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Case Study

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Association between Takayasu arteritis and ulcerative colitis – case report and review of serological HLA analysis

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A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: Takayasu arteritis and ulcerative colitis are immune-mediated inflammatory diseases; genetic factors are assumed to play an important role in the pathogenesis of these 2 diseases. However, the coexistence of these 2 diseases has rarely been reported.

Case Report: In this report, we present a rare case of a 29-year-old man with a 4 years history of ulcerative colitis who developed Takayasu arteritis. He was found to carry the following human leukocyte antigens (HLA): A11, A24, B52, B62, DR4, and DR9.

Conclusions: We present a case report and review of the pertinent literature on serological analysis of HLA haplotype of the patients who exhibit both these diseases. In patients with both Takayasu arteritis and ulcerative colitis, high frequency of HLA-A24, B52, and DR 2 is observed. The pathological relevance of HLA-A24, B52, and DR2 to concomitant Takayasu arteritis and ulcerative colitis requires further investigation.

key words: takayasu aortitis • ulcerative colitis • HLA analysis

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Background

Takayasu arteritis is a chronic inflammatory disease that primarily affects large elastic arteries such as the aorta and its major branches; this disease is rare in North America and Europe but common in Japan and Southeast Asia. Females less than 40 years are predominantly affected. Although the cause of this disease is unclear, many case reports and studies have indicated that immunological abnormalities may be involved in the pathogenesis of this form of vasculitis. Numerous studies have suggested that immunological factors are involved in ulcerative colitis and that the coexistence of lupus erythematosus, autoimmune hemolytic anemia, and chronic hepatitis with ulcerative colitis is suggestive of an autoimmune phenomenon. Moreover, many reports have described that genetic factors are important in the pathogenesis of the 2 diseases. However, occasional case reports have revealed an association between Takayasu arteritis and ulcerative colitis, but the complicated coexistence of the 2 diseases might be rare.

In this report, we describe a case of a 29-year-old Japanese man with ulcerative colitis complicated by Takayasu arteritis and present a genetic review of the pertinent literature on the serological analysis of human leukocyte antigen (HLA) haplotypes in the patients with both Takayasu arteritis and ulcerative colitis.

Case Report

A 29-year-old Japanese man was admitted to our hospital in March 2007 for cardiovascular examination. The patient was experiencing diarrhea and bloody bowel discharge since he was at high school. At the age of 20 years, the patient was diagnosed with ulcerative colitis at a local hospital. Subsequently, at the age of 24 years, when the patient was admitted to the hospital due to injury, he was diagnosed with Takayasu arteritis at the same hospital unexpectedly. At the time of admission to our hospital, the patient was receiving predonisolone (20 mg/day) and mesalazine (2250 mg/day) therapy.

On admission to our hospital, his height was 167 cm and body weight was 66.9 kg. His body temperature was 36.5°, and blood pressure was 148/50 mmHg and 100/44 mmHg in the right and the left upper limbs, respectively. His heart rate was 67 beats/min. Both Lungs of the patient were clear to auscultation. Heart examination revealed Levine grade III/VI diastolic murmur at the right sternal border. Vascular bruit was audible over the left subclavian artery, abdominal aorta, and both right and left carotid arteries.

Electrocardiogram revealed a heart rate of 70 beats/min, sinus rhythm, and left ventricular hypertrophy. Chest radiograph revealed mild cardiomegaly (cardiothoracic ratio: 53%).

The laboratory findings were as follows: hemoglobin level, 14.1 g/dl; white blood cell count, 14600/mm^3 with 76.2% neutrophils; erythrocyte sedimentation rate, 3 mm/1st h, and 7 mm/2nd h, and serum C-reactive protein level ⩽0.2mg/dl. Hepatic and renal functions, and immunoglobulin and serum complement levels were within the normal limits. Antinuclear antibody, anti-neutrophil cytoplasmic antibodies, and rheumatoid factor were not detected. Serological test for syphilis was negative. The level of brain natriuretic peptide was 42.6 pg/ml (normal level, ⩽20 pg/ml).

