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Aortic Valve Replacement in a Patient with Morquio Syndrome

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ABSTRACT

Cardiac involvement in Morquio syndrome, mucopolysaccharidosis IV, is characterized by aortic and mitral valve thickening and infiltration of the coronary arteries. There are few reports concerning surgical interventions in patients with mucopolysaccharidoses. We report a case of a patient affected by Morquio syndrome who underwent aortic valve replacement surgery for severe aortic valve stenosis, with an uneventful postoperative course. Cardiac surgery appears safe and feasible in these patients and improves the quality of life, even if the future prognosis related to the underlying disorder should be considered.

INTRODUCTION

Morquio syndrome, mucopolysaccharidosis IV, is an autosomal recessive disorder characterized by excess excretion of keratan sulphate in the urine, caused by the accumulation of mucopolysaccharides in lysosomes [Brailsford 1929; Morquio 1929]. This syndrome is characterized by severe skeletal changes and respiratory involvement related to a restrictive effects of thoracic cage deformity and upper airway obstruction due to thickening of tissues from mucopolysaccharide accumulation. Associated aortic valve insufficiency [Dangel 1998] and mitral stenosis [Ireland 1981] have been described, and mucopolysaccharides infiltration of the coronary arteries may occur.

Few reports have addressed surgical interventions in patients affected by mucopolysaccharidoses [Hachida 1996; Minakata 1998]. We describe a patient with Morquio syndrome who underwent aortic valve replacement surgery for severe aortic valve stenosis.

CASE REPORT

A 41-year-old man with Morquio syndrome was admitted because of echocardiographic findings of severe calcific aortic stenosis. The patient was first evaluated at the age of 3 years for a history of ingravescent bilateral muscular weakness of the lower extremities. The patient had no mental deficiencies. During growth the patient's skeletal habitus was characterized by short stature with short trunk, broad mouth, prominent lower third of the face, pectus carinatum, kyphosis, gibbus, scoliosis, and joint abnormalities. Ophthalmogical examination revealed corneal opacities due to accumulation of mucopolysaccharides. X-ray examination showed osteopenic bones with cortical thinning, dorsolumbar spine kyphosis, coarse appearance of the second cervical vertebral body, and anterior hypoplasia of second lumbar vertebral body. Upper extremities were characterized by widened metaphyses and hypoplasia of metacarpal bone IV and lower extremities by genu-valgus deformity. The diagnosis of mucopolysaccharidosis type IV was ultimately made on the basis of urinary examination showing pathologic excretion of keratan sulphate, with a value of 0.54 mg/24 hours (normal range 0-0.17 mg/24 hours).

The onset of cardiac symptoms occurred approximately 1 month before the admission and consisted of ingravescent dyspnoea and signs of heart failure. Echocardiography showed an aortic valve area of 0.43 cm^2 with mean systolic gradient of 65 mm Hg. Severe left ventricle concentric hypertrophy was detected, and the left ventricular ejection fraction was 52%. Coronary angiography excluded significant coronary artery disease. Cardiopulmonary bypass was instituted with ascending aorta and right atrium cannulation, and myocardial protection was performed with intermittent normothermic blood cardioplegia. After the removal of a tricuspid aortic valve with severely fibrotic, thickened, and calcified cusps, the patient underwent 19-mm mechanical Sorin Bicarbon prosthesis implantation. Cardiopulmonary bypass time was 120 minutes, and aortic cross-clamping time was 84 minutes. Weaning from mechanical ventilatory support required 15 hours, and the patient remained in the intensive care unit for 2 days. Postoperative echocardiogram showed normal function of the implanted prosthesis and normal heart contractility. The postoperative course was uneventful and the patient was discharged on day 7 after surgery. At 3 months' follow-up the patient was alive and asymptomatic.

Histologic examination showed a marked thickening of the aortic valve leaflets, due mainly to diffuse ialine fibrosis with foci characterized by neoangiogenesis (Figure 1A) consisting of arteriolae, venulae, or dilated thin-walled vessels. The above sclerotic tissue showed scarce spindled fibroblasts

