Aortic Valve Replacement in a Patient With Myelodysplastic Syndrome and Interstitial Pneumonia

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There are a few reports of cardiac surgery in patients with myelodysplastic syndrome (MDS). It is difficult to control bleeding and prevent infection in the presence of pancytopenia. Interstitial pneumonia, which is treated by steroid medication, is also a risk factor in cardiac surgery. Aortic valve replacement was successfully performed in a patient with severe thrombocytopenia associated with MDS, interstitial pneumonia and scleroderma. (Circ J 2007; 71: 1826–1828)

Key Words: Aortic valve replacement; Interstitial pneumonia; Myelodysplastic syndrome

Although the clinical outcome of cardiac surgery in a patient with many complications is poor, scheduled treatment and careful management of each underlying problem may give a good result. Myelodysplastic syndrome (MDS) is clinical condition with pancytopenia caused by dysplasia of the bone marrow. Because the patients with MDS has risks of bleeding and infection,1-5 cardiac surgery using extracorporeal circulation (ECC) increases those risks. Interstitial pneumonia is also a risk factor in cardiac surgery, because it exacerbates lung function after surgery, and steroid therapy for interstitial pneumonia associated with scleroderma is necessary, but that also increases the morbidity and mortality.3,4 We present a successful case of aortic valve replacement (AVR) in a patient with severe thrombocytopenia related to MDS, scleroderma and interstitial pneumonia.

Case Report

A 73-year-old woman was referred for surgical treatment of aortic valve stenosis. She had been suffering from dyspnea on exertion for several years. In 1988 she was treated by dermatologist for scleroderma, and had been taking 5 mg of prednisolone sodium for interstitial pneumonia since 2000. In December 2002, she was referred for hematological examination because of pancytopenia. Chromosomal analysis of her bone marrow aspirate showed an abnormal karyotype: 47,XX,+8. She was diagnosed as having MDS with a subtype of refractory anemia (RA) and had been followed for 3 years without medication because of slow progression of the disease and in consideration of her age. Physical examination revealed a systolic heart murmur at the 2nd right intercostal space and bilateral fine crackles over the whole lung field. Laboratory investigations revealed severe pancytopenia: white blood cell (WBC) count was 1,860/mm³; red blood cell (RBC) count 215×10⁴/mm³; hemoglobin 7.5 g/dl, and platelet count was 1.5×10⁴/mm³; serum lactate dehydrogenase was 295 U/L, serum KL-6 level was 1,210 U/ml (normal <500 U/ml) and SP-D was 33.7 ng/ml (normal <110 ng/ml), which reflected the severity of the interstitial pneumonia. Respiratory function analysis was normal: vital capacity was 1,980 ml (87.2%), 1-s forced expiratory volume was 1,570 ml (93.4%). We judged the interstitial pneumonia to be inactive and well controlled by steroid therapy. Chest roentgenogram revealed bilateral diffuse reticular shadows on the lung fields. Chest computed tomography findings were consistent with interstitial pneumonia (Fig 1). Cardiac catheterization revealed aortic valve stenosis with a mean pressure gradient of 78 mmHg, and the aortic valve area was 0.4 cm². Although she and her family hoped for surgery, we hesitated to perform it, because the combination of these rare medical illnesses meant that an unfavorable outcome was very likely. To accomplish the operation safely, a perioperative management program was instituted for each potential complication. To control the bleeding diathesis, 20 units of platelet concentrate (PC)
were transfused prior to operation in order to keep the platelet count over 50,000/mm³. Intravenous administration of glucocorticoid (100 mg hydrocortisone) was done on the day of surgery and first postoperative day, until the patient could take medicine orally. A urinary trypsin inhibitor, ulinastatin 300,000 units, was administered for 3 days to prevent worsening of the interstitial pneumonia. Granulocyte colony-stimulating factor (G-CSF) was not given, as per the published guideline. Prophylactic administration of antibiotics was done as usual.

