CASE REPORT

Rapid Progression of Aortic Regurgitation with Thoracic Aortic Aneurysm due to Takayasu Arteritis Associated with Ulcerative Colitis

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Abstract

A 25-year-old woman with ulcerative colitis developed heart failure due to severe aortic regurgitation. Although chest X-ray 18 months previously showed a normal cardiac shadow, thoracic aortic aneurysm progressed due to Takayasu arteritis. Aortic valve and ascending aorta replacement were performed successfully, but re-valve replacement for severe aortic regurgitation due to prosthetic valve detachment and aortic root replacement for valsalva sinus rupture were required. Human leukocyte antigen analysis showed B35 and B52, the typical haplotype in cases with coexistence of both diseases and associated sustained inflammation. Close observation and early aortic root replacement were needed in this case.

Key words: aortic valve replacement, aortitis syndrome, inflammation, human leukocyte antigens (HLA)

Introduction

Takayasu arteritis (TA) and ulcerative colitis (UC) are types of idiopathic vasculitis occurring in young individuals. However, only a few reports have described the clinical course of patients with both diseases. A higher frequency of the human leukocyte antigens (HLA) Bw52 and DR2 was demonstrated in patients with these two diseases (1-6). Herein, we describe a patient treated with three aortic surgeries during one year due to aortic regurgitation, prosthetic valve detachment, and sinus rupture of the valsalva associated with TA and UC.

Case Report

A 25-year-old woman who had been treated for UC was admitted to our hospital with chest pain, palpitation, and malaise. After she was diagnosed with UC at age 15 years old, treatment with prednisolone (PDN) was carried out for eight years, and immunosuppressive therapy with salazosulfapyridine (SASP; 4 g per day) was used as a replacement which resulted in remission. The patient was sick for two weeks prior to admission. Physical examination at the time of admission showed alert consciousness, body temperature of 36.2°C, regular pulse rate (105 beats/min), and a blood pressure at the brachial artery of 102/49 mmHg on the right and of 93/47 mmHg on the left. A grade 3 to-and-fro murmur was heard on the third left sternal border, and rales on both lung fields. No bruits were audible around the cervical region. The pulses of other superficial arteries were well palpable. The patient was free from abdominal symptoms, which suggested remission of UC. Chest X-ray on admission showed pulmonary congestion and protrusion of the ascending aorta when compared with X-ray taken 18 months prior (Fig. 1A, B), while electrocardiogram showed a nega-
Figure 1. Chest X-ray on admission (A) showed pulmonary congestion and protrusion of the ascending aorta (arrow) when compared with X-ray taken 18 months prior (B).

Figure 2. Volume-rendered image of multislice computed tomography revealed an aneurysm of the ascending aorta (A, arrow). Dilatation of the ascending aorta (57.1×48.6 mm) was shown on computed tomography (B).

tive T wave on V3 to V6 suggestive of volume overload. Enlargement of the ascending aorta was observed on computed tomography (Fig. 2A, B), and hyperplasia of the media and intima of the carotid artery were detected on ultrasound. Cardiac ultrasound examination revealed dilatation of the aortic root and severe aortic regurgitation with mild pulmonary hypertension (Fig. 3A, B); left ventricular (LV) diastolic dimension was 55 mm, LV ejection fraction was 46%, ascending aorta was 47 mm, and estimated right ventricular (RV) pressure was 52 mmHg. Laboratory findings were as follows: C-reactive protein (CRP) 2.61 mg/dL, erythrocyte sedimentation rate (ESR) 105 mm/h, white blood cell count 12,620/mm$^3$ (92.0% neutrophils, 4.9% lymphocytes, 2.3% monocytes), red blood cell count 371×10$^4$/mm$^3$, hemoglobin 10.8 g/dL, and platelet count 37.2×10$^4$/mm$^3$. Fibrinogen was increased to 728 mg/dL, while prothrombin time and active partial thrombin time were within normal limits. Brain natriuretic peptide (BNP) was elevated to 626.2 pg/mL (normal= <18.0 pg/mL), but no other abnormal values were seen including results for liver function, renal function analysis, and immunological studies. HLA typing showed B 35, B 52.

The patient was diagnosed with congestive heart failure due to aortic regurgitation associated with aortitis syndrome, and treatment with diuretics and catecholamine was performed, and steroid therapy with PDN at 30 mg/day was restarted immediately. Sixteen days after admission, aortic valve and ascending aorta replacement was performed. At operation, an aneurysm of the ascending aorta was observed (52 mm in diameter) with a thickened wall, and enlargement of the sinotubular junction was the likely cause of aortic regurgitation. Because the sinus of valsalva exhibited a normal appearance, a metallic valve (On-X 21 mm) was chosen and the vascular graft (Gelweave 24×10 mm) was replaced. Histological findings of the aortic wall showed infiltration of lymphocytes with marked fibrosis, which were compatible with TA. Having no clinical findings suggestive of Marfan syndrome, other connective tissue diseases, or vasculitis, she had a definite diagnosis of TA associated with UC.

