

Morquio's Syndrome: Severe Aortic Regurgitation and Late Pulmonary Autograft Failure

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A 44-year-old woman underwent a Ross procedure for severe aortic regurgitation at the age of 32 years. She had been diagnosed in childhood with spondyloepiphyseal dysplasia and a bicuspid aortic valve. At surgery, a tricuspid aortic valve with chondroid metaplasia and fibrosis was reported. Biochemical and genetic evaluation in this patient confirmed the diagnosis of mucopolysaccharidosis IV type B (MPS IV), otherwise known as Morquio's syndrome. This autosomal-recessive inherited syndrome is characterized by the accumulation of keratin sulfate in connective tissue and various other organs. Cardiac (notably valvular) involvement has been well described in the literature. To the authors' knowledge, this is the first reported case of valve replace-

The mucopolysaccharidoses (MPS) are a group of hereditary disorders resulting from defective enzymatic activity leading to an accumulation of incompletely degraded glycosaminoglycans. Mucopolysaccharidosis IV, also called Morquio's syndrome, was first described in 1929 (1). This rare metabolic disorder, which has an autosomal-recessive inheritance pattern (2), is characterized by the accumulation of keratin sulfate in connective tissue and various other organs. MPS IV is divided into two subtypes, A and B, as a result of different enzymatic defects (3).

There is wide variability in the clinical presentation of MPS IV. Typically, these patients have severe skeletal abnormalities including dwarfism, pigeon breast, genu valgum, and kyphoscoliosis (4). Bony abnormalities of the thoracic cage predispose to restrictive lung physiology and recurrent pulmonary infections. Obstructive pulmonary defects may occur from tracheal or laryngeal stenosis (5). Cervical spine laxity

ment or Ross procedure for this condition. This woman presented 12 years after her initial valve surgery with progressive dyspnea. Echocardiographic examination revealed severe pulmonic autograft regurgitation without a dilated aortic root, together with severe stenosis of the pulmonary homograft. It is postulated that the underlying metabolic abnormality may have led to progressive pulmonary autograft failure and to accelerated dysfunction and stenosis of the pulmonary homograft. It is likely that a mechanical prosthesis would have been a better therapeutic option if the preoperative diagnosis of MPS IV had been made.

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leads to atlanto-axial instability and high risk for subluxation. Other clinical features include corneal clouding, hearing loss, dental defects, and hepatosplenomegaly (6). The average life expectancy is less than 30 years, and treatment to date has been supportive (1).

Cardiac involvement with MPS IV has historically been described as isolated aortic regurgitation (7,8). Recent studies have reported potential involvement of all four cardiac valves (most commonly left-sided valves), which manifests as either stenosis and/or regurgitation (7,9-11). Additional cardiac abnormalities of coronary intimal sclerosis, endocardial fibrosis and ventricular hypertrophy have been reported (9,12). It is believed that the valve disturbances and other cardiac abnormalities are a result of both keratin sulfate deposition and intrinsic collagen derangements (13). Despite the described valvulopathy, there is a paucity of information regarding valve replacement therapy.

Herein are presented the details of a 12-year echocardiographic follow up of a patient with Morquio's syndrome who underwent a Ross procedure for aortic regurgitation.

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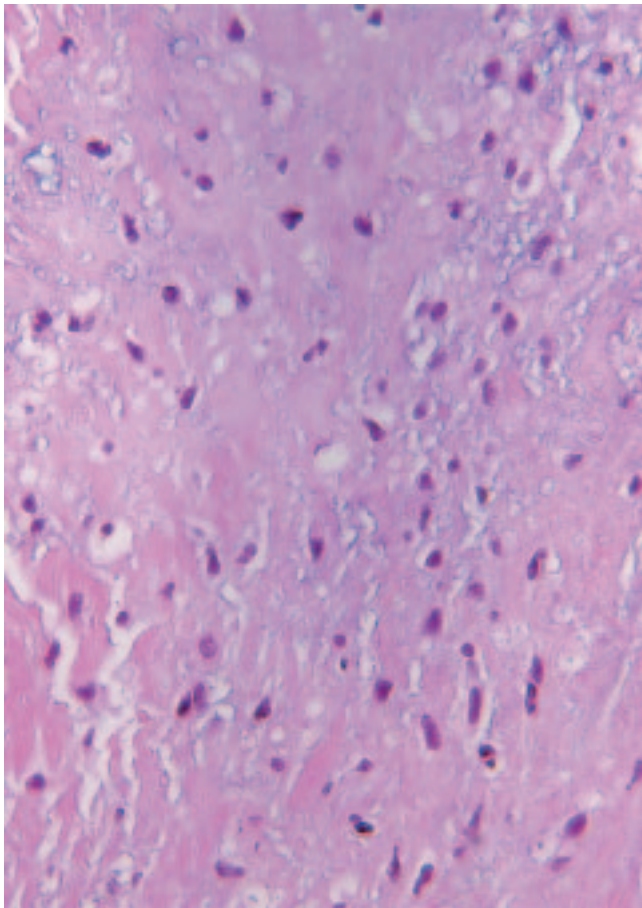


