Morquio syndrome

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Summary
Morquio syndrome (mucopolysaccharidosis (MPS) type IV) is a rare inherited cause (autosomal recessive) of short-trunk dwarfism. Skeletal manifestations of this spondylo-epiphyseal dysplasia include severe growth retardation, odontoid hypoplasia, thoracolumbar kyphosis, hip dysplasia, genu valgum and marked skin and joint laxity. Mental function is normal, and the coarse facial features associated with the other MPS types are not present. Treatment is supportive only, with most affected individuals living until early adulthood.

Introduction
In 1929, Luis Morquio (1867–1935), a paediatrician in Montevideo, Uruguay, described a “familial skeletal dystrophy” in four out of five children of a consanguineous family of Swedish origin. Simultaneously but independently, James Brailsford (1888–1961), a radiologist in Birmingham, UK, described the clinical and radiological features of a child with “chondro-osteo dystrophy”. Both are thought to be descriptions of patients with Morquio syndrome (also known as Morquio-Brailsford syndrome), a cause of short-trunk dwarfism.

It is one of a group of inherited metabolic disorders, the mucopolysaccharidoses (MPSSs) (Table 1). Each is due to a specific lysosomal enzyme defect leading to incomplete breakdown of complex proteoglycans, causing accumulation of glycosaminoglycans (previously called mucopolysaccharides) that interfere with cell function. They are defined by the enzymatic defect, the type of glycosaminoglycan excreted in the urine and by the clinical features. Skeletal effects are particularly marked in MPS types I H (Hunter), I S (Scheie) and IV (Morquio).

Epidemiology and genetics
Morquio syndrome (MPS IV) is rare with an overall incidence of 1 in 40,000. The syndrome is found in all ethnic groups, but with higher incidence in French Canadians. Two types have been described—type A (more severe form) with a deficiency in N-acetyl-galactosamine-6-sulphatase (chromosome 16q) and a rarer type B with a deficiency in β-d-galactosidase (chromosome 3p). A variety of different gene mutations that result in defective enzymes have been identified. The inheritance pattern is autosomal recessive, with parents therefore unaffected by the disease. Laboratory diagnosis is possible with detectable enzyme deficiencies in fibroblasts and amniocytes, allowing pre-natal diagnosis in subsequent pregnancies.

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Clinical presentation

Children with Morquio syndrome have skeletal manifestations that result from a unique spondylo-epiphyseal dysplasia with ligament laxity. Growth and development are normal in the first year or two of life and the diagnosis is usually made between 2 and 4 years of age, although the severity of the features varies and milder forms of the syndrome may go undiagnosed. They can be distinguished from other MPSs at an early age as they have normal mental function and do not have coarse facial features.

There is severe growth retardation, usually with disproportionate short stature (short trunk), a large head and short neck, a prominent maxilla with wide-spaced teeth, thoraco-lumbar kyphosis with other spine and rib abnormalities (see “radiological features”), hip dysplasia, genu valgum and marked joint and skin laxity. The combined abnormalities result in a “duck-waddling” gait. Corneal clouding, deafness, aortic incompetence and hepatomegaly are all typical. Keratan sulphaturia is present, but decreases with age. Lifespan is variable, depending on disease severity, but many die in early adulthood with cardiopulmonary disease or the sequelae of neurological deficits.

Radiological features

Axial skeleton (Figs. 1–3)
- Hypoplastic/absent odontoid with atlanto-axial subluxation
- Thoracolumbar kyphosis with wedging of apical vertebrae
- Anterior vertebral beaking at other levels
- Platsypophyly (flattened vertebrae)
- Pectus carinatum
- Rib flaring
- Constricted iliac wings—“wine-glass” pelvis

Appendicular skeleton (Figs. 3–5)
- Acetabular dysplasia with coxa valga
- Genu valgum
- Epiphyseal and metaphyseal irregularity (advanced stages)
- Metacarpals small and irregular with pointed proximal ends

Treatment

The management of Morquio syndrome is currently limited to supportive care. Affected children need regular range of movement exercises and night splintage to limit progressive loss of motion. If surgery is contemplated, careful anaesthetic planning is required to address potential cervical instability, silent aortic incompetence, and respiratory insufficiency caused by spinal and thoracic deformities.

Spine

Spinal surgery is often necessary, as odontoid hypoplasia and the consequent C1-2 instability, if untreated, gives rise to myelopathy, quadriplegia or even sudden death. Hence posterior C1-2 fusion is often performed prophylactically aged 9–10 to regain stability and protect the spinal cord.

The thoraco-lumbar spinal deformity can be braced if necessary, but may need anterior decompression and strut grafting and posterior instrumented fusion if severe.

Lower limbs

Hip dysplasia may require containment osteotomies of the acetabulum and proximal femur. Genu valgum can be addressed with medial stapled semi-epiphysiodesis, but realignment osteotomies may also be required, usually of the proximal
tibia. Contractures around the hip, knee and ankle are difficult to address, as soft-tissue releases rarely successful.

Other

Gene therapy research promises new future treatments. The deficient enzyme N-acetylgalactosamine-6-sulfatase can be transferred via a recombinant retroviral factor, leading to correction of the metabolic defect in Morquio syndrome fibroblasts in the laboratory, but there has been no success yet in vivo. Bone marrow transplantation and enzyme
replacement therapy have been partially successful in the treatment of Hurler syndrome with increased lifespan, but the musculoskeletal condition is unchanged.

References