**CASE REPORT**

**Bilateral hip replacement in three patients with lysosomal storage disease: Mucopolysaccharidosis type IV and Mucolipidosis type III**

The management of joint replacement in lysosomal storage diseases has not been well reported. We present three patients with progressive degenerative changes of the hips who required bilateral total hip replacement in early childhood. The stature of the patients make it essential to have access to appropriately scaled prostheses. Consideration has to be given to associated disorders of the skeleton which must be carefully screened to ensure safety in providing appropriate anaesthesia as well as ensuring that there is no cardiac abnormality. In one patient, a periprosthetic fracture was sustained in one hip in the early post-operative course requiring internal fixation.

The patient made a full recovery and all six hips were clinically and radiologically satisfactory at mid-term review.

Lysosomal storage diseases are an inherited group of heterogeneous human disorders characterised by the accumulation of partially degraded macromolecules intra-lysosomally. This results in an increase in the size and number of these organelles and ultimately in cellular dysfunction and clinical abnormalities. They can be generally classified by the accumulated substrate and they include Mucolipidoses and Mucopolysaccharidoses amongst others. Mucopolysaccharidosis Type IV, also referred to as Morquio disease, first reported by Morquio, and Brailsford, shows an autosomal recessive hereditary pattern with a reported incidence varying between 1:76 000 and 1:450 000. Defective degradation of keratan sulphate and chondroitin-6-sulphate leads to damage of connective tissue resulting in spondyloepiphyseal dysplasia, including dysplasia of the vertebrae, hypermobility of the joints and ligaments, cardiac valve lesions and corneal opacities. Two types have been described: a more severe form, type A, which is caused by a deficiency in N-acetylgalactosamine-6-sulphatase (chromosome 16q) and the rarer form, type B, which is caused by a deficiency in β-D-galactosidase (chromosome 3p). The most severe form presents with spinal deformities, which occasionally lead to paralysis, dwarfism, hip dysplasia and damage to the cardiac valves. The major orthopaedic manifestations include shortening of the trunk and limbs, spinal curvature, abnormal hip development and malalignment of the lower limbs. The pelvis typically shows dysplastic acetabula, flared ilia, dysplastic femoral heads, short and wide femoral necks with valgus deformity and subluxation of the hip with the development of a neocacetabulum and a wide symphysis pubis. Neurological dysfunction, due to cervical cord compression, can also occur. The presence of odontoid hypoplasia may allow atlantoaxial subluxation with the consequent of the spinal cord being crushed on C1 as the hypoplastic dens slips under the anterior arch of C1 during sudden forward flexion of the head. This can be prevented by operative craniocervical stabilisation. The major anaesthetic consideration is cervical hyperextension during intubation with subsequent spinal cord compression.

Mucolipidosis II and III are disorders of lysosomal enzyme phosphorylation and localisation caused by deficiency of N-acetylgalacosaminyl-1-phosphotransferase, leading to accumulation of glycosaminoglycans and sphingolipids in cells. There are two phenotypically different diseases: Mucolipidosis II (I-Cell Disease) and the rarer form, Mucolipidosis III (pseudo-Hurler polydystrophy). Both are autosomal recessive, Hurler-like disorders. Skeletal involvement is prominent, in particular, dysplasia of the vertebral bodies, pelvis and proximal femora.
The most significant orthopaedic consideration in these storage diseases is hip dysplasia leading to secondary degenerative arthritis. The treatment of this specific hip pathology with bilateral hip replacement has not been extensively reported and we present three cases of bilateral hip replacement in patients with these diseases.

**Case reports**

**Case 1.** This seven-year-old girl presented with an increasingly abnormal gait. Radiographs of the lumbar spine showed characteristic flattening of the vertebral bodies with central projection suggestive of Morquio disease. There were also irregular acetabula with shortened thick femoral necks and flattening of the capital femoral epiphyses. Confirmation of the diagnosis by enzyme assay was not undertaken due to the distinctive clinical features. Despite physiotherapy her condition deteriorated and she developed a marked Trendelenberg gait.

