MYOSITIS OSSIFICANS PROGRESSIVA

Report of a Case in which A.C.T.H. and Cortisone Failed to Prevent Reossification After Excision of Ectopic Bone

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Myositis ossificans progressiva is a rare disease. Strictly, it is misnamed, for the essential pathological change is a metaplasia of connective tissue in and between muscles, leading to the progressive formation of embryonic connective tissue, adult connective tissue, cartilage and bone. Degeneration of muscle fibres and sarcolemmal proliferation follow; the bone formed may contain marrow and is not chemically different from ordinary bone. Sites of this metaplasia may be indicated first by localised, sometimes haemorrhagic, swellings in muscle, appearing spontaneously or after injury. Occasionally familial or twin incidence has been reported and males are affected slightly more often than females. Onset may be in the first year of life, is common in early childhood and rare after adolescence. If tendons are ossified the radiographic appearance may suggest diaphysial aclasis. There is commonly an associated microdactyly affecting the great toes. The main sites of ossification are the muscles of the trunk, the masseters, and the upper arms; the neck and external laryngeal muscles may also be involved. Those of the eye, face, diaphragm, heart, perineum, sphincters and larynx have not been observed to be affected. Excision of ectopic bone has usually been followed by recurrence. Death has commonly followed increasing rigidity leading to pneumonia or chronic sepsis from bed sores. The blood chemistry (including estimation of the serum alkaline phosphatase) has previously been reported to be normal.

This rare disease has recently been reviewed by Fairbank (1950) and Maudsley (1952), and Briggs and Illingworth (1952) have added further cases, the latter recording the results of cortisone treatment. In the case to be described here the patient's metabolic state was investigated fully before and after excision of a mass of bone from the neck (Fig. 1). It was hoped to prevent subsequent reossification by A.C.T.H. and cortisone.

CASE REPORT

The patient was a girl twelve years old at the time of investigation. When she was four she had a cervical abscess after an attack of tonsillitis; the abscess was drained. Soon afterwards localised nodules were noticed in the neck and shoulders. Further swellings developed during the next few months in the neck, back and pectoral and axillary regions. A nodule was excised for pathological examination. The appearances were mostly those of a granulation tissue response to an inflammatory lesion, but the examination did not throw any further light on their cause. Radiographs at that time showed a calcified shadow in the axilla suggestive of myositis ossificans. Other areas of ectopic ossification were subsequently demonstrated.

Limitation of movement in the neck and shoulders increased progressively, and by the time she was eleven there was also a fixed flexion deformity of the left hip which was treated by X-ray therapy with some improvement.

Detailed clinical description—Abnormal areas of new bone formation were present in the posterior cervical region, extending from the occiput to the upper thoracic vertebrae. Neck movement was severely restricted and movements of the neck were accompanied by movements of the right scapula. There was some lateral rotation to the right but only a very small
range of flexion. Nodules of bone were present in both axillae, in the lower thoracic region posteriorly, and in the anterior abdominal wall. In the lower limbs, hip movements were fairly free on the right, but on the left there was a flexion deformity of 50 degrees and the range of flexion was through only a few degrees. A good range of knee and ankle movements was retained. The tendon reflexes were not impaired. In the upper limbs, shoulder abduction was limited to 30 degrees on the right and 50 degrees on the left. Flexion was similarly reduced. The pectoral muscles were diffusely infiltrated with bone.

No abnormality was found in the cardiovascular system. The lungs were normal. Chest expansion was two inches.

Radiographic examination—The pituitary fossa was not enlarged. The neck showed a solid bar of bone extending from the occiput to about the level of the spine of the second and third thoracic vertebrae (Fig. 2); there was a further smaller bar on the right side of the neck behind. There was evidence of congenital fusion of all the cervical vertebrae except the first and seventh. The cervical vertebral bodies and spinous processes were poorly formed. There were irregular masses of bone in both axillae and scapular regions. The shoulder joints, forearms and hands appeared normal. In the lower limbs the shafts of the long bones were normal, but there were multiple slender exostoses round the knee joints.

In the trunk a solid mass of bone extended downwards from the right lower thoracic region posteriorly, where it was attached to several ribs (Fig. 5). It reached down to the level of the fourth lumbar vertebra. Additional smaller pieces of bone were present on the left side. The lumbar spine showed multiple congenital abnormalities of the articular facets and pedicles. There appeared to be partial fusion of the sacro-iliac joints with a few small plaques of bone in the soft tissues: these were most marked around the neck of the left femur. Both femoral necks were deformed and the acetabula were shallow.