Figure 1: Histologic examination of the resected native aortic valve demonstrated periodic acid-Schiff-positive material, chondroid metaplasia, and dystrophic calcification.

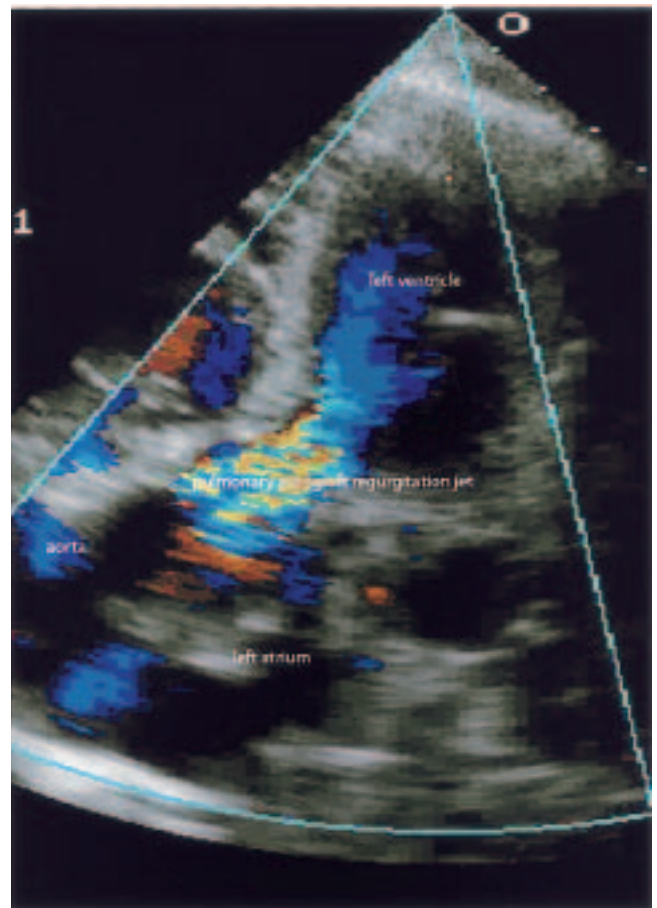


Figure 2: Transthoracic echocardiographic apical five-chamber view showing severe pulmonary autograft regurgitation by color-flow Doppler.

Case report

A 44-year-old female was diagnosed with spondyloepiphyseal dysplasia as a child. At the age of 23 years, she required bilateral hip arthroplasty, but nine years later developed dyspnea on exertion and was noted to have aortic regurgitation. Her echocardiogram was interpreted as a bicuspid aortic valve with severe aortic regurgitation and left ventricular enlargement. She underwent a Ross procedure (pulmonary autograft replacement of the aortic valve and 29-mm pulmonary homograft replacement). At surgery, the aortic valve was described as tricuspid with thickening and retraction of the leaflets, but no abnormalities were noted in the pulmonary valve. Pathology of the aortic valve revealed fibrosis, basophilic degeneration, and chondroid metaplasia (Fig. 1). Metabolic and genetic evaluations were performed which confirmed the diagnosis of MPS IV type B (Morquio's syndrome).

The patient's postoperative course was complicated by a sternal wound infection which responded to

antibiotic therapy. She underwent routine transthoracic echocardiography (TTE) seven years after the valve replacement, whereupon the examination showed moderate pulmonary autograft regurgitation and mild stenosis of the pulmonic homograft, and a gradient of 16 mmHg. The aortic root was not dilated.

The patient re-presented approximately 12 years after her initial valve surgery with a prosthetic hip infection. She acknowledged progressive shortness of breath over the past year, and TTE revealed severe pulmonary autograft regurgitation. The aortic annulus and root were not dilated, and no vegetations were apparent (Fig. 2). Additionally, her pulmonic homograft had severe calcific stenosis, with mean and peak gradients of 36 and 75 mmHg, respectively. There was a hyperdynamic left ventricle, a dilated hypokinetic right ventricle, and marked right atrial enlargement (Fig. 3).