Cardiac ultrasound examination revealed preserved LV...
Figure 3. Echocardiography on admission showed severe aortic regurgitation due to aortic root dilatation. Parasternal long axis view (A-1) and color Doppler imaging (A-2). Short axis view (B-1) and color Doppler imaging (B-2). LV: left ventricle, Ao: aorta, LA: left atrium, RV: right ventricle

Figure 4. Echocardiography on second admission showed aortic regurgitation due to prosthetic valve detachment of the aorta (arrow). Parasternal long axis view (A-1) and color Doppler imaging (A-2). Echocardiography on third admission revealed dilatation of the valsalva sinus (44 mm), and shunt flow to the RV indicated rupture of the valsalva sinus (arrowhead). Parasternal short axis view (B-1) and color Doppler imaging (B-2). Ao: aorta, LA: left atrium, RV: right ventricle

function without aortic regurgitation following surgical treatment. No abnormal abdominal findings were observed, SASP at 4 g/day was continued, and anticoagulation with warfarin potassium was started. Based on ESR, the 30 mg/day dosage of PDN was decreased gradually. Thirty-three days after surgery the patient left the hospital receiving 15 mg/day PDN and showed only slightly elevated ESR (31 mm/h).

Seven months later, a reoperation for severe aortic regurgitation due to flail prosthetic valve was required. Cardiac ultrasound examination showed detachment of the prosthetic valve and regurgitation at that region (Fig. 4A). The patient had taken 12 mg/day PDN, and exhibited a normal ESR level (6 mm/h) without anemia (Hb 14.5 g/dL). Re-aortic valve replacement (SJM 23A) was performed urgently, and a minimum invasive strategy was chosen because the valsalva sinus showed a normal appearance and had no remarkable changes in diameter (35 mm).

Cardiac ultrasound three months later revealed dilatation of the valsalva sinus (44 mm) and shunt flow to the RV (Fig. 4B). A third operation for the valsalva rupture was required, which was unexpected from the appearance of the valsalva sinus at the second operation. Aortic root replacement (Gelweave 26 mm and SJM 23A), direct suture clo-
sive therapy, and coronary artery bypass grafting to the left main trunk were performed successfully. Forty-six days after the third surgery, the patient left the hospital receiving 20 mg/day PDN and showed an almost normal ESR level (20 mm/h).

**Discussion**

TA is a chronic vasculitis mainly involving the aorta and its branches, and presents with various ischemic symptoms of the upper extremities and cervical lesion. UC is an inflammatory bowel disease involving the colonic mucosa accepted as a type of autoimmune disorder. Pathological findings of TA were found in 100 (0.04%) out of 293,315 general autopsies, whereas the incidence of UC was reported as 7.85/100,000 in Japan. The coincidence of TA and UC is a rare condition, with only 39 Japanese cases reported.

The pathogenic association of TA with UC is unclear, although a common genetic basis has been speculated because of the high frequency of specific HLA A2, A24, B52, and DR2 (1-6, 10, 11). Patients with this haplotype are prone to accelerated inflammatory progression and resistance to steroid therapy. The present patient was positive for HLA B 35 and B 52, which is the typical haplotype observed in cases with coexistence of both diseases. On the other hand, previous histopathological analysis has revealed inflammatory cell infiltration in the adventitia and the media, and granulomatous changes of the vessel walls in TA (12). Park et al (13) also reported that levels of inflammatory cytokines, including serum interleukin (IL)-18 and IL-6, were elevated in patients with TA, especially in those with active disease, and that serum IL-18 levels correlated well with disease activity. Furthermore, Nishimoto et al (14) reported successful treatment of a patient with refractory active TA complicated by UC using an anti-IL-6 receptor antibody. The disease activity in the present case seemed elevated, although inflammatory markers such as CRP and ESR were almost normalized due to steroid therapy. Thus, monitoring of serum IL-6 and IL-18 may be useful.

Surgical treatment of aortic regurgitation associated with TA can be complicated with occurrence of prosthetic valve detachment or formation of pseudoaneurysm at the suture line. Late dilatation of the ascending aorta after aortic valve replacement is a clinically important finding. Active inflammation could be related to valve or graft detachment. Matsuura et al (15) reported that detachment of the valve or graft occurred in four of ten patients confirmed with active inflammation in intraoperative pathological specimens. Adachi and colleagues (16) analyzed the surgical management of aortic regurgitation in 15 patients with aortitis syndrome, and reported that the incidence of prosthetic valve detachment or aortic root dilatation was higher after aortic valve replacement than after aortic root replacement. In the present case, aortic valve and ascending aorta replacement, but not aortic root replacement, was performed because the appearance of the vasa vasorum was normal. However, we should have performed aortic root replacement considering the incidence of prosthetic valve detachment and the rupture in cases with coexistence of TA and UC even if the sinus of vasa vasorum exhibited a normal appearance.

The prognostic factors for patients with TA were reported as progressive clinical course and major complications such as retinopathy, hypertension, aortic regurgitation, and aneurysm, and the 15-year survival rate was 66.3% versus 96.4% for patients with and without a major complication (17). Although the present patient achieved remission of UC, she had almost all of these prognostic factors, which suggested a poor prognosis. Further studies are required to elucidate the pathophysiological background, genetic mechanisms, and appropriate management in patients with both TA and UC.

**References**


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