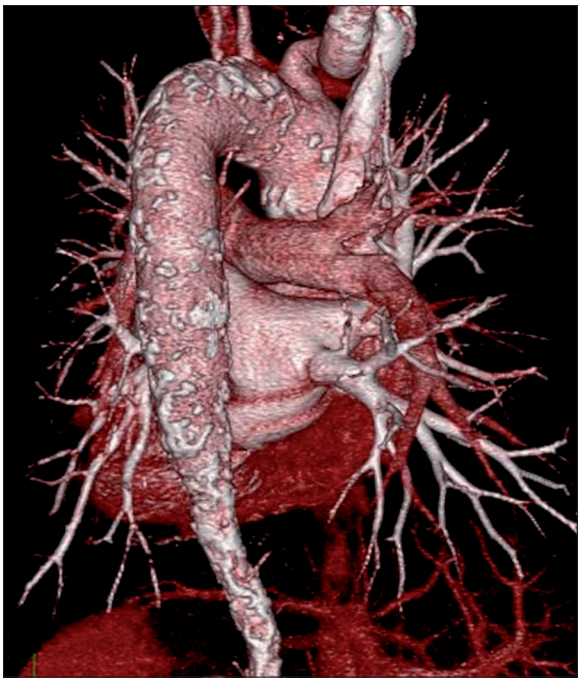

Figure 1. 3-dimensional reconstruction of the great arteries by computed tomography, which demonstrates the dilatation of the ascending aorta and stenosis of the left subclavian artery, descending aorta with severe calcification of arterial wall.

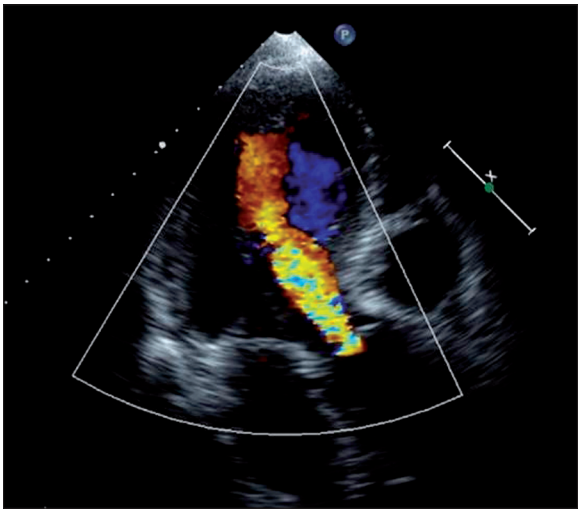

Figure 2. Apical long-axis view of left ventricle in 2-dimensional transthoracic echocardiograpy, which demonstrates severe aortic valve regurgitation.

Contrast-enhanced computed tomography and magnetic resonance angiography revealed dilatation of the ascending aorta and stenosis of the left subclavian artery, descending aorta, and superior mesenteric artery with severe calcification of arterial wall (Figure 1). Multidetector computed tomography showed almost normal epicardial coronary arteries.

Transthoracic echocardiogram revealed severe aortic valve insufficiency (Figure 2) with mild left ventricular hypertrophy (left ventricular end-diastolic diameter: 52 mm, end-systolic diameter: 31 mm, left ventricular ejection fraction

Table 1. Review of published cases of Takayasu arteritis associated with ulcerative colitis who underwent serological HLA analysis.

