Aortic Root Replacement for Takayasu Arteritis Associated With Ulcerative Colitis and Ankylosing Spondylitis

— Report of a Case —

Shigeaki Aoyagi, MD; Hidetoshi Akashi, MD; Takemi Kawara, MD;
Kenji Ishihara, MD; Atsuhisa Tanaka, MD; Seiji Kanaya, MD;
Yoshinori Koga, MD; Ritsuko Ishikawa, MD

A 26-year-old man was admitted for treatment of congestive heart failure resulting from aortic regurgitation. The patient had been on medical treatment for ulcerative colitis (UC) since he was 14 years old and for ankylosing spondylitis (AS) since he was 20 years old. On admission, gradients of blood pressure among the extremities were observed. Echocardiography revealed marked dilation of the left ventricle (LV), hypokinetic wall motion of the LV, slightly prolapsed aortic cusps with annular dilatation, and severe aortic regurgitation. Computed tomographic scans demonstrated an aneurysmal dilation of the ascending aorta and thickening of the descending and abdominal aortic wall. Digital subtraction angiography demonstrated an aneurysmal dilation of the ascending aorta; however, there was no clear evidence of steno-occlusive lesions in the brachiocephalic vessels. Blood studies showed positive inflammatory signs and negative rheumatoid factor. HLA typing showed A2, 24(9), B27, 67, Cw1, 7, and DR1, 2. Based on these data, the diagnosis of Takayasu arteritis associated with UC and AS was made. Aortic root replacement was performed. Steroid therapy was restarted immediately after surgery. Histologic studies of the aortic wall showed findings compatible with Takayasu arteritis. The combination of these rare diseases suggests that they have a common pathophysiologic background.

(Jpn Circ J 1998; 62: 64–68)

Key Words: Takayasu arteritis; Ulcerative colitis; Ankylosing spondylitis; Overlapping syndrome; Aortic regurgitation

Takayasu arteritis, ulcerative colitis (UC), and ankylosing spondylitis (AS) are chronic inflammatory diseases of unknown etiology. These 3 diseases are not very common in Japan. However, several cases in which these diseases coexisted in the same patient have been described^{1–3}. On the other hand, Takayasu arteritis, UC and AS all often affect the aorta and the aortic valve, being most often manifested clinically as aortic regurgitation (AR) and aortic aneurysms^{4,5}. These cardiovascular complications frequently require surgical treatment.

We report here a case of a young Japanese man who underwent aortic root replacement for severe AR and an ascending aortic aneurysm resulting from Takayasu

arteritis complicated by long-standing UC and AS. To our knowledge, this is the first reported description of the coexistence of these 3 diseases in the same patient.

Case Report

A 26-year-old man was referred to our hospital for treatment of AR. The patient had been treated with non-steroidal anti-inflammatory drugs after the initial diagnosis of UC with total colonic involvement as a result of clinical, endoscopic, and histologic evaluations when he was 14 years old. At 20 years old, he was also diagnosed as having moderate AR and AS based on the positive findings of clinical evaluations

(Received April 16, 1997; revised manuscript received June 30, 1997; accepted July 7, 1997)

Department of Surgery and Third Department of Medicine, Kurume University School of Medicine, Kurume, Japan

Mailing address: Shigeaki Aoyagi, MD, Department of Surgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume 830, Japan

Fig 1. Computed tomographic scans showed aneurysmal dilatation of the ascending aorta and thickening of the descending aortic wall (left), and also revealed thickening of the abdominal aortic wall without dilatation (right).

Table 1 Laboratory Data on Admission

ESR	110 mm/h
CRP	18.1 mg/dl
WBC	9170
RBC	466×10^4
Hb	11.7 g/dl
Ht	39.0%
Plt	37.0×10^4
TP	9.4 g/dl
Alb	3.45 g/dl
A/G	0.58
Glb	36.8%
α_1 -Glb	4.5%
α_2 -Glb	10.1%
β -Glb	9.8%
γ -Glb	38.8%
GOT	15 IU/L
GPT	15 IU/L
LDH	186 IU/L
BUN	10.2 mg/dl
Cr	0.7 mg/dl
Na	137 mequiv/L
K	4.8 mequiv/L
Cl	96 mequiv/L
T. chol	124 mg/dl
TG	39 mg/dl
LE test	(-)
ANA	(-)
Anti-DNA	45
RA	(-)
IgG	3713 mg/dl
IgA	567 mg/dl
IgM	297 mg/dl
C ₃	90 mg/dl
CH ₅₀	39.9 U/ml
Stool: occult blood	(-)

