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Brief Report

Aortic stenosis in a patient with Hurler's syndrome after bone marrow transplantation

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Abstract We describe a case of severe aortic stenosis in a 16-year-old male with Hurler's syndrome who had prior bone marrow transplantation. The excised aortic valve leaflets showed characteristic pathologic findings of Hurler's syndrome. This is the first case report of aortic valve replacement in a patient with Hurler's syndrome treated with bone marrow transplantation that demonstrates progression of the aortic valve disease despite treatment.

Keywords: Mucopolysaccharidosis; aortic valve replacement; valvular disease

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Hurler's syndrome, the most severe form of type I Mucopolysaccharidosis, is a lethal autosomal recessive disease characterised by absent enzymatic activity of the lysosomal enzyme a-L-iduronidase. The incidence of Hurler's syndrome is approximately 1 in 144,000 live births.[1] Without treatment, patients with the most severe forms of the disease have a median survival of 6.8 years.[2] In the early 1980s, Hobbs and associates proposed allogenic bone marrow transplantation as a way to reverse the clinical features and improve the outcomes in patients with Mucopolysaccharidosis.[3] Whether BMT improves the progression of valvular disease in patients with type I Mucopolysaccharidosis is controversial.[4,5] Here, we report the case of a patient with Hurler's syndrome, who developed aortic valve stenosis necessitating valve replacement after bone marrow transplantation.

Case report

A 16-year-old male with Hurler's syndrome presented with limited exercise capacity and a recent syncopal episode after walking quickly up a 100-yard incline. The patient's past medical history was significant for unrelated bone marrow transplantation at ages 1 and 2 years after pre-conditioning with busulphan and total body irradiation. The most recent engraftment study at age 12 years showed 95% donor blood. His past surgical history was significant for multiple prior orthopaedic procedures, including surgeries for clubfoot, spondylolithiasis, and hip dysplasia. He had a balloon aortic valvuloplasty 4 months before presentation.

The pre-operative echocardiogram showed a thickened and dysplastic bicuspid aortic valve with moderate aortic stenosis and mild aortic regurgitation. The peak valve gradient was 65 millimetres of mercury and mean valve gradient was 43 millimetres of mercury. The aortic annulus was 18 millimetres. Cardiac catheterisation confirmed the findings of mixed aortic valve disease with a left ventricular systolic pressure of 189/9 millimetres of mercury and simultaneous aortic pressure of 92/54 millimetres of mercury. No other valvular abnormalities were noted.

Surgical repair was performed through a median sternotomy with full cardiopulmonary bypass. After cardioplegic arrest, the aorta was partially transected high above the sinotubular junction. The aortic wall was thick and indurated, and had limited elasticity

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making exposure of the aortic valve difficult. The aortic valve on inspection was quite different from a typical stenotic bicuspid aortic valve: there were mild calcifications at the base of the valve cusps. The free margins of both cusps were oedematous and irregular with small cauliflower-type protrusions, and there was severe restriction to their mobility, with a very small effective orifice area and a small aortic annulus. A mechanical aortic valve replacement was performed using a 19-millimetre St. Jude Medical Hemodynamic Plus aortic valve prosthesis (St. Jude Medical Inc., St. Paul, Minnesota, United States of America) with posterior enlargement of the annulus with treated pericardium. The pressure gradient across the aortic valve decreased from 97 millimetres of mercury to 10 millimetres of mercury. At an interval of 3 months after the operation, a repeat echocardiogram showed a peak gradient across the prosthetic valve of 15.4 millimetres of mercury, a left ventricular ejection fraction of 72.8%, and a decrease in the left ventricular mass index from pre-operative 92.4–55.3 grams per square metre. The valve is functioning properly without abnormal pannus formation.

Discussion

Since the 1980s, bone marrow transplantation is utilised to correct the inborn error in patients with Hurler's Syndrome by replacing the patient's defective macrophages by marrow-derived donor macrophages.[2] The short-term cardiac effects of bone marrow transplantation in patients with Hurler's syndrome include regression of ventricular hypertrophy and stabilisation of the aortic and mitral valve anomalies.[3] However, Braunlin et al reported that the long-term cardiac beneficial effects of bone marrow transplantation appear not to extend to the cardiac valves. The mitral and aortic valves continue to thicken and develop prolapse, insufficiency, or stenosis despite documented successful engraftment.[4] The reason for this is unknown. In contrast to the myocardium, valve leaflets are relatively avascular. It is possible that after successful engraftment, the degradation of glycosaminoglycans deposited in the leaflets is hindered by the lack of vascularity and limited access to the phagocytic cells.

The patient presented in this report had severe aortic stenosis with small aortic annulus 14 years after bone marrow transplantation. The aortic valve was dysplastic on gross inspection and the abnormal features of the cusps were quite different from the typical degeneration of a congenital bicuspid valve. Moreover, Elastic-van Gieson staining showed attenuated areas of elastin framework (Fig 1a) and the Alcian blue stain showed deposits of acidic mucopolysaccharides (Fig 1b), both characteristic pathologic findings of Hurler's syndrome. This provides further evidence to support that in patients with Hurler's syndrome, the beneficial effects of bone marrow transplantation may not extend to the structural degeneration of the cardiac valves. These patients must have regular cardiology follow-up and need to be considered for surgical intervention when they develop significant valvular disease.

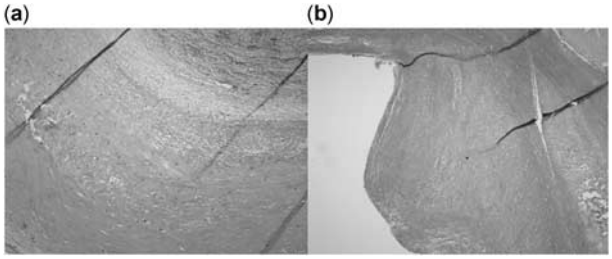

Figure 1.
*(**a**) Elastic-van Gieson staining shows attenuated areas of elastin framework, (**b**) Alcian blue stain deposits of acidic mucopolysaccharides.*

The annulus of the aortic valve was markedly calcified and small, and the exposure of the aortic valve as well as the performance of an aortic valve replacement was very challenging. The surgical outcome in this case was excellent and the patient had an uneventful recovery despite his multiple comorbidities and the technical difficulty of the valve replacement.

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