Orthopaedic management in four cases of mucolipidosis type III

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Four patients with mucolipidosis type III, three of them brothers, were seen initially in the first two decades of life. Their main symptoms were carpal tunnel syndrome, trigger fingers and generalized joint stiffness. Radiographs showed spinal deformities and hip dysplasia, but these were not causing pain. Carpal tunnel syndrome was treated surgically but joint stiffness and hip and knee contractures were managed by physiotherapy. Up to the age of 24 none of these patients has had pelvic osteotomy for hip dysplasia; this operation, not yet reported in mucolipidosis type III, may eventually be necessary.

INTRODUCTION

Mucolipidosis type III, first described by Maroteaux and Lamy in 1966[1] is of milder severity than the Hurler syndrome and similar to the Scheie syndrome but without hepatosplenomegaly, cloudy cornea or mucopolysaccharidiuria[2]. The basic defect is in post-translational modification of lysosomal enzymes, leading to a failure of targeting to the lysosome. The severe form of the defect is usually known as I cell disease (mucolipidosis type II). We review four patients with this rare condition, three of whom were from the same family, with particular reference to the orthopaedic complications and their management.

CASE HISTORIES

Case 1

This patient was referred because of short stature when 16 years old. His parents were first cousins. He had three brothers, two of whom were also short for their age. On examination he had claw hands, mandibular prognathism, lumbar hyperlordosis and fixed flexion deformities of both hips and knees. There was no excess of mucopolysaccharides in the urine but the finding of raised plasma hexosaminidase and alpha and beta mannosidase with normal plasma acid phosphatase suggested a mucolipidosis. His three brothers were also assessed and two of these (cases 2 and 3) had similar clinical and enzymatic pictures. He was then referred for an orthopaedic assessment.

Bilateral clinodactyly and brachydactyly was noted, with wasting of the thenar muscles on the left. Nerve conduction studies indicated median nerve entrapment at the wrist. Wrist, elbow and shoulder movements were all restricted and he was unable to raise his arms above his shoulders; radiographs showed glenohumeral and acromioclavicular dysplasia (Figure 1). Similarly spinal movements were restricted, with a lumbar hyperlordosis. On radiography of the thorocolumbar spine there was beaking and hypoplasia of the vertebral bodies (Figure 2). He had fixed flexion deformities of 30° affecting both hips and 15° affecting both knees. Radiographs of the pelvis showed hip dysplasia (although both femoral heads appeared well covered), flaring of the iliac wings, and platyspondyly of the lower lumbar vertebrae. Initial management was conservative except for the median nerve entrapment, treated by carpal tunnel decompression with initial success. Physiotherapy seemed of some benefit in that the deformities did not progress, although there was no real improvement in the

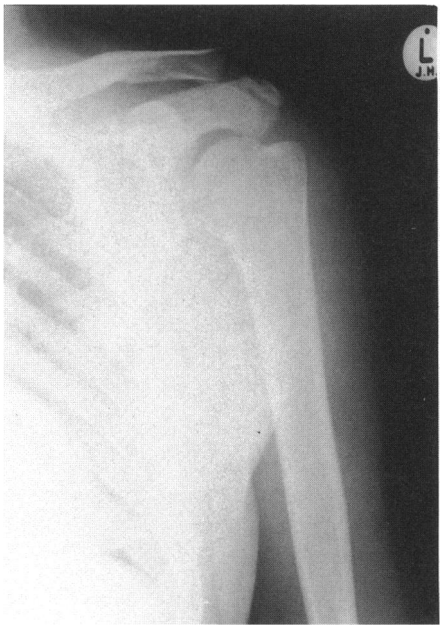

Figure 1 **Shoulder dysplasia in case 1, age 16**

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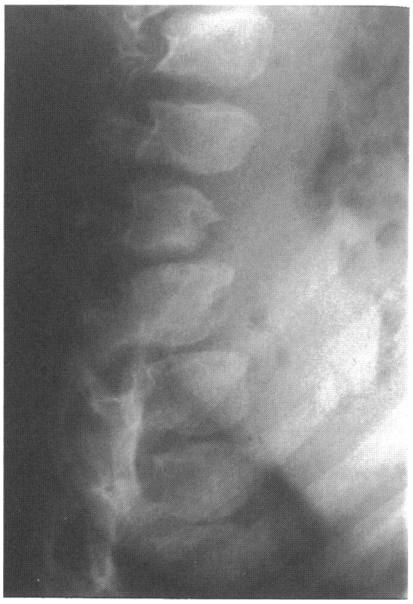

Figure 2 **Vertebral hypoplasia and beaking in thoracolumbar spine, case 1**

range of movement. The patient is now 24 and works as a petrol attendant.