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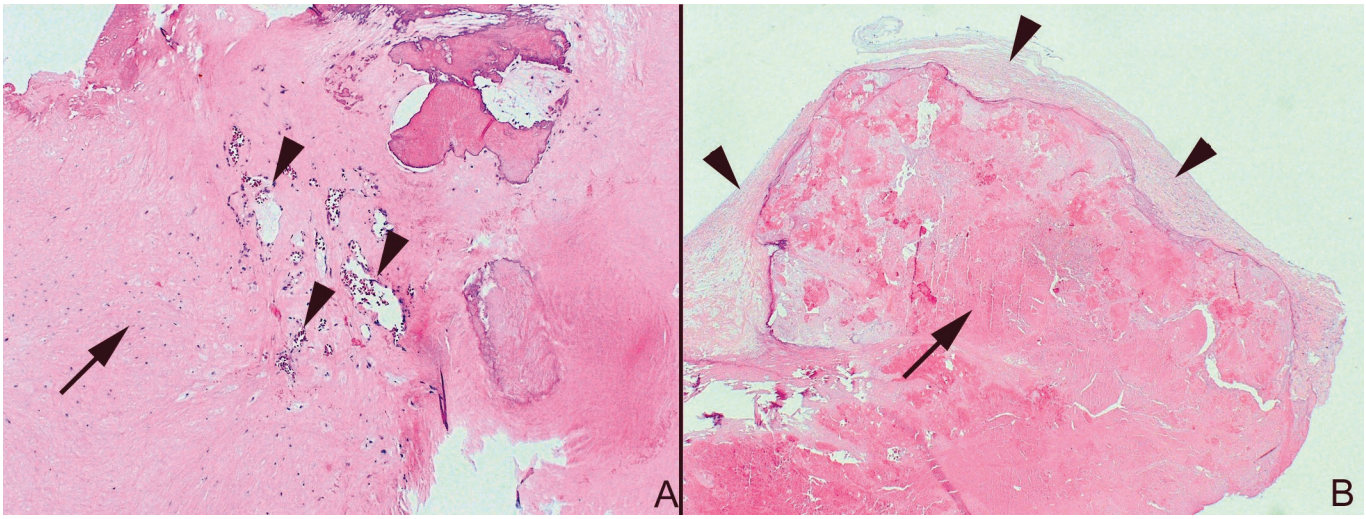

Figure 1. A. This aortic valve leaflet is characterized by diffuse fibrosis (arrow) with scattered foci of new-formed blood vessels throughout (arrowheads). B. Low-power magnification of the aortic valve showing a large vegetation (arrow) that both substitutes and deforms the leaflet architecture. A thin rim of fibrous tissue often encircles this vegetation (arrowheads). Hematoxylin-eosin staining; original magnification ×2.

as well as scattered mesenchimal elements with early signs consistent with cartilagineous metaplasia. The valvular surface was often deformed by vegetations (Figure 1B) containing necrotic and sometimes calcific amorphous material. In addition, scattered chronic inflammatory aggregates were detectable throughout the aortic leaflets. These were often related to the newly formed blood vessels.

DISCUSSION

In 1929, Morquio, a pediatrician in Uruguay, and Brailsford, a radiologist in England, simultaneously described clinical cases now believed to be Morquio syndrome [Brailsford 1929; Morquio 1929]. This syndrome is a member of a group of metabolic disorders, collectively termed mucopolysaccharidoses, with a chronic progressive course caused by the accumulation of partially degraded glycosaminoglycans, with resulting thickening of tissue and compromising of cell and organ function over time. Glycosaminoglycans accumulate in lysosomes and extracellular tissue and are excreted in the urine. In Morquio syndrome, also termed mucopolysaccharidosis IV, the degradation of keratan sulfate is defective because of deficiency of N-acetyl-galactosamine-6-sulfate sulfatase in mucopolysaccharidosis IV A, or deficiency of β-galactosidase in mucopolysaccharidosis IV B. Variability in clinical expression within both groups is apparent, and no clear clinical differentiation exists between Morquio syndrome types IV A and IV B.

Patients with mild manifestations of Morquio syndrome, regardless of subtype, survive into the seventh decade of life. Patients with severe manifestations, related to cervical instability and pulmonary compromise, often do not survive beyond the second or third decade of life.

Cardiac involvement has been described in all types of mucopolysaccharidoses, occurring in 72% of patients, although clinical signs and symptoms are often mild and uncharacteristic [Dangel 1998]. Cardiac involvement in Morquio syndrome is commonly characterized by aortic and mitral leaflet thickening with valve insufficiency; infiltration of the coronary arteries with mucopolysaccharides can lead to cardiac ischemia. As described in the literature, pathologic accumulation of glycosaminoglycans cause thickening and calcifications, with more localization on aortic cusps than on the aortic annulus, compared to degenerative senile aortic stenosis. Few reports address surgical interventions in patients with mucopolysaccharidoses [Hachida 1996; Minakata 1998]; in our experience cardiac surgery appears safe and feasible in these patients and improves the quality of life. Special attention to anesthesiological procedures is needed because of potential difficult airway management [Shinhar 2004]. These patients may have a prominent mandible or maxilla, macroglossia, and a short neck with or without cervical scoliosis. Deposits of mucopolysaccharides in the soft tissues of the oropharynx, floor of the mouth, and tracheal wall can distort the airway. Moreover, pulmonary dysfunction associated with Morquio syndrome is multifactorial; a restrictive component derived from the kyphoscoliosis can result in decreased lung volumes, ventilation-perfusion mismatching, and obstructive sleep apnoea with consequent pulmonary hypertension and potential sudden death. Preoperative sedation should be avoided or minimized in case of an airway prone to obstruction. Personnel must be prepared for immediate action in case of difficulty with mask ventilation or during intubation. Careful positioning of the patient is mandatory to avoid atlanto-axial subluxation. With a thorough understanding of the disease process and potential consequences, it is possible to evaluate and manage these patients with a high margin of safety in the perioperative period.

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