

## Aortic Valve Replacement for Aortic Stenosis with a Small Aortic Annulus in a Patient having Werner's Syndrome and Liver Cirrhosis

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**Werner's syndrome is a rare genetic disease characterized by premature aging and scleroderma-like involvement of the skin. We report a case of aortic valve replacement for severely calcified aortic valve stenosis with a small annulus in a patient suffering from Werner's syndrome and liver cirrhosis. (Ann Thorac Cardiovasc Surg 2001; 7: 378–80)**

**Key words:** Werner's syndrome, aortic stenosis, small annulus, liver cirrhosis

### Introduction

Werner's syndrome is a rare autosomal recessive disease of unknown etiology. It affects connective tissue and produces widespread manifestations throughout the body. Precocious generalized arteriosclerosis and coronary artery disease manifested by congestive heart failure, angina, and myocardial infarction in patients with Werner's syndrome have been described.

### Case Report

We describe a 41-year-old man who was treated for rupture of the esophageal varices secondary to liver cirrhosis eight years ago. At that time, Werner's syndrome and aortic stenosis also had been diagnosed. Thereafter he received several treatments for gastro-esophageal varices, including sclerotherapy, distal spleno-renal shunt, spleno-pancreatic dissection, gastric dissection, partial splenic embolization, and clipping of the gastric varices. The latter was performed 5 months before the cardiac surgery. He had been hospitalized a few times for treatment

of congestive heart failure secondary to aortic stenosis. Recently, his hospital admissions had become frequent so that surgical treatment was considered and he was referred to our hospital.

At the time of admission, the patient was suffering from anginal pain. He presented with scleroderma-like skin with neither skin ulcers or abscesses, premature cataracts, premature leucotrichosis, short stature (157.5 cm), and low weight (34 kg). His voice was high pitched and his visage was "bird-like." In his past medical history, an ulcer had appeared on the right ankle and flexion contracture developed four years ago. An investigation of his family history disclosed consanguinity; his parents are second cousins. The patient has an elder sister who is also affected with Werner's syndrome but not with heart diseases. Laboratory findings showed anemia with red blood cell levels at  $274 \times 10^4/\mu\text{l}$ ; lowered cholinesterase, at 2230 U/l; and hyperglycemia at 215 mg/dl. A preoperative echocardiogram revealed left ventricular hypertrophy (thickness of interventricular septum, 19 mm; posterior wall, 13 mm) and calcification in the aortic valves and the mitral annulus. Mild aortic and mitral insufficiency were also detected. The mitral valve area was calculated to be 1.4 cm<sup>2</sup> from the pressure-half time, indicating moderate mitral stenosis. The pressure gradient between the left ventricle and the aorta measured 131 mmHg with Doppler echocardiography. Electron beam computed tomographic scans with volume scanning mode (Imatron C-150XP; Imatron Inc., San Francisco, CA) confirmed the findings of calcification in the aortic valves and the mitral annulus as well as in the ascending aorta (Fig. 1). The cardiac catheterization showed a consider-

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Received February 21, 2001; accepted for publication May 21, 2001.

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**Fig. 1.** Electron beam computed tomographic scans with volume scanning mode (Imatron C-150 XP; Imatron Inc., San Francisco, CA) indicated diffuse calcific deposits in the aortic and mitral annulus. The diameter of the sinuses of Valsalva as well as aortic annulus was smaller than 19 mm.

able increase in the transaortic valve pressure gradient (98 mmHg), with elevated pulmonary artery wedge pressure (21 mmHg). The calculated mitral valve area was 1.7 cm<sup>2</sup>. Mild mitral regurgitation was noted and it may have exaggerated the elevation of pulmonary artery wedge pressure. The coronary arteries were normal in angiography. The severity of liver cirrhosis was graded as class A according to the criteria of Child.<sup>1)</sup> The cause of liver cirrhosis is unknown; however, it was apparently not related to either alcohol or hepatitis B and C viruses. Because tricuspid regurgitation was not detected and the mean right atrial pressure was not high (3 mmHg), cardiac cirrhosis was unlikely. Preoperative pulmonary function tests showed restrictive pulmonary dysfunction with the forced expiratory volume in one second, 1500 ml; vital capacity, 1870 ml; and % estimated vital capacity, 51%.