No	Auther	Published year	Patient's age	Sex	HLA typing
1	Miwa Y	1979	43	F	A2, A9, B5, B13, Cw3
2	Achar KN	1986	35	F	A11, B5, B7, DR2, DR4
3	Ichikawa M	1988	24	F	A2, A24, B51, B52, Cw3
4	Goto M	1991	19	F	A24, A31, B52, Bw 61, Cw3
5	Yoshida H	1992	21	M	A11, A24, B52, DR2, DQm1
6	Ishikawa H	1993	27	F	A2, A24, B52, Bw 61
7	Oyanagi H	1994	25	F	A24, A33, B52, B44, DR2
8	Sato R	1994	14	F	A11, A24, B48, B52, DR2, DR9, DQ1, DQ3
9	So S	1995	27	F	A11, A24, B52, DR2, DR6
10	Morita Y	1996	19	F	A24, B51, B52, DR2, DR12
11	Aoyagi S	1998	26	M	A2, A24, B27, B67, Cw1, Cw7, DR1, DR2
12	Ito Y	2001	21	F	A24, A26, B52, B61, Cw3, DR2, DR8, DQ1
13	Suzuki T	2001	14	M	A24, A33, B52, DR2
14	Shibata C	2002	42	F	A24, A26, B35, B52, Cw3, DR2, DR 4
15	Fukunaga	2002	18	F	B52, DR2
16	Masuda H	2002	41	F	A2, A31, B52, DR2
17	Masuda H	2002	20	F	A2, A31, B52, B61, DR2, DR4
18	Bansal R	2003	15	F	A24, B15, B52, DR4, DR15
19	Hokama A	2003	36	F	A2, B35, Cw3
20	Nakano H	2004	49	M	A24, A26, B52, B4, DR51, DQ6
21	Katsinelos P	2005	36	F	B52, DR2
22	Present case	2010	29	M	A11, A24, B52, B62, DR4, DR9

measured by using modified Simpson method: 68%, interventricular septum: 13 mm, posterior wall: 12 mm, Left ventricular mass index 152 g/m^2). HLA typing revealed demonstrated the following antigens: A11, A24, B52, B62, DR4, and DR9.

The patient was discharged in May 2007, and he has been in good health for the subsequent 2 years.

Discussion

There are some reports about the relationships between Takayasu arteritis and HLA. The association between susceptibility to Takayasu arteritis and HLA haplotype was first reported in 1976 [1]. Naito et al. first reported the significant association of HLA-B52 with Takayasu disease [2]. Till date, HLA-A24, B52, and DR 2 have been generally associated with Japanese Takayasu arteritis patients. The aforementioned haplotypes are more common in the Orientals and are rarely found in the Europeans, thus explaining the geographical distribution of Takayasu arteritis.

Since the first report of association of HLA haplotype with inflammatory bowel disease in 1972 [3], there have been some reports indicating the association between ulcerative colitis and HLA haplotype. Asakura et al. reported a significant association between ulcerative colitis and HLA-B52 and DR 2 haplotypes in Japanese populations [4].

The coexistence of Takayasu arteritis and ulcerative colitis has been reported occasionally, mostly in Japan. Few such cases have been reported in other areas of the world till date. To the best of our knowledge, results of HLA typing have been reported only 22 cases until now [5–24]. The results of serological analysis of HLA haplotypes of patients with Takayasu arteritis and ulcerative colitis are presented in Table 1. Nineteen patients were from Japan, among whom 17 were females; the average age of patients was 27 years. For locus A, 16 cases of 20 patients were positive for A24 or 9 (80%). For locus B, 20 cases of 22 patients were positive for B52 or 5 (91%). For locus DR, 14 cases of 17 patients were positive for DR2 (82%). In our study, although the pathological association of Takayasu arteritis and ulcerative colitis is not clear, a common genetic basis of these 2 diseases has been speculated because of high frequency of specific HLA alleles, namely, HLA-A24, B52 and DR 2. Interestingly, HLA-A24-B52-DR2 haplotype is a characteristic of the Japanese population (8.7%) [25]. Thus, it appears

that a genetic factor plays an important role in the pathogenesis of concomitant Takayasu arteritis and ulcerative colitis.