Case 2

When first examined at age 15 this patient had severe clawing of the hands and wasting of the thenar eminences bilaterally. He described paraesthesiae and pain in both hands, and nerve conduction studies confirmed median nerve entrapment at the wrist bilaterally for which he underwent decompression. More recently he reported intermittent triggering of the left ring finger. Radiographs of his hands and wrists show dysplastic ends to radius and ulna bilaterally and small dysplastic carpal bones. The metacarpals have flattened ends whilst the phalanges are rectangular in shape, the clawing clearly visible (Figure 3). Wrists, elbows and shoulders were also stiff, and like his older brother the patient was unable to lift his arms above his shoulders. He had a lumbar hyperlordosis with reduced spinal movements and fixed flexion deformities affecting hips and knees.

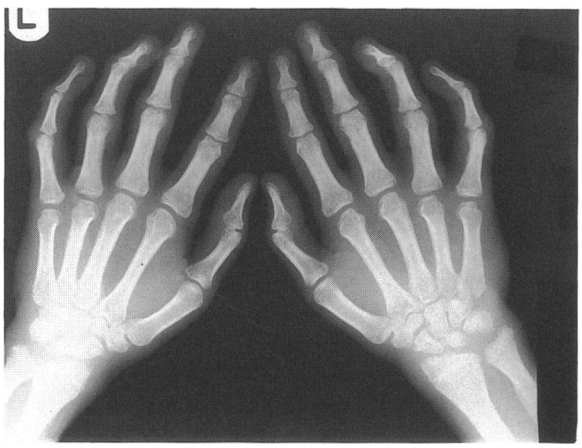

Figure 3 **Flattening of the metacarpal heads and rectangular shape of phalanges, case 2**

At age 23 he is now 4 ft 11 in (1.5 m) tall. His upper limb symptoms have changed little but his spinal disease seems to have deteriorated. He now has a fixed lumbar scoliosis, although without neurological deficit. His hip and knee flexion deformities have improved with physiotherapy. Lately he has developed clawing of the lesser toes and flexion deformities of the interphalangeal joints of the great toes. He has also acquired callosities at the ends of the great toes but currently feels that he can manage with padded insoles. Radiographs of his feet show flattening of the ends of the metatarsals and cystic changes to the interphalangeal joint of the left great toe.

Case 3

The third brother, diagnosed at 14 years old, seemed the worst affected. He had similar changes in his upper limbs although there was no median nerve entrapment. Spinal movements were reduced and he had the most severe lumbar hyperlordosis. He also had the greatest degree of fixed flexion deformity to the hips and knees. Neurological examination suggested weakness in both lower limbs, though magnetic resonance imaging of the spine did not indicate root or cord compression at any level. Remarkably the flexion contractures improved dramatically with physiotherapy. At presentation there was severe hip dysplasia with poorly covered femoral heads, but follow-up radiographs showed improved containment despite the conservative approach (Figure 4). Clawing of all toes was managed with padded insoles. He is now 20 years old and a student.

Case 4

This girl was referred at 4 years old with pain in her right hip and knees. She was the first baby and had been born normally at full term. Her parents are unrelated. She was late to walk at 23 months. On examination she was seen to walk with in-toing on the right side; hip movement was normal apart from reduced external rotation; and she had clawing of the hands and stiff upper limbs such that she was unable to raise her arms above her shoulders. Enzyme studies revealed features consistent with mucolipidosis type III. Figure 5 shows severe right sided hip dysplasia with a poorly covered femoral head. The patient might benefit from a pelvic osteotomy but, since there are no hip symptoms, no decision regarding surgery has been made.