AVR was performed in November 2005. Heparin was administered as usual during cardiopulmonary bypass (CPB) and the activated clotting time was kept over 400 s. After excision of the severely calcified aortic valve, a 19-mm Carpentier-Edwards pericardial bioprosthesis (Edwards Lifescience, Irvine, CA, USA) was implanted. Partial endarterectomy of the calcified aortic root was performed simultaneously. The operation time was 260 min, CPB time 100 min, and aortic cross-clamping time 87 min; 40 units of PC, 6 units of RBCs, and 3 units of fresh frozen plasma were transfused during the operation. Endotracheal tube was extubated 12 h after surgery. The postoperative course was uneventful and there was no untoward bleeding, because of the timely infusion of platelet-rich plasma (Fig 2). We transfused PC when the platelet count went below 10,000/mm³. Both the platelet count and WBC count returned to preoperative levels on the 43rd postoperative day. The patient was administered a β-blocker and an angiotensin-converting enzyme inhibitor in order to prevent myocardial remodeling as a result of hypertrophied cardiomyopathy. The patient was doing well at 15 months after surgery.

**Discussion**

MDS is a clonal hemopathy characterized by ineffective hematopoiesis and cellular dysfunction! It has been classified by the French-American-British Cooperative Group into 5 categories: RA with ringed sideroblasts (RARS); RA with excess blasts (RAEB); RAEB in transformation (RAEBIT); and chronic myelomonocytic leukemia (CMML). Survival is intermediate for patients with RAEB and CMML, and poor for patients with RAEBIT! Among the various types of MDS, a subtype of RA has a relatively favorable prognosis. The present patient was not taking any medication with regard to MDS and as there is no effective medication for the treatment of MDS, we pondered whether AVR was indicated. The problems associated with MDS are bleeding and infection because of the thrombocytopenia and leukopenia. Surgery in patients with severe thrombocytopenia less than 30,000/mm³ may be accompanied by a high risk of intractable bleeding during and after surgery. The present patient had a platelet count of 15,000/mm³, which is the bleeding diathesis level in ordinary daily life. As we had no experience doing cardiac surgery using CPB in a patient with such severe thrombocytopenia, we investigated the literature. There are several reports of cardiac surgery in patients with MDS: 3 cases of RA and 1 of RAEB. In the patients with the RA or RARS of MDS, it was possible to perform surgical treatment with replacement of blood cell components. Therefore, we prepared for bleeding and impaired oxygen transportation by supplementing the patient’s blood components. As for the severe thrombocytopenia, PC was given on the day before surgery and during surgery (Fig 2). According to advice from a hematologist, G-CSF was not used because it might induce malignant transformation of leukopoietic cells. The European Society for Medical Oncology recommends that G-CSF should be avoided in patients with MDS because of the possible transformation to acute myeloid leukemia with increased mortality. Even in the absence of G-CSF, the patient’s WBC count actually increased by approximately 4,000/mm³ after operation (Fig 2). Although postoperative surgical site infection and bacterial pneumonia did not occur with the routine administration of prophylactic antibiotics, this issue remains controversial because of the extremely rare nature of this experience, even among the experts. Essentially, body defense mechanisms, not just the leukocyte count, are important in this situation. We conclude that G-CSF may be unnecessary for infection-free cardiovascular surgery in MDS patients. On the other hand, Yamamoto et al reported a case of mycotic abdominal aortic aneurysm in a diabetic patient and use of G-CSF before surgery which we thought was rational use in that case because the patient already had a severe infection.

Interstitial lung disease occurs in approximately 40% of patients with scleroderma and is a leading cause of morbidity and mortality. In the present patient, proliferative...
changes in the lungs were not progressive because she was taking daily steroids. Generally, cardiac surgery using ECC causes a systemic inflammatory response, resulting in deterioration of lung function. It has been reported that various cytokines, such as interleukin 6 and tumor necrosis factor, play important roles in the blood-surface interaction. To prevent progression of the lung disease, we administered ulinastatin during surgery. Sato et al. reported that ulinastatin treatment during CPB attenuated the elevation of interleukin-6 and interleukin-8 release. Sivelestat sodium hydrate prevented acute lung injury after ECC in a rabbit model; however, although in commercial use, administration of sivelestat during surgery is not permitted, so we selected ulinastatin. In fact, the KL-6 value improved from 1,210 U/ml before surgery to 621 U/ml after surgery. Perioperative intravenous steroid replacement therapy was continued the next day until she could take medicine orally. Care was taken not to prolong mechanical ventilation after surgery because it may induce ventilator-related lung injury and pneumonia. As a result of these multidisciplinary treatments, her interstitial pneumonia did not worsen.

In conclusion, scheduled treatment and careful management for each potential complication made it possible to perform cardiac surgery with ECC safely in a patient with severe MDS.

References