ABSTRACT

The treatment of recurrent prosthetic valve endocarditis is extremely difficult. Heart transplantation (HT) may save the patient's life. Recurrent endocarditis, however, can occur after HT. This report described a patient who had undergone four conventional valve surgeries and three HTs successfully. In May 2000, a 14-year-old boy suffered from endocarditis with severe aortic valve regurgitation. He underwent aortic valve replacement (AVR) at another hospital. Due to prosthetic valve endocarditis, he displayed a severe paravalvular leakage and was transferred to our hospital where he underwent Bentall's operation in October 2000. Despite a full antibiotic course, he experienced a relapse of the prosthetic endocarditis with significant deterioration of the heart function and a progressively more severe paravalvular leak. Considering the difficulties of repair and the poor heart function, he underwent an HT in June 2003 and recovered well. Unfortunately, endocarditis with aortic valve regurgitation attacked him again after 3 years. Remarkably, all blood cultures were negative. A second AVR was performed in October 2006 with a Second Bentall's procedure 1 year later in 2007. In November 2009, the patient suddenly displayed cardiogenic shock with collapse. He was transferred to our hospital and needed extracorporeal membrane oxygenation (ECMO) support. Two days later, he underwent a second HT. However, the donor heart was nonfunctional due to the prolonged ischemia time. ECMO support was continuously needed after the HT. A third HT was performed successfully 10 days later. Due to previous reported experiences of culture-negative endocarditis, minocycline was prescribed twice daily continuously after the third HT/seventh cardiac surgery. The patient was discharged 2 months later. To date he takes minocycline every day and lives a healthy life.

CASE REPORT

A 14-year-old boy with Marfan's syndrome and valvular heart disease was transferred from another tertiary hospital, due to progressive chest tightness and dyspnea in September 2000. His medical history showed a diagnosis of IE with severe aortic valve regurgitation (AR). In May 2000, cardiac surgery was performed as an AVR with a metallic valve after 4 weeks of antibiotic treatment. He was discharged home. Four months later, he suffered chest tightness and dyspnea with progression to low-grade fever. Echocardiogram showed preserved heart function, metallic aortic...
cardiac surgeons decided that a high-risk HT would be the only ventricular (LV) dysfunction. A conference of cardiologists and conduit dehiscence with severe AR and moderate to severe left thromboembolism in the left main graft as well as a valvular caused by thrombosis of the prosthetic aortic valve, which was during the hospitalization showed negative results. He recovered rapidly after surgery, but remained febrile despite antibiotics. On December 3, 2000, antibiotics had to be discontinued due to a drug allergy with a skin rush and itching on the trunk and extremities. He was discharged 5 days later. All blood cultures during the hospitalization showed negative results.

In April 2003, he was admitted due to symptoms of heart failure caused by thrombosis of the prosthetic aortic valve, which was treated with a urokinase infusion. Cardiac catheterization showed a thromboembolism in the left main graft as well as a valvular conduit dehiscence with severe AR and moderate to severe left ventricular (LV) dysfunction. A conference of cardiologists and cardiac surgeons decided that a high-risk HT would be the only lifesaving option for the patient. He underwent elective HT on June 23, 2003, with the standard immunosuppressive regimen.

Routine echocardiograms followed every half year due to the past history of endocarditis showed no evidence of endocarditis recurrence. On October 17, 2006, he was admitted because of vegetation (more than 1 cm²) over the aortic valve with moderate AR. Antibiotic treatment with vancomycin and amikacin was started for the diagnosis of transplant IE. The follow-up echocardiogram showed the vegetation to be bigger. He underwent a fourth cardiac surgery, namely placement of a metallic valve for AVR. Spiking fevers were noted postoperatively and antibiotic treatment was shifted to linezolid and gentamicin. After 4 weeks of antibiotic treatment, he was discharged home without oral antibiotics. The patient reported a poor appetite and dyspnea at the outpatient department. An echocardiogram revealed AV dehiscence severe AR, as well as moderate to severe mitral and tricuspid valve regurgitation. The fifth cardiac surgery, a Bentall's procedure with a stentless valvular conduit, was performed on October 8, 2007. During the operation abscess formation was noted with annular disruption. The annulus was reconstructed using bovine pericardium and the stentless valvular conduit sutured to the annulus. Six weeks of antibiotic treatment was prescribed thereafter.

Four months later, a paravalvar leakage of AV recurred with severe AR. Separation between implanted right coronary artery and the valvular conduit with strong flow in the gap of the native aorta and the conduit were noticed to be accompanied by moderate LV dysfunction in August 2008. However, his health remained marginal for a while. On November 24, 2008, he presented to another hospital with acute collapse. He was transferred to our emergency department and placed immediately on mechanical support. He was kept on MCS with ECMO and intra-aortic balloon pumping for 10 days before undergoing the seventh cardiac surgery/third HT. During the hospitalization, he was on ECMO support for 16 days and received eight operations, including setup and removal of ECMO, two HTs, and pericardiectomy to check bleeds. There was neither a sternotomy nor an ECMO wound infection; he was free of acute renal failure and other complications. Remarkably, all blood cultures in his medical course showed negative results. Because of the culture-negative IE, the prescribed antibiotics were fluconazole to treat a fungal infection after the third HT. Due to the severe facial acne, infectious disease specialists suggested to prescribe minocycline. Until now, he has been taking minocycline and Cotrimoxazole regularly for infective prevention. He has also been prescribed low dosages of immunosuppressants to prevent rejection.

**DISCUSSION**

This patient is one of the few cases of persistent endocarditis in the native or transplanted heart. The cumulative incidence of transplant endocarditis is 1.5% to 1.7%. Noticeably, the incidences of endocarditis in heart, liver, and kidney transplant recipients is equal. Endocarditis-associated mortality is about 60% to 80% in this group.

The most common pathogen for transplant patients is *Staphylococcus aureus* (40% of cases), as in the general population. The second common pathogen is *Aspergillus fumigatus* (30%), which is different from the general population (coagulase-negative *Staphylococcus*, such as *Staphylococcus epidermidis* and *Staphylococcus lugdunensis*). About 15% of PVE, especially after 1 year of surgery, are culture-negative endocarditis (CNE). American Heart Association/American College of Cardiology guidelines recommend to use broad-spectrum antibiotics for CNE patients for at least 6 weeks. However, small, sporadic studies with a few case reports have suggested various therapeutic methods for CNE in transplanted patients. At present, we believe that 6 weeks of antibiotic treatment perioperatively is not sufficient.

Considering the shortage of donor hearts, HreT might not have been the right choice for the present case of CNE and heart failure. Since the first successful HreT in 1974, only 2% to 3% of primary transplant recipients have received HreT. Transplanted coronary vasculopathy is the major cause. No HreT due to IE has been reported to our knowledge, probably since IE is considered to be a contraindication to HT. After multiple reports have summarized experiences, IE with cardiogenic shock may be an absolute contraindication for HT and even HreT. However, HT and HreT was performed emergently in this 25-year-old man, under inotropic and mechanical support.

In conclusion, mortality of PVE is high despite advanced surgical technology and material. We successfully treated the present case of persistent native, prosthetic, and transplanted endocarditis. From this experience, we suggest that heart replacement can completely eradicate the intratable infective source in the intracardiac cavity. The length of antibiotic treatment for PVE is unclear, especially for transplanted heart cases. Oral antibiotics should last life-long and, any infectious disease may be an absolute contraindication for HT in some cases, but HT or even HreT may be a therapeutic option for IE. The present case is now healthy without sequela, with a regular job and social life.
REFERENCES