Additionally, among these patients, Takayasu arteritis followed the occurrence of ulcerative colitis in 15 cases of 21 patients (71%), ulcerative colitis tended to occur simultaneously or prior to the development of arteritis. These results suggest that Takayasu arteritis is one of the complications of the extra intestinal tract of ulcerative colitis.

There have been some reports on the association of clinical manifestations of Takayasu arteritis and HLA haplotypes. The incidence of aortic valve regurgitation in patients with Takayasu arteritis is between 13% and 25%; therefore, aortic valve regurgitation is now considered an important risk factor of mortality in patients with this disease [26]. Moriwaki et al. reported that the frequency of aortic valve regurgitation was markedly increased in HLA-B52 positive patients; further, B52 positive patients required higher dose of steroids for a longer periods as compared to B52 negative patients [27]. Kasuya et al. also reported that the incidence of left ventricular dysfunction was more common in B52 positive patients than in B52 negative Takayasu arteritis patients. In these studies, it was concluded that B52 positive patients are affected more seriously and developed these complications more rapidly than B52 negative patients (28). Kitamura et al. reported that aortic valve regurgitation, pulmonary infarction, and ischemic heart disease were commonly observed in B52 positive and B39 negative patients, and the incidence of renal artery stenosis was significantly high in B52 negative and B39 positive patients [29]. Similarly, Futami et al. reported that HLA-DR2 (DRB1 1502) was associated with the severity of the disease in patients with ulcerative colitis [30].

Therefore, HLA haplotype was suggested to be important in the pathogenesis of Takayasu arteritis and ulcerative colitis; further, HLA haplotype might determine not only the susceptibity of patients to Takayasu arteritis and ulcerative colitis but also the clinical manifestation of these diseases.

Conclusions

In patients with both Takayasu arteritis and ulcerative colitis, high frequency of HLA-A24, B52, and DR 2 is observed. The pathological relevance of HLA-A24, B52, and DR2 to concomitant Takayasu arteritis and ulcerative colitis requires further investigation. Moreover, further studies are required to identify other genetic factors and environmental agents that contribute to the pathogenesis of these diseases.

References:

