Cardiol Young 2002; 12: 67–70

ISSN 1047-9511

Brief Report

Multiple valvar replacements for hypereosinophilic syndrome

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Abstract A boy with familial eosinophilia had the hypereosinophilic syndrome, with involvement of mitral and tricuspid valves. Between the ages of 11 and 20 years, he underwent eight surgical procedures on his atrioventricular valves. The pathology included recurrent thrombotic vegetative masses related to hypereosinophilia. Initial repair of the mitral valve was shortlived, but recurrent repairs of the tricuspid valve were helpful. Mechanical prostheses inserted in the mitral position thrombosed despite anticoagulant therapy, and bioprosthetic valves deteriorated with thrombus, fibrosis, or tearing. The hypereosinophilic syndrome is unusual in children, and produces additional problems with valvar surgery.

Keywords: Hypereosinophilic syndrome; familial eosinophilia; thrombotic vegetations; heart valve surgery; mitral valve replacement

THE HYPEREOSINOPHILIC SYNDROME CONSISTS of unexplained eosinophilia lasting more than six months. It is associated with damage to several organs, particularly the heart.[1] The cardiac pathology is eosinophil-mediated damage producing necrosis, thrombosis, and fibrosis. This manifests variably as endomyocardial fibrosis, involvement of the mitral and tricuspid valves, and restrictive or dilated cardiomyopathy. It is more common in men, in a ratio of 9 to 1, and tends to present between the ages of 20 and 50 years.[1] Presentation in childhood is unusual.[2,3] We report a boy with hypereosinophilic syndrome and familial eosinophilia who has undergone eight procedures involving the mitral valve between the ages of 11 and 20 years.

Case history

The boy came to medical attention at the age of 10 years when he was involved in a motor vehicle accident and sustained a compound fracture of his left tibia and fibula. A heart murmur was heard, and he developed a fever. An echocardiogram demonstrated apparent vegetations on his mitral and tricuspid valves, both of which were incompetent. He was treated for bacterial endocarditis with intravenous antibiotics. When he developed signs of cardiac failure, he was referred for surgery. At his first operation, in 1991, the diagnosis was thought to be rheumatic heart disease with treated endocarditis. An old calcified vegetation was seen on the mural leaflet of the mitral valve, and vegetations were found on all leaflets of the tricuspid valve. Both valves were repaired and a 25 mm Duran ring was placed in the tricuspid annulus. A re-repair was performed the same day because of dehiscence of the mitral valve. Histology of a removed vegetation was reported as compatible with chronic endocarditis, but stains failed to show any micro-organism.

He was followed as an outpatient, but within two years he developed clinical and echocardiographic evidence of severe mitral stenosis and moderate tricuspid stenosis. He also had hepatosplenomegaly. At the third operation in 1993, the mitral valve was described as containing vegetations around its circumference, leaving an orifice of no more than 8–9 mm. The subvalvar apparatus was totally fused posteromedially with additional vegetative material. The valve was replaced with a 27 mm St Jude prosthesis, the tricuspid annuloplasty ring was removed, and a tricuspid valvotomy performed. He went home on warfarin, digoxin and diuretics. Less than 3 weeks later, he was readmitted acutely with abdominal

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Accepted for publication 27 June 2001

pain, vomiting, pallor, cool peripheries, pulsatile hepatomegaly and a marked right ventricular lift. There was echocardiographic evidence of thrombosis of the St Jude mitral valvar prosthesis. He was rushed to surgery and found to have thrombus and pannus around the hinges of the discs, fixing one disc in the closed position with the other opening slightly. The valve was replaced using a xenotech bioprosthesis. Microscopy of the removed valve confirmed thrombus. He remained on warfarin therapy for a further three months after that operation.

One month later, he was readmitted with fever, malaise, tachypnoea, cool peripheries and echocardiographic evidence once more of severe obstruction to the mitral valve. His white cell count was 34×10^9/L, with 18×10^9 eosinophils and 6.5×10^9 neutrophils. Procoagulant haematological factors were not found. His sedimentation rate was 2. It was noted that he had always had a mildly elevated eosinophil count and that the family, which was widely separated, had been investigated elsewhere for eosinophilia. There was no evidence of parasitic infestations, and leukaemia was excluded by bone marrow examination. A diagnosis of familial eosinophilia had been made, with his father, brother and two step-brothers being affected.