and of radiographic examinations, and negative serum rheumatoid factor. Since 1994, the patient has been on steroid therapy with prednisolone (7.5 mg/day). In the

middle of November 1996, he experienced dyspnea and palpitation on exertion. On admission, blood pressure was 112/60 mmHg in the right arm, 92/52 mmHg in the left arm, and 140/30 mmHg in both legs. The pulse rate was 108 beats per min with a regular rhythm. A grade 2 to-and-fro murmur was heard on the 3rd left sternal border, and there were rales on both lung fields. A chest radiograph showed moderate cardiomegaly with moderate pulmonary congestion. Echocardiography showed marked dilation of the left ventricle (LV), severely hypokinetic LV wall motion (ejection fraction=30%), and slightly prolapsed aortic cusps with annular dilation. Doppler color flow mapping revealed severe AR and mild mitral regurgitation. Computed tomographic (CT) scans demonstrated aneurysmal dilation of the ascending aorta of 6.0 cm in diameter and thickening of the descending and abdominal aortic wall without dilation, as shown in Fig 1. Blood studies showed an accelerated erythrocyte sedimentation rate, positive C-reactive protein, and an increase in the white blood cell count, as shown in Table 1. HLA typing showed A2, 24(9), B27, 67, Cw1, 7, and DR1, 2. Digital subtraction angiography performed after regression of the inflammatory signs with an increase in prednisolone to 30 mg/day, and demonstrated aneurysmal dilation of the ascending aorta. However, there was no clear evidence of stenocclusive lesions in the brachiocephalic vessels (Fig 2). Based on gradients of blood pressure among the extremities, and the findings of CT scans and angiograms, an additional diagnosis of Takayasu arteritis with AR and an ascending aortic aneurysm to both UC and AS was made.

Because of severely limited physical activity, urgent operation was scheduled before performing cardiac catheterization. To prevent prosthetic valve detachment, aortic root replacement with the modified

Fig 2. Intravenous digital subtraction angiography showed aneurysmal dilatation of the ascending aorta (left), however stenotic lesions in the arch vessels were not clearly found (right).

Bentall technique, which included prosthetic valve translocation, was planned.⁶ At operation, an aneurysm of the ascending aorta with a diameter of 8 cm was confirmed. The aortic wall was strongly thickened, edematous, and had patchy sclerosing lesions. Annular dilation and prolapse of the aortic cusps caused AR. After resection of the aortic cusps, the aortic root was replaced with a composite graft formed by a 26-mm vascular graft (Hemashield, Meadox Medicals, Oakland, NJ) and a 23-mm St Jude Medical valve (St Jude Medical, St Paul, MN). The coronary arteries were reconstructed with a short segment of an 8-mm vascular graft (Hemashield, Meadox Medicals, Oakland, NJ) to the right coronary artery and a saphenous vein graft to the left anterior descending artery because, when an aortic button was made, the left main trunk of the coronary artery was injured. Intra-aortic balloon pumping (IABP) was necessary for weaning off cardiopulmonary bypass; however, the patient recovered uneventfully with the assistance of IABP for 2 days postoperatively. Steroid therapy (prednisolone 30 mg/day) was begun immediately after surgery.

Histologic studies of the aortic wall showed fibrosis and marked infiltration of the inflammatory cells, including monocytes and lymphocytes, with edema and severely destroyed elastic fibers in the intima and media and fibrotic thickening of the intima and adventitia. These findings are considered to be compatible with those of Takayasu arteritis.

Discussion

Takayasu arteritis, UC, and AS are chronic inflammatory diseases of unknown etiology. Although the incidence of Takayasu arteritis is relatively higher

in Japan than in Western countries, these 3 diseases are not very common in Japan. Since the original description by Takayasu,⁷ epidemiologic, pathologic, medical and surgical interventions have been performed, and various terms have been used to describe this disease. A research committee, sponsored by the Japanese government's Ministry of Health and Welfare, has been studying this disease and has given it the name of "Takayasu arteritis."⁸

Pathologic findings of Takayasu arteritis were found in 100 (0.04%) out of 293,315 general autopsies in Japan.⁹ The incidence of UC in Japan was reported to be 7.85/100,000,¹⁰ that is nearly 1/10 to 1/20 of the prevalence in Western countries.¹¹ On the other hand, true prevalence of AS is not known; an epidemiologic study,¹² however, indicated that the prevalence might be in the range of 1% of the population, and that AS occurred rarely in black Africans and Japanese. Therefore, the likelihood of simultaneous occurrence of these 3 diseases is considered to be extremely small. Nevertheless, several cases in which 2 of these 3 diseases coexisted in the same patient have been described.¹⁻⁴ In our patient, all 3 rare diseases coexisted. Although the precise etiology of these 3 diseases is unknown, familial aggregation and the association of these diseases suggest some common pathophysiologic background, particularly the contribution of a genetic mechanism or an immune process to the development of the diseases.