Biochemical investigations (Fig. 1)—Examinations six years before the present investigation had shown serum calcium level of 8.7 milligrams per 100 millilitres, phosphorus 3.8 milligrams per 100 millilitres, alkaline phosphatase 20-9 phenol units per 100 millilitres, and erythrocyte sedimentation rate 7 millimetres in one hour. Investigations at the time of her admission
to the metabolic ward (Fig. 1) gave the following results. *Serum constituents* (per 100 millilitres)—calcium 9:6 milligrams, magnesium 2:4 milligrams, phosphorus 4:8 milligrams, albumin 3:5 grammes, globulin 3:2 grammes, $\text{CO}_2$ combining power 64 vols., alkaline phosphatase 23:5 phenol units, and vitamin C 1:5 milligrams. *Renal function tests*—Blood urea 43 milligrams per 100 millilitres, urea clearance 100 per cent of normal, phosphorus clearance 13 millilitres per minute (normals range from 8–25 millilitres per minute) increased
to 19 millilitres per minute after parathormone. Urine contained a trace of albumin and a few pus cells but no excess of amino-acids. **Calcifying tendency of serum**—Incubation of a slice of a tibial epiphysis of a rachitic rat in the patient's serum by Robison's (1932) technique showed greatly increased tendency to deposition of bone salt compared with the serum of a normal child of about the same age which contained calcium 10 milligrams and phosphorus 4 milligrams per 100 millilitres.

*Treatment and progress*—The child was placed on a low calcium diet containing 0.35 grammes of calcium, 0.48 grammes of phosphorus, and 50 grammes of protein, on which she appeared to be in equilibrium. Her serum calcium 9.6 milligrams per 100 millilitres and phosphorus 4.8 milligrams per 100 millilitres, giving $\text{Ca} \times \text{P}$ of 46, suggested that the rather high serum phosphorus value was contributing to the high calcifying tendency. Another factor influencing calcification by the humoral mechanism is the concentration of magnesium (a high magnesium value inhibiting), but the serum magnesium of 2.4 milligrams per 100 millilitres was in the normal range.

After one week a diet containing 0.89 grammes of calcium, 1.25 grammes of phosphorus, and 70 grammes of protein was given; on this diet she maintained a slight positive balance of each constituent. It was thought that the calcifying tendency of her serum might be decreased if a lower phosphate level could be produced. Attempts to do this were made by administering alumina to reduce phosphate absorption from the gut. Aludrox (5.6 per cent aluminium hydroxide) was given, the dose being increased from 1 ounce per day initially to 2 ounces after three days and thereafter four ounces daily for one week. At the same time the phosphorus intake was reduced to 0.4 gramme daily. On this regimen the blood phosphorus was not appreciably changed, but the urine phosphorus was reduced from 600 milligrams per diem to 60 milligrams.
Operation—Four weeks after her admission to hospital the middle two-fourths of the bony bar running down the back of the neck was excised by Mr J. A. Cholmeley in an attempt to restore lateral flexion of the neck (Fig. 3).

Pathological examination of excised bone (Dr H. A. Sissons)—The specimen consisted of normal dense lamellar bone, and showed a central "marrow cavity." It was too dense to be suitable for histochemical examination. The surface of the surrounding fibrous tissue showed a layer of osteoblasts and recently formed bone trabeculae, and in the immediate neighbourhood of these a considerable amount of alkaline phosphatase could be demonstrated. The remainder of the fibrous tissue and muscle was entirely devoid of bone, and no alkaline phosphatase could be demonstrated in it. No abnormal metachromasia was demonstrable in the fibrous tissue. Chemical analysis showed water 20 per cent, ash 52 per cent, calcium 18.7 per cent, phosphate 26 per cent, protein 21 per cent, carbonate 3.05 per cent. These values are within the limits accepted for normal bone.

Post-operative treatment—From one week after operation 15 milligrams of ACTH were given four times a day for twenty-five days. The diet contained 600 milligrams of calcium and 1,100 milligrams of phosphorus, on which a slight positive calcium balance was maintained.

Thereafter cortisone was given by mouth in the following dosage: 50 milligrams six-hourly for three days; 25 milligrams six-hourly for three days; and 25 milligrams eight-hourly for seven days. No demonstrable change in the metabolism of calcium, phosphorus or nitrogen was produced by ACTH or cortisone (Fig. 1).

Further progress—The patient was discharged from hospital after completion of the treatment described, but she continued to take cortisone in doses of 12.5 milligrams four times a day (50 milligrams a day) for a further three months.

Up till that time (four months after operation) there was no clinical evidence of reossification in the area from which the bone had been excised. There was a range of 45 degrees rotation of the head to the right and 30 degrees to the left; a small range of flexion and extension was possible. A month later the range of movement was unchanged. But after a further two months (seven months after operation) the patient reported that she had noticed a swelling deep to the scar on the back of the neck for a previous three weeks. Radiographs showed a zone of irregular ossification at the site of operation (Fig. 4). Critical re-examination of the earlier post-operative radiographs showed that progressive ossification had in fact begun to occur nine weeks after the operation.

Comment—There are no exact data on the rapidity of reossification at the sites of injury or operative intervention in myositis ossificans progressiva. Nevertheless it seems certain that in this case cortisone in the dosage given had no effect in retarding the process of re-ossification, which was manifest only nine weeks after excision of a bar of bone.

SUMMARY

1. A metabolic study in a case of myositis ossificans progressiva is reported.
2. The serum showed an increased power of calcification of rachitic rat cartilage.
3. Estimations of alkaline phosphatase showed slightly raised values.
4. Surgical removal of a bony bar was followed by prolonged administration of ACTH and cortisone, but no effect on the calcium-phosphorus balance or on the re-ossification within the area of operation was observed.

REFERENCES