He proceeded to his fifth operation in November 1994 with the diagnosis of hypereosinophilic syndrome. The bioprosthetic mitral valve was narrowed by tough thrombotic material which extended into the left atrium and wall of the left ventricle. The valve was excised and a 29 mm St Jude valve inserted. Histology of the thrombotic material demonstrated large clusters of eosinophils. Bone marrow examination showed increased myeloporesis, particularly with eosinophils, but no evidence of malignant cells. He had an uneventful postoperative course. He was initially heparinized and then given warfarin again. The hypereosinophilic syndrome was treated with prednisolone and hydroxyurea. The eosinophil count fell to 3.57×10^9/L and his blood count was closely monitored at home.

He represented several weeks later, again severely ill, with signs of severe obstruction of the mitral prosthesis, pulmonary hypertension and tricuspid regurgitation. On admission, his international normalised ratio for prothrombin time, which should be in the therapeutic range for oral anticoagulant therapy of 2.0–4.5, was greater than 9, and he was given vitamin K before undergoing his sixth operation as an emergency in December 1994. The hinges of the St Jude valve had thrombosed, causing severe obstruction. The valve was excised and replaced with a 29 mm Carpentier-Edwards xenograft sewn into a supra-annular position. He was given intravenous heparin for two weeks and resumed hydroxyurea in an increased dose to lower his eosinophil count. Warfarin was then resumed. He was followed as an outpatient for another 4 years. By then, he had evidence of moderate mitral stenosis and incompetence, and severe tricuspid incompetence. He presented with abdominal pain from pulsatile hepatomegaly. The seventh operation in 1998, involved insertion of another Carpentier-Edwards xenograft mitral valve, and repair of the tricuspid valve with annuloplasty.

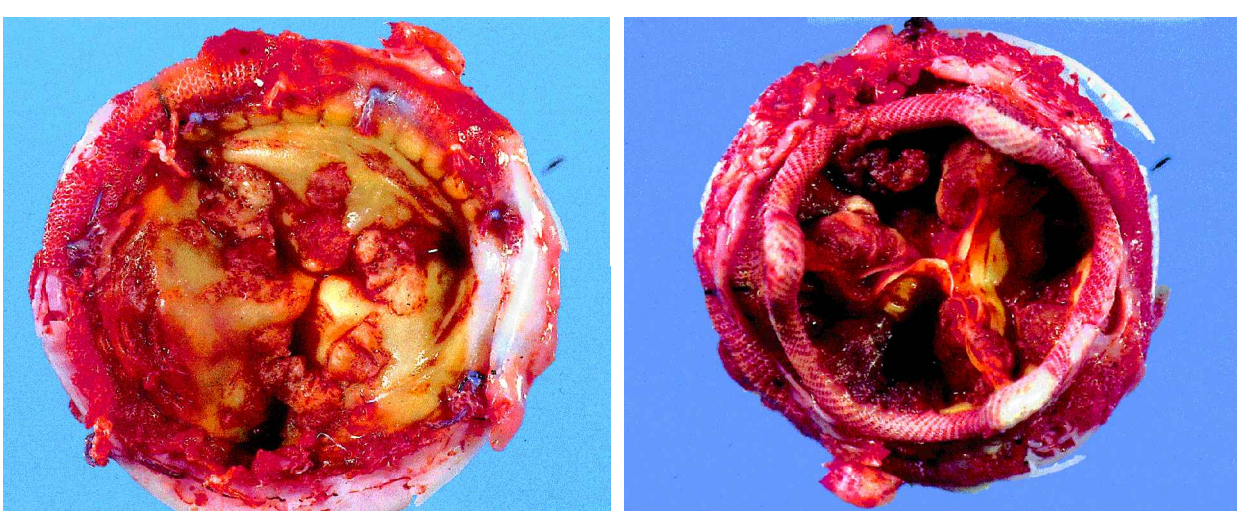

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Figure 1.
Surgical specimen from the eighth operation. The explanted mitral xenograft had been in place for 28 months. It is covered with reddish-brown thrombotic material which caused severe stenosis. The gradient across the valves was 32 mmHg. (A) shows atrial surface and (B) the ventricular surface of the valve.

https://doi.org/10.1017/S1047951102000136 Published online by Cambridge University Press

He remained on warfarin and hydroxyurea. In 1999, he was treated for Streptococcus viridans endocarditis. In February 2001 he again had evidence of significant mitral valvar stenosis, with pulmonary hypertension and early pulmonary oedema. In his eighth procedure, a xenograft mitral valve (29 mm Mosaic) was inserted via a right thoracotomy. The excised valve showed reddish-brown thrombotic material on both atrial and ventricular surfaces (Fig. 1). He is currently well, with echocardiographic evidence of a mean gradient of 11 mmHg across the xenograft mitral valve. The tricuspid valve has thickened leaflets, a mean gradient of 4 mmHg, and is moderately incompetent. His eosinophilia has varied between 1.97×10^9/L and 3.56×10^9/L, never reaching the reference range of $< 0.60 \times 10^9$/L. His reliability with drugs is also questionable.