The association of Takayasu arteritis and UC has occasionally been reported,¹ and a higher frequency of HLA haplotypes Bw52 and DR2 has been demonstrated in patients with these 2 diseases. HLA analysis of Japanese patients with Takayasu arteritis previously showed a higher frequency of HLA A9 or Aw24, B5 or Bw52, and DR2 than in healthy Japanese subjects.¹³

On the other hand, HLA Aw24, B5 or Bw52, and DR2 have also been demonstrated in Japanese patients with UC.¹⁴ Thus, HLA haplotypes of Aw24(9), B5 or Bw52, and DR2 are associated with both Takayasu arteritis and UC. Interestingly, the HLA Aw24-Bw52-DR2 haplotype is a characteristic type in the Japanese population¹⁵ and Takayasu arteritis is also one of the characteristic diseases of the Japanese.⁹ The present patient was positive for HLA Aw24 and DR2, but negative for HLA Bw52.

The coexistence of AS and inflammatory bowel disease (IBD), including UC and Crohn's disease, is well known, and the striking association of AS with HLA haplotype B27 has also been demonstrated by a number of workers.^{3,16} Mallas et al³ emphasized the likelihood of HLA B27 being a pathogenetic discriminator between the arthropathies in IBD and its prognostic significance with respect to the extent and severity of the disease. In their study, the incidence of HLA B27 was increased in the patients in whom both UC and Crohn's disease were complicated by AS. Furthermore, AS was found with significantly higher frequency in UC patients with the HLA B27 haplotype than in non-B27 patients. In addition, the incidence of total colonic involvement of IBD was significantly higher in HLA B27 UC patients with than in non-B27 patients. These data support the suggestion that patients with IBD with HLA B27 are more likely to develop AS than others who do not possess this antigen. Our patient had HLA B27 antigen, in addition to HLA Aw24 and DR2 antigens, and also had total colonic involvement of UC.

The association of Takayasu arteritis and AS has been described in several English-language journals.² Although HLA typing was, unfortunately, performed in only 2 patients, both patients were negative for HLA B27. However, all of the previously reported 3 patients who underwent aortic valve replacement for AR due to AS were positive for HLA B27.⁵ Contrary to predominance of Takayasu arteritis in young females, AS has always been thought to be primarily a disease of males. However, current investigations¹² indicate that the sex ratio in patients with the HLA B27 haplotype, especially in those with AS complicating IBD, may be as close as 1:1. Considering these data, it seems possible that a genetic mechanism plays an important role in the pathogenesis of the overlapping of Takayasu arteritis, UC, and AS that was observed in our young male patient. Abnormalities of the humoral immune response have also been described in these 3 diseases. Increased concentrations of serum immunoglobulins are commonly found in these diseases;¹⁷ as was observed in our patient.

Although depletion of complements was not detected in our patient, the presence of circulating immune complexes has had much attention in the pathogenesis of the unusual combination of these diseases.¹⁸

Aortic valve replacement in inflammatory cardiovascular diseases, such as Takayasu arteritis and Behçet disease, deserves special attention because valve detachment, paravalvular leakage, and pseudoaneurysm formation are not rare postoperative complications.¹⁹ Yamauchi et al²⁰ employed the modified Bentall technique, which included translocation of the prosthetic valve to 1.5–2.0 cm above the proximal extremity of the vascular graft. They emphasized that the key to repairing valve detachment in Takayasu arteritis was to reduce the tension on the suture line and aortic annulus and suggested that aortic root replacement, especially with an allograft, might provide favorable results. Thus, we performed aortic root replacement with translocation of the prosthetic valve to 1.5 cm above the proximal extremity of the vascular graft.

In conclusion, we performed aortic root replacement in a young male Japanese patient with AR and an ascending aortic aneurysm resulting from the overlapping of Takayasu arteritis, UC and AS, and we believe that a combination of these 3 rare diseases suggests some common pathophysiologic background, in particular a genetic mechanism or a certain immune process.