At 25 years of age she had increasing disability caused by pain in the right hip. Her walking distance was reduced and she had pain at rest. Her height was 154 cm, suggesting that she was unusually mildly affected, and probably suffered from Morquio type B disease.

Examination revealed a fixed flexion deformity of the right hip of 15° with flexion to 70°. It was not possible to abduct or adduct the hip and there was little rotation. Radiologically there was complete loss of the joint space. Radiographs of the cervical spine showed a hypoplastic dens and atlanto-axial subluxation on forward flexion of 5 mm.

Right total hip replacement (THR) was performed with a cemented Ogee acetalubar component (DePuy, Leeds, United Kingdom) and cemented Elite CDH femoral stem (DePuy) under spinal anaesthetic and post-operative recovery was uneventful. At follow-up at 16 weeks post THR, the right hip was pain-free but mobility remained severely restricted because of pain arising from the left hip. Radiographs revealed marked degenerative change (Fig. 1). She underwent a cemented left THR 15 months after her first operation using the same hip system. Once again the recovery was uneventful.

At follow-up after seven years she was mobilising independently without aids and had no symptoms in her hips. The radiographs revealed no signs of loosening (Fig. 2).

**Case 2.** This ten-year-old girl presented with widespread restriction in the movement of the fingers, wrists, shoulders and spine. Her hips had reduced rotation and abduction. Intensive physiotherapy was prescribed. As the progressive nature of the disease manifested itself, Mucolipidosis Type III was suggested as the diagnosis. Radiographs revealed delayed bone age, atypical carpal bones, wedging of the T6 and T9-11 vertebrae, and marked bilateral acetabular dysplasia with subluxation of the femoral heads. The diagnosis was confirmed by elevated plasma lysosomal enzymes. Conservative management was continued, including pain management. At age 13 years her flexion contractures had progressed to 40° at the right hip and 30° at the left, and she was only able to mobilise using elbow crutches. At 17 years the pain from her right hip was severely restricting her walking distance and she was unable to attend school. Her height was now 127 cm and her right leg was shorter than the left by 2 cm with marked restriction of movement. Radiographs revealed destruction of the right femoral head and neck, with a shallow acetabulum. THR was recommended. Radiographs of the cervical spine showed no atlantoaxial subluxation. Electro- and echocardiograms showed no evidence of a cardiomyopathy or aortic valve involvement.
Right THR was performed under general anaesthetic using Charnley acetabular component (DePuy) and a cemented custom-made Exeter femoral component (Stryker, Newbury, United Kingdom). The post-operative period was uneventful and she was discharged from hospital mobilising with two crutches. At the six-week review, pain and range of hip movement were much improved although she was still mobilising with two crutches. Unfortunately following this review (eight weeks post THR) she fell, and sustained a periprosthetic fracture Vancouver grade C. This was reduced and internally fixed with a Dall-Miles plate and cable system (Stryker). She was touch weight-bearing on two crutches for six weeks post-operatively.

By four months post-operatively she was mobilising freely full weight-bearing with two crutches. At nine months following the right THR she presented with further symptoms in the left hip and radiographs showed marked degenerative changes. Aged 18 years she underwent a left THR with a cemented Charnley acetabular component (DePuy), and a cemented C-Stem femoral implant (DePuy).

At the five-year follow-up she was walking without crutches, albeit with a slight Trendelenberg gait and she had no pain in her hips.

**Case 3.** This seven year-old girl presented with an eight-week history of increasing flexion deformity of the fingers in both hands, decreased range of movement in both wrists and shoulders and decreased rotation in both hips. Over the course of the following year there was significant deterioration in function. Second line rheumatoid arthritis treatment was commenced after a diagnosis of juvenile chronic arthritis was made. Her shoulders were the most affected joints and she had developed bilateral triggering of the thumb and index fingers which required surgical release. At the age of ten years she complained of pain in the left hip but mobility was unaffected. Because of complications her rheumatoid medication was progressively withdrawn. By the age of 11 years she was referred for further assessment because of decreased rotation in both hips and valgus deformity of both knees. Examination showed slight limitation of rotation and abduction and radiologically both hips were dysplastic.