Intraoperative measurement of the aortic annulus indicated that it was slightly smaller than 19 mm. Annular enlargement was performed to pass metal dilators through the aortic annulus changing from a smaller size to a larger one. Finally, a mechanical prosthetic valve (St. Jude Medical 19 mm; St. Jude Medical Inc., St. Paul, MN) could be inserted. Total bilirubin increased to 5.3 mg/dl on the second postoperative day but gradually returned to the preoperative value. The diminishment of postop-

erative hepatic protein synthesis appeared with total protein, 5.4 g/dl; cholinesterase 1439 IU/l. Otherwise, the postoperative course was uneventful and he is doing well with neither anginal pain nor dyspnea two years after the operation. Warfarin was started on the first postoperative day, keeping the international normalized ratio (INR) of the thrombo test between 1.6 and 2.8. The daily dose of warfarin is stabilized to be 2.5 mg.

A postoperative echocardiogram at two weeks showed good functioning of the aortic prosthetic valve and an ejection fraction of 0.56. Moderate mitral stenosis and mild mitral insufficiency remained unchanged. Histopathological findings of the excised aortic cusps are not specific but indicated fibrous and hyalinous thickening with calcification.

## Discussion

Otto Werner first described a family with Werner's syndrome in 1904. Since then, approximately 400 cases have been reported in the world. Khraishi et al. estimated that the prevalence of patients with Werner's syndrome is 1:500,000.<sup>2)</sup> The average life span of patients with Werner's syndrome is 47 years, and the principal causes of death are vascular disease (cardiovascular or cerebrovascular) and malignancy.

The cardiac manifestations previously described include coronary artery disease, calcification in the annulus or cusps of the mitral and/or aortic valves with resultant valvular dysfunction. Our patient not only has valvular dysfunction but also liver cirrhosis with gastroesophageal varices. Concomitant fatty liver is reported but liver cirrhosis is very rare in patients with Werner's syndrome.<sup>3)</sup> To our knowledge, this is the first report of aortic valve replacement in a patient with Werner's syndrome and concomitant liver cirrhosis in the world. Liver cirrhosis with esophageal varices increases the mortality and morbidity of cardiac operations with respect to postoperative liver dysfunction and rupture of the varices. Klemperer et al. reported that patients with liver cirrhosis have numerous complications and a high mortality rate (31%) after cardiac operations.<sup>4)</sup> We accomplished aortic valve replacement for the patient without major postoperative complications.

Our institution has an electron beam computed tomography, which is more competent in detecting calcific deposits in the heart than conventional computed tomography. We often perform the electron beam computed tomography as a preoperative evaluation of calcific deposits in valve apparatus as well as coronary arteries.

To avoid massive bleeding from the gastroesophageal varix when it is ruptured, a biological prosthetic valve may be preferable to a mechanical valve, which requires taking an anticoagulant. However, the patient has small sinuses of Valsalva as well as the aortic annulus, which were smaller than 19 mm. We were afraid that a high profile prosthetic valve such as stented biological valves could not be inserted. We also considered stentless biological valves but a stentless biological valve smaller than 19 mm is not available. It is difficult to obtain homografts of aortic valves in our country. Furthermore, inaccurate sizing of prosthetic valves is reported. Christakis et al. demonstrated that external diameter varies in each pros-

thetic valve and external diameter of St. Jude Medical mechanical valve (standard type) is not larger than other prosthetic valves including biological prosthetic valves in a certain labeled size.<sup>5)</sup> Several techniques for enlarging the aortic annulus, including Manouguian's and Nick's are available, but we thought these procedures are too invasive for the patient who has liver cirrhosis and other organic dysfunction. For these reasons, we chose a St. Jude Medical mechanical valve (standard type) for the aortic valve replacement. As for postoperative anticoagulation, the patient receives 2.5 mg of warfarin with well-controlled INR. The dose of warfarin is smaller than that in patients with normal liver function. Anticoagulation is kept on because of higher incidence of cerebral infarction in patients with Werner's syndrome.

Because cardiovascular disease is one of the main causes of death, we consider that aggressive surgical treatment for valvular dysfunction in patients with Werner's syndrome is justified.

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