The patient was deemed not to be an operative candidate and died a few days later. No autopsy was performed.

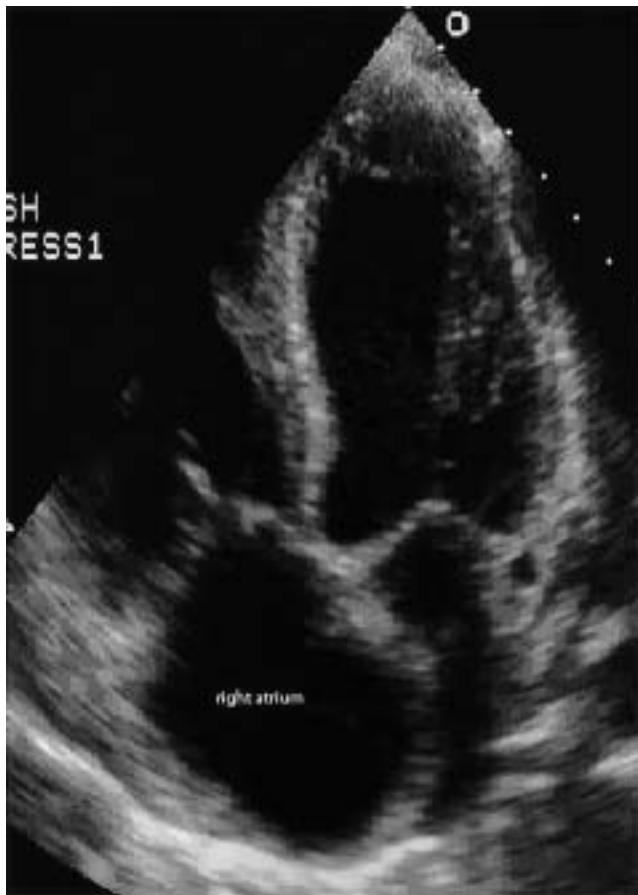


Figure 3: Transthoracic echocardiographic apical four-chamber view with prominent right ventricular hypertrophy and right atrial enlargement with a bowed intra-atrial septum related to pulmonary homograft stenosis.

Discussion

Mucopolysaccharidosis is a rare disease with systemic involvement; cardiac involvement has been described as either stenotic and/or regurgitant lesions (7). Historically, the life expectancy of MPS patients is limited and valve replacement has not been an option. However, with improved surgical and medical therapy, and perhaps milder phenotypes, some patients with MPS are surviving longer and their cardiac abnormalities may become more prominent (9). Despite the advancing age of some MPS patients, there is a paucity of literature regarding valve replacement (14-16). With regard specifically to MPS IV, to the present authors' knowledge there are no reported valve replacement cases. The present patient underwent a Ross procedure for suspected bicuspid aortic valve, and the diagnosis of MPS IV type B (Morquio's syndrome) was only made after surgery.

Previous studies concerning the Ross procedure

illustrate an actuarial freedom from reoperation for autograft regurgitation or left ventricular obstruction of approximately 90% between five and eight years after surgery (17,18). Historically, when the pulmonary autograft fails it is related to progressive root dilatation and subsequent autograft regurgitation (19).

It is postulated that this patient's autograft failed because of progressive valvular degeneration related to her MPS IV. While no autopsy was performed, it seems much less likely that autograft failure was responsible for this patient's autograft lesion, especially given the normal aortic root caliber. Previous pathological studies have verified that MPS IV may involve all heart valves (10). Through serial echocardiographic examinations, MPS IV cardiac involvement has proven to be a progressive phenomenon (7). Although no autopsy was performed in the present case, it is believed that the same pathology of intrinsic collagen abnormalities and keratin sulfate deposition that occurred in her original native aortic valve may also have occurred in the autograft, and this led to recurrent severe pulmonary autograft regurgitation. Furthermore, keratin sulfate deposition in a calcific-prone pulmonic homograft may have accelerated the stenotic process.

In conclusion, MPS IV is a rare condition which may lead to significant valvular dysfunction. This is the first report to date of heart valve replacement in a patient with confirmed MPS IV. Because the condition was not recognized before surgery, the patient underwent a Ross procedure, which failed over a relatively short time. Based on this experience, MPS should perhaps be considered a relative - if not absolute - contraindication to the Ross procedure.

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