DISCUSSION

The most troublesome features of mucolipidosis type III, in the first two decades of life, are orthopaedic in nature. Carpal tunnel syndrome has been well documented[4].

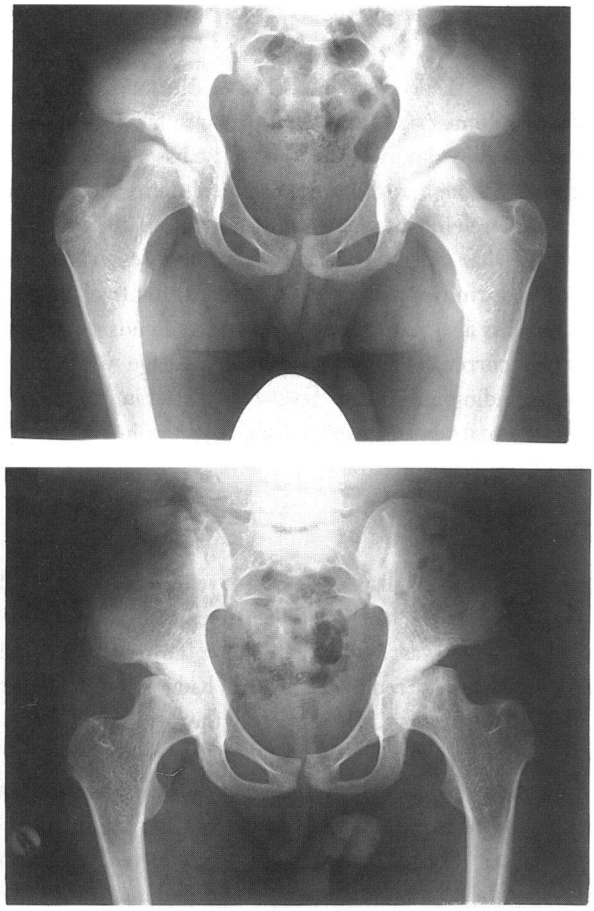

Figure 4 **Radiographs of pelvis, case 3: (*a*) Poor acetabular cover of femoral heads bilaterally, worse on the right; (*b*) follow-up radiograph 6 years later, showing improved cover to both femoral heads**

Recurrent intermittent triggering of the fingers is less of a nuisance in this group, perhaps because of the stiffness already present. Generalized joint stiffness is difficult to treat. Despite intensive physiotherapy there was little increase in the range of movement except in the hips and knees, where flexion contractures improved sufficiently to avoid the need for soft tissue releases. Spinal complications were limited to the lower thoracic and lumbar spine, no

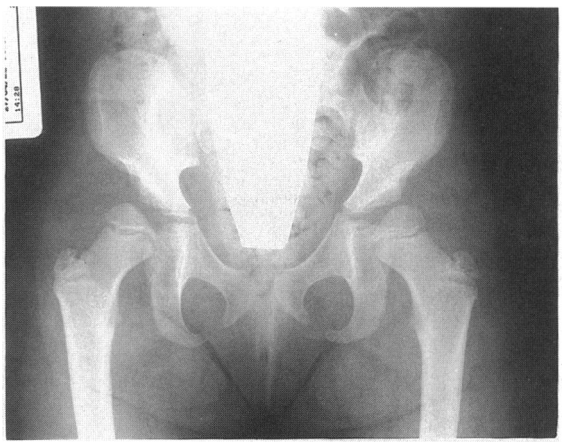

Figure 5 **Radiograph of 4-year-old girl (case 4) with dysplastic hips**

patients in our series having the cervical involvement reported previously[3]. There was no obvious relation between the radiological findings in the spine and the degree of clinical involvement, patients complaining little if at all of back pain. Hip pain and stiffness were universal features. Flexion contractures improved consistently with physiotherapy. Severe dysplasia may be an indication for surgery but this approach has not been reported. Foot deformities, a late complication, can initially be managed conservatively.

Overall, young patients with mucolipidosis type III complain little despite substantial musculoskeletal disease.

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