feature of the affected joints. The presence of osseous deformity as seen at the lower end of the femur in this case is exceptional. There can be no doubt that this deformity, as well as that of other joint elements, is secondary to the muscle defect and the fact that bony changes occur so seldom suggests that the condition does not arise until late in foetal life.

There can be no doubt that the present case was one of mongolism, despite some minor discrepancies, such as the shape of the head and the curly hair. Mongolism is remarkable for the large number of its physical signs and for the fact that no one of them is invariably present. Despite this there is usually sufficient evidence, as in this case, to make the picture unmistakable.

The maternal and pre-natal history shows no evidence of early amniotic infection, a possibility suggested by Price, unless the previous miscarriage be considered as suggestive of low-grade uterine infection.

Diagnosis.

The diagnosis of amyoplasia congenita cannot be considered as certain in this case, but several factors point very strongly to this condition. The main features of amyoplasia congenita may be said to be:—

- (1) Congenital joint rigidities of varying degree, usually symmetrical and always without inflammatory change.
- (2) Hypoplasia or degeneration of those muscles which normally produce the movements which the child is unable to perform.
- (3) Absence of any hypertonia or hypertrophy of antagonistic muscles, showing that the immobility is not attributable to muscular overaction.
- (4) Sudden checking of movement at the affected joints, which no application of force can increase, pointing to bony or fibrous changes of the joint structures. The fact that mobility is not increased under general anaesthesia corroborates the last two points.
- (5) Weak or absent faradic responses in affected muscles, but no reaction of degeneration.
- (6) No sensory or trophic changes.
- (7) Normal intelligence.
- (8) Extensive fibro-fatty changes in the affected muscles.

The present case illustrated the characteristic type of joint rigidity, sudden checking of movement, and absence of hypertonia and sensory or trophic change. Electrical reaction tests were unfortunately not available at the hospital and the child was physically unfit to travel. Only one

previous case appears to have suffered from mental defect, but in the present case this was but a part of the syndrome of mongolism, the association of which with amyoplasia congenita must now be considered. The characteristic fibro-fatty changes were found in the muscle tissue in the neighbourhood of the knee-joint.

Mongolism and amyoplasia congenita.

There would appear to be no obvious association between mongolism, which is probably caused by some defect of maternal or foetal metabolism in the early weeks of intra-uterine life, and amyoplasia congenita, which appears to be due to a more or less localized muscular maldevelopment; and it may be said at once that etiological connection is unlikely. There are, however, individual points of similarity. The pseudo-oedematous appearance, due to a generalized subcutaneous fatty deposit is common to both conditions. Sections show this deposit to be true fat. The musculature shows a certain superficial similarity, but microscopy reveals a very different picture. No gross abnormalities are found in mongol muscle, whereas the affected muscles in amyoplasia congenita show only a few healthy muscle fibres, the remainder being replaced by fat and fibrous tissue. It is worthy of mention that neither syndrome shows any hereditary or familial tendency, although a definitely hereditary condition occurs in lambs (Roberts^{3, 4}), which is clinically and pathologically akin to amyoplasia congenita. The age of the mother and other etiological factors significant in mongolism have yet to be ascertained in cases of amyoplasia congenita. Lastly the facial resemblance between the present case and Fairbank's third case⁹ is not without interest.

In the present case only the characteristic deformity of the knee joints and to a lesser degree of the ankles was peculiar to amyoplasia congenita. The condition of the muscles, except in the immediate neighbourhood of the knee joints, could equally well be attributed to mongolism. On the other hand, the local picture is so typical of amyoplasia congenita that this diagnosis cannot be reasonably withheld.

Pathogenesis.

The various theories of the causation of this condition have been reviewed and discussed by Sheldon, who maintains that the joint-structure deformities are secondary to the muscle changes and that the primary defect is in the nature of a developmental aplasia or hypoplasia of certain muscle groups. More recently Middleton¹ has described atrophic changes in the affected muscles more suggestive of a degeneration in the later stages of intra-uterine life than an actual hypoplasia. The changes resembled those seen in some cases of muscular dystrophy and Middleton believes amyoplasia congenita (myodystrophia foetalis deformans) to be a pre-natal form of myodystrophy. It is true that his evidence is drawn from a single case, which was complicated by what appeared to be an upper motor neurone

lesion, but he has also described a similar, though more active process of muscle degeneration in the closely related condition of congenital 'stiff jointed lambs,' described by Fraser Roberts^{3,4}. This condition differs from the one under discussion in that it is definitely hereditary and has been proved to be due to a simple autosomal recessive factor.

In other cases of amyoplasia congenita there has been found a simple replacement of muscle by fat and fibrous tissue, mainly the former, and when muscle fibres remain, they are of normal appearance. When a somatic structure fails to develop or when it has completely atrophied, it is usual for fat to take its place, so that the fatty changes seen in the affected muscles do not favour the one theory more than the other. The evidence in favour of Middleton's myodystrophic theory rests almost entirely upon the finding of actually degenerating as opposed to hypoplastic muscle tissue in one case. The absence of degenerative changes in other examined cases may, however, be due to the atrophic process having been completed, and therefore invisible, at the time of histological examination. If muscle sections could be examined in the later stages of intra-uterine life, as was done in that case of Roberts's lamb disease which showed actively degenerating muscle, a similar picture of atrophic process might well come to light.

The possibility of a nervous origin has been suggested by the case, originally published by Dorothy Price², in which Middleton found atrophic changes. In this case atrophy of certain muscle groups and limitation of joint movements were associated with a generalized spasticity, with adduction spasm of the legs, in fact, a congenital spastic diplegia. The pathological findings of a diffuse chronic meningo-myelitis and mild hydrocephaly support this conclusion and the fact that 'the anterior horn cells appeared to be normal in size and number' is directly antagonistic to a neuronie conception of the origin of the muscle defect. In uncomplicated amyoplasia congenita there is no spasticity and no hypertonia of antagonistic or other muscles, the limitation of movement being entirely mechanical and not due to muscular spasm.

It would appear that both Price's and the present case are true examples of amyoplasia congenita, the former complicated by congenital spastic diplegia and the latter by mongolism. There is at present no valid evidence that amyoplasia congenita is due to a lesion of nervous structure, all available histological findings pointing to the muscle as the primary pathogenic site. It has not, however, been definitely established whether the lesion is hypoplastic or, as seems more probable, atrophic.

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NOTICE TO CONTRIBUTORS.

It is proposed to publish from time to time reports of single cases which are of special interest and importance.