1. Ohtawa T: HLA antigens in arterial occlusive diseases in Japan. Jpn J Surg, 1976; 6: 1–8
2. Naito S, Arakawa K, Saito S et al: Takayasu's disease: association with HLA-B5. Tissue Antigens, 1978; 12: 143–45
3. Gleeson MH, Walker JS, Wentzel J et al: Human leukocyte antigens in Crohn's disease and ulcerative colitis. Gut, 1972; 13: 438–40
4. Asakura H, Tsuchiya M, Aiso S et al: Association of the human lymphocyte-DR 2 antigen with Japanese ulcerative colitis. Gastroenterology, 1982; 82: 413–18
5. Miwa Y, Nagasako K, Sasaki H et al: Aortitis syndrome associated with ulcerative colitis: report of a case. Gastroenterol Jpn, 1979; 14: 492–95
6. Achar KN, Al-Nakib B: Takayasu's arteritis and ulcerative colitis. Am J Gastroenterol, 1986; 81: 1215–17
7. Ichikawa M, Onizuka T, Ichikawa K et al: A case of ulcerative colitis associated with Takayasu's arteritis. Jpn J Gastroenterol, 1988; 85: 1690–93
8. Goto M, Nakano I, Sakai K: A case of ulcerative colitis with aortitis syndrome, scroilitis, and pancreatic cancer. Kyusyu J Rheumatol, 1991; 10: 144–47
9. Yoshida H, Tomokuni T, Tamura K et al: A surgical case of thoracic aortic aneurysm due to Takayasu's aortitis associated with ulcerative colitis. Jpn J Throracic Surg, 1992; 40: 1135–39
10. Ishikawa H, Kondo Y, Yusa Y et al: An autopsy case of ulcerative colitis associated with Takayasu disease with a review of 13 Japanese cases. Gastroenterol Jpn, 1993; 28: 110–17
11. Oyanagi H, Ishihara R, Ishikawa H et al: Ulcerative colitis associated with Takayasu's disease. Intern Med, 1994; 33: 127–29
12. Sato R, Sato Y, Ishikawa H et al: Takayasu's disease associated with ulcerative colitis. Intern Med, 1994; 33: 759–63
13. So S, Okabe N, Maeda K et al: A case of ulcerative colitis associated with aortitis syndrome. Nippon Shokakibyo Gakkai Zasshi, 1995; 92: 175–79
14. Morita Y, Yamamura M, Suwaki K et al: Takayasu's arteritis associated with ulcerative colitis; Genetic factors in this association. Intern Med, 1996; 35: 574–78
15. Aoyagi S, Akashi H, Kawara T et al: Aortic root replacement for Takayasu arteritis associated with ulcerative colitis and ankylosing spondylitis. Jpn Circ J, 1998; 62: 64–68
16. Ito Y, Kume H, Goto K et al: Aortitis syndrome associated with ulcerative colitis preceded by pulmonary infarction involvement. J Jpn Respir Soc, 2001; 39: 287–91
17. Suzuki T, Kaneko H, Tabata M et al: Association of aortitis syndrome and ulcerative colitis. Case report and review of literatures. Jpn J Pediatr Gastroenterol Hepatol Nutr, 2001; 15: 88–93
18. Shibata C, Funayama Y, Naito H et al: Takayasu's arteritis after total proctocolectomy for ulcerative colitis. Dis Colon Rectum, 2002; 45: 422–24
19. Fukunaga K, Sawada K, Fukuda Y et al: A case report: First case of filtration leukocytapheresis for a patient of aortitis syndrome associated with ulcerative colitis. Ther Apher, 2002; 6: 93–98
20. Masuda H, Ishii Y, Aoki H et al: Ulcerative colitis associated with Takayasu's disease in two patients who received proctocolectomy. J Gastroenterol, 2002; 37: 297–302
21. Bansal R, Aggarwal P, Handa R et al: Ulcerative colitis associated with Takayasu arteritis. Int J Cardiol, 2003; 88: 91–93
22. Hokama A, Kinjo F, Arakaki T et al: Pulseless hematochezia: Takayasu's arteritis associated with ulcerative colitis. Intern Med, 2003; 42: 897–898
23. Nakano H, Ikeuchi H, Uchino M et al: Takayasu's arteritis associated with ulcerative colitis. J Jpn Soc Coloproctol, 2004; 57: 396–401
24. Katsinelos P, Tsolkas P, Beltsis A et al: Takayasu's arteritis and ulcerative colitis in a young non-Asian woman: a rare association. Vasa, 2005; 34: 272–74
25. Tokunaga K, Juji T: [Distribution of MHC alleles in Japanese]. Nippon Rinsho, 1984; 42(Suppl.): 335 [in Japanese]
26. Matsuura K, Ogino H, Kobayashi J et al: Surgical treatment of aortic regurgitation due to Takayasu arteritis: long-term morbidity and mortality. Circulation, 2005; 112: 3707–12
27. Moriwaki R, Numano F: Takayasu arteritis: followup studies for 20 years. Heart Vessels Suppl, 1992; 7: 138–45
28. Kasuya K, Hashimoto Y, Numano F: Left ventricular dysfunction and HLA Bw 52 antigen in Takayasu arteritis. Heart Vesels Suppl, 1992; 7: 116–19
29. Kitamura H, Kobayashi Y, Kimura A, Numano F: Association of clinical manifestations with HLA-B alleles in Takayasu arteritis. Int J Cardiol, 1998; 66: S121–26
30. Futami S, Aoyama N, Honsako Y et al: HLA-DRB1*1502 allele, subtype of DR 15, is associated with subceptibility to ulcerative colitis and its progression. Dig Dis Sci, 1995; 40: 814–18