References

1. Sato R, Sato Y, Ishikawa H, Oshima Y, Suzuki T, Watanabe S, et al: Takayasu's disease associated with ulcerative colitis. *Int Med* 1994; **33**: 759–763
2. Hull RG, Asherson RA, Rennie JAN: Ankylosing spondylitis and an aortic arch syndrome. *Br Heart J* 1984; **51**: 663–665
3. Mallas EG, Mackintosh P, Asquith P, Cooke WT: Histocompatibility antigens in inflammatory bowel disease: their clinical significance and their association with arthropathy with special reference to HLA-B27 (W27). *Gut* 1976; **17**: 906–910
4. Yamaguchi A, Kitamura N, Otaki M, Minoji T, Tamura H: A case of Bentall's operation for annuloaortic ectasia complicated with ulcerative colitis and aortitis syndrome (in Japanese with English abstract). *J Jpn Assoc Thorac Surg* 1988; **36**: 578–582
5. Kawasaki M, Hetzer R, Oelert H, Stauch G, Borst HG: Aortic valve replacement and ascending aorta replacement in ankylosing spondylitis: report of 3 surgical cases and review of the literature. *Thorac Cardiovasc Surg* 1982; **30**: 310–314
6. Aoyagi S, Kosuga K, Fukunaga S, Akashi H, Oryoji A, Oishi K: Valve detachment after aortic valve replacement – a successfully reoperated case with the Cabrol technique.

- Jpn Circ J* 1996; **60**: 377–381
7. Takayasu M: Case with unusual changes of the central vessels in the retina (in Japanese). *Acta Soc Ophthal Jap* 1908; **12**: 554–555
 8. Numamo F, Lee KT, Hong YC (editors): Takayasu's arteritis 1992. *Heart Vessels* 1992; Suppl 7
 9. Nasu T: Takayasu's truncoarteritis. Pulseless disease or aortitis syndrome. *Acta Pathol Jpn* 1982; **32**(Suppl 1): 117
 10. Utusnomiya T, Suzuki K, Shinohara H: Epidemiology of ulcerative colitis (in Japanese). *Clin Gastroenterol* 1987; **2**: 187
 11. Calkins BM, Lilienfeld AM, Garland CF, Mendeloff AI: Trends in incidence rates of ulcerative colitis and Crohn's disease. *Dig Dis Sci* 1984; **29**: 913
 12. Calin A and Fries J: The striking prevalence of ankylosing spondylitis in "healthy" W27 positive males and females: a controlled study. *N Engl J Med* 1975; **293**: 835
 13. Wakisaka A: Present status of intractable disease and HLA in Japan (in Japanese). *Clin Immunol* 1982; **14**(Suppl 4): 2
 14. Shiwaku Y, Morita N, Sakaguchi T, Inoue M, Tsuji K: HLA antigens in ulcerative colitis (in Japanese). *Clin Immunol* 1982; **14**(Suppl 4): 76
 15. Tokunaga K, Juji T: Distribution of MHC alleles in Japanese (in Japanese). *Nippon Rinsho* 1984; **42**(Suppl): 335
 16. Scarpa R, Puente AD, D'Arienzo A, di Girolamo C, della Valle G, Panarese A, et al: The arthritis of ulcerative colitis: clinical and genetic aspects. *J Rheumatol* 1992; **19**: 373–377
 17. Ito I, Saito Y, Nonaka Y: Immunological aspects of aortitis syndrome. *Jpn Circ J* 1975; **39**: 459–462
 18. Peeters AJ, van den Wall Bake AW, Daha MR, Breedveld FC: Inflammatory bowel disease and ankylosing spondylitis associated with cutaneous vasculitis, glomerulonephritis, and circulating IgA immune complexes. *Ann Rheum Dis* 1990; **49**: 638–640
 19. Isomura T, Hisatomi K, Yanagi I, Shimada S, Uruguchi K, Aoyagi S, et al: The surgical treatment of aortic regurgitation secondary to aortitis. *Ann Thorac Surg* 1988; **45**: 181–185
 20. Yamauchi M, Eishi K, Sasako K, Nakano K, Isobe F, Kawashima Y: A case of aortitis operated twice Bentall's operation due to valve (graft) detachment (in Japanese with English abstract). *Jpn J Thorac Surg* 1994; **47**: 1083–1085