When she was 14 years old the diagnosis of Mucolipidosis Type III was proposed but could not be confirmed because she had a severe needle phobia. At this stage she had severe pain in the right hip and was unable to bear weight. She was treated with skin traction and her symptoms improved. She had an intra-articular steroid injection under radiological control and became pain-free.

After three months the symptoms returned in the left hip requiring readmission to hospital. Further traction was instituted which was beneficial. Radiographs showed a dysplastic left acetabulum with a steep, shallow roof and flattening of the femoral head (Fig. 3). She was prescribed a course of hydrotherapy. Urinalysis excluded the diagnosis of Mucopolysaccharidosis. At follow-up her shoulders were her main concern and radiography revealed underdeveloped glenoids, diminution of the humeral heads and dysplastic clavicular heads.

At 18 years old she consented to blood analysis and the diagnosis of Mucolipidosis Type III was confirmed. MRI showed changes compatible with bilateral femoral head avascular necrosis. She was 150 cm tall. Radiographs of the cervical spine showed atlantoaxial subluxation of 4 mm on forward flexion. She underwent a right THR under general anaesthetic with a cemented Charnley acetabular component (DePuy) and cemented Elite Plus CDH Stem (DePuy). Her acetabulum was reconstructed with her femoral head (bulk graft screwed). She made an uneventful post-operative recovery and had an identical procedure for her left hip three months later. The post-operative recovery was uneventful.

At follow-up at three years she was mobilising, pain-free, with crutches. Radiological investigation revealed no signs of loosening and well seated THRs (Fig. 4).

**Discussion**

A search of the current literature using MEDLINE (Medical Literature Analysis and Retrieval System online, Bethesda,
Maryland) and the Cochrane Library,15 using the terms ‘hip arthroplasty’, ‘bilateral’, ‘lysosomal storage’, ‘Mucopolysaccharidosis type IV’, ‘Mucolipidosis type III’ and ‘Morquio’ has not revealed any case reports of patients with lysosomal storage diseases, undergoing bilateral THR at such a young age. Hunter16 and other authors17-19 have described the outcome of the management of hip pathology with hip replacements in chondrodysplasias, of which Morquio disease and Mucolipidosis are two of many. However, we present these specific cases because of their encouraging mid-term results. These disorders present a wide spectrum of disease and although hip pathology is well recognised, in the milder forms, particularly Morquio disease, it is occasionally misdiagnosed as Perthes’ disease.20 It is important to remember that in cases of early bilateral arthritis of the hips, bone dysplasia should be suspected and radiographs of the other joints, including the spine, hands and feet should be undertaken along with a physical examination and obtaining a family history.21 Milder forms of these conditions with hip disorders have been successfully treated with bilateral varus osteotomies although long-term follow-up has not been conducted.21 In these three patients, although femoral osteotomy was considered, the degree of destruction of the hips precluded this option.

All three patients were of short stature. Two patients had radiological evidence of atlantoaxial instability, although in only one was this considered to present a significant risk to their management. None had any neurological defect. The hips were markedly dysplastic with dysplastic femoral heads, shallow dysplastic acetabula and short femoral necks. The bones were small and osteoporotic requiring appropriately scaled implants. The acetabular preparation was difficult as they were very shallow but in each hip it was possible to site the acetabular component in an anatomical position, and in only two hips was it necessary to augment the acetabular side with a bone graft.

Although the mid-term results have been satisfactory it is appreciated that in the long term these patients will undoubtedly require revision. The involvement of many joints will restrict the activities of these patients and this may serve to prolong the period of satisfactory function from the primary THRs.

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References