Discussion

The heart is involved in three-fifths of cases of the idiopathic hypereosinophilic syndrome, and is the major cause of morbidity and mortality.[1] Typical manifestations include endomyocardial fibrosis, formation of thrombus, scarring of the tendinous cords, and development of mitral and tricuspid valvar incompetence.[4]

Our patient was atypical in presenting at such a young age with apparent vegetative masses. Such pathology, with organizing thrombus causing vegetation-like masses on the atrio-ventricular valves, is unusual and has rarely been seen in the hypereosinophilic syndrome. It was described at autopsy in one report concerning a 68-year-old Japanese woman.[5] With our patient, there was an undue delay in diagnosis of the condition because the initial pathology was thought to be rheumatic and infective. His haematology, although investigated, was not correlated with the cardiac pathology. Even when therapy with prednisolone, hydroxyurea and warfarin was commenced, he continued to have rapid and recurrent problems with the cardiac valves. These relate to multiple factors. He was not always totally reliable with his therapy. Thrombotic events did occur when he was well anticoagulated. Bioprosthetic valves deteriorate more rapidly in young patients than in older recipients. Eight operations by the age of 20 years, nonetheless, is excessive. The need for recurrent surgery has been reported previously in a 38-year-old woman who required four operations in 4½ years.[6] She also had repeated thrombotic obstruction despite anticoagulant therapy.

The choice of valve used for surgical replacement is difficult.[1] Table 1 gives a summary of valve operation. Mechanical valves when used in this condition, have been known to obstruct with thrombus and pannus.[6–9] Such obstruction has been rapid, within days or months of surgery, and to occur despite anticoagulant therapy. The recommended valve for replacement is a porcine heterograft bioprosthesis used with warfarin therapy.[8,9] This attempts to overcome the problems of susceptibility to thrombotic

Table 1. Summary of valve operations.

No.	Date	Procedure	Indication for operation
1	13.02.1991 Age 11	Mitral valve repair Tricuspid valve repair and insertion of Duran ring 25 mm	Severe mitral and tricuspid regurgitation Apparent vegetations on MV and TV Pulmonary hypertension
2	13.02.1991 Age 11	Re-repair of MV same day	Mitral regurgitation from valve dehiscence
3	24.06.1993 Age 12	St Jude 27 mm mitral valve replacement (MVR) Removal of TV annuloplasty ring Tricuspid valvotomy	Severe mitral stenosis with incompetence Moderate tricuspid stenosis and incompetence
4	20.07.1993 Age 12	Removal of St Jude MVR Xenotech bioprosthesis MVR 27 mm	Thrombosis of St Jude MVR Severe pulmonary hypertension
5	09.11.1994 Age 14	Xenotech MV removed St Jude MVR 29 mm	Severe mitral stenosis with tough thrombotic material
6	27.12.1994 Age 14	Removal of St Jude MVR 29 mm Carpentier-Edwards xenograft 29 mm MVR in supra-annular site	Severe mitral stenosis due to thrombosis on hinge mechanism
7	02.11.1998 Age 18	Removal of xenograft MVR Carpentier-Edwards xenograft MVR TV repair and annuloplasty	Severe mitral regurgitation due to a leaflet tear Severe tricuspid regurgitation
8	20.02.2001 Age 20	Removal of xenograft MVR 29 mm Mosaic MVR via right thoracotomy	Severe mitral stenosis Mean echo gradient = 32 mmHg Early pulmonary oedema

https://doi.org/10.1017/S1047951102000136 Published online by Cambridge University Press

obstruction despite adequate anticoagulation, and prevention of the thromboembolism, which also occur in hypereosinophilic syndrome.[1] When there is associated tricuspid valvar involvement, repair or annuloplasty is preferable, as was done in our patient on three occasions. The additional problem in children is the rapidity of deterioration of bioprosthetic valves. Young age is a known significant risk factor for reoperation with such valves.[10] Drug therapy for hypereosinophilia aims to achieve a near normal eosinophil count, as the eosinophils are responsible for the pathology. It is highly probable that the eosinophils will also cause an increased rate of deterioration of xenograft valves in this condition.

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