Does a common pathophysiological basis exist in the association of ulcerative colitis and Takayasu's aortitis? – report of a case

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Summary: A case of a young Japanese woman with long-standing ulcerative colitis complicated by preinfarction angina due to Takayasu's aortitis is presented. Successful emergency aorto-coronary bypass operation was performed. Whether the association of these two diseases can be explained by a common mechanism is discussed.

Introduction

Since ulcerative colitis and Takayasu's aortitis are relatively uncommon disorders, the likelihood of their simultaneous occurrence is extremely small. Nevertheless, there have been several cases in which these two diseases have coexisted, suggesting some common pathophysiological background between them.

We describe here a case of a young Japanese woman with long-standing ulcerative colitis complicated by preinfarction angina due to Takayasu's aortitis. Successful emergency aorto-coronary bypass operation was performed. We discuss whether the combined occurrence of these two diseases can be explained by a common mechanism.

Case report

A 23 year old Japanese woman was admitted to Hiratsuka City Hospital, Kanagawa, Japan, in March 1988, for treatment and evaluation of precordial pain precipitated by physical exertion and a positive double Master test. In 1963, when she was 8 years old, she developed refractory diarrhoea with blood and mucus. She was diagnosed as having ulcerative colitis by colonoscopy, colonic biopsy and barium enema examination, and was treated with salicylazosulphapyridine and prednisolone. In 1979, prednisolone was stopped, and she remained well until December 1987, when the precordial pain appeared. There was

no history of smoking or use of oral contraceptives.

Figure 1 shows a colonic biopsy histology performed in April 1984. Although the typical 'crypt abscess' is not seen, ulceration without granulomas or epithelioid cells confirmed the diagnosis of ulcerative colitis.

On examination, the pulses of all extremities were normal and the blood pressure was 126/70 mmHg in both arms. A grade 2 systolic murmur was heard along the left sternal border. No vascular bruits were audible. The optic fundi were normal.

Laboratory findings were as follows: erythrocyte sedimentation rate 57 mm/h, C-reactive protein 4+, white cell count $8.7 \times 10^9/l$ with a normal differential, haemoglobin 11.4 g/dl, haematocrit 35.6%, platelets $54.0 \times 10^9/l$, fasting glucose 117 mg/dl, and the cholesterol 117 mg/dl. Serum protein electrophoresis revealed polyclonal hypergammaglobulinaemia. Serum IgG, IgA, and IgM were 1310 mg/dl, 405 mg/dl, and 164 mg/dl, respectively. C₃ and C₄ were within the normal range. Anti-nuclear antibody test and serological test for syphilis were negative. Circulating immune complexes were not detected. The urine was normal and stool specimens were trace positive for occult blood and negative for ova of parasites.

On the eighth hospital day, cardiac catheterization was performed. Selective coronary angiograms disclosed severe narrowing of the ostia of both the left main and right coronary arteries. The remaining vessels were entirely normal in calibre (Figure 2).

Soon after examination, she complained of severe precordial pain and hypotension developed. Electro-

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Figure 1 Biopsy of the sigmoid colon. Although the typical crypt abscess is not seen, ulceration covered by non-specific granulation tissue and the stromal inflammatory infiltrate composed of lymphocytes, plasma cells and neutrophils are compatible with the diagnosis of ulcerative colitis. There are no granulomas or epithelioid cells.

Figure 2 Selective coronary angiograms showing severe narrowing of the ostia of both the left main coronary artery (a) and the right coronary artery(b).

cardiogram (ECG) showed ST segment elevation in leads II, III, and aVF, and ST segment depression in leads I, aVL, and V1 through V5. Since intensive medical therapy, including intra-aortic balloon counter pulsation, could not control the pain, emergency aorto-coronary bypass operation was performed.

At surgery, the aortic wall was thickened, oedematous, and had patchy sclerosing lesions. There was a tight adhesion between the ascending aorta and pulmonary artery trunk. Saphenous vein grafts from the aorta to the anterior descending artery and the right coronary artery were implanted, choosing the most inactive site for the anastomosis and a wide arteriotomy of 7 mm.

A tiny piece of aortic tissue sampled at operation was examined microscopically. There was severe fibrosis in the media and adventitia, and the elastic fibres in the media were completely fragmented. Slight infiltrations of mononuclear cells, particularly lymphocytes, were seen around the vasa vasorum in the outer media and adventitia. The intima was fibrotic and thickened. All of these pathological findings were compatible with the diagnosis of Takayasu's aortitis.

She was discharged on the twentieth hospital day and has been followed up as an outpatient while undergoing administration of prednisolone. No recurrence has been observed to the end of 1988.

Discussion

Takayasu's aortitis is a nonspecific inflammatory process of unknown aetiology affecting segmentally the aorta and its main branches. The incidence of coronary artery involvement has been reported to be approximately 10%^{1,2} and although uncommon, angina pectoris is one of the early symptoms, which include fever, fatigue, dizziness, headache, dyspnoea, and hypertension.^{3,4} Narrowing of the coronary

arteries is produced mainly by contraction of the fibrotic media and adventitia in the aorta. Therefore, stenosis is characteristically limited to the ostia and proximal segments of the coronary arteries,³ as seen in our case.

Both inflammatory bowel disease and Takayasu's aortitis are relatively uncommon disorders. Since Soloway *et al.*⁵ first reported a case in 1970, there have been 9 cases, including ours, of ulcerative colitis in association with Takayasu's aortitis.⁵⁻¹² Six of the nine were Japanese, in whom the incidence of Takayasu's aortitis is relatively high. Crohn's disease is another major form of inflammatory bowel disease and 8 cases have been described in association with Takayasu's aortitis.¹³⁻²⁰ According to Yassinger,¹⁴ assuming the incidence of Takayasu's aortitis to be 1 per one million persons, the chance of inflammatory bowel disease and Takayasu's aortitis occurring in the same patient is 1 in 10 trillion. The actual rate of association is more than ten thousand times higher than that of the estimated value, suggesting that some common pathophysiological background may exist.

Anti-colon antibodies and anti-aortic antibodies have been demonstrated in ulcerative colitis and Takayasu's aortitis, respectively,²¹⁻²³ and a number of workers have directed their attention to the role of immune complexes. Lenhoff *et al.*¹⁸ and Achar *et al.*¹⁰ proposed a hypothesis that immune complexes associated with Takayasu's aortitis may induce chronic colitis in certain susceptible individuals. Chapman *et al.*⁸ noted the possibility that immune complexes absorbed from the diseased colon might induce vasculitis. Table I summarizes the reported cases with both Takayasu's aortitis and ulcerative colitis which have occurred in either sequence. Neither circulating immune complexes nor depletion of complement has been detected. We did not find these serological abnormalities either, and in our case, the onset of ulcerative colitis preceded that of Takayasu's aortitis by as long as 15 years. Therefore, it seems highly

Table I Clinical findings of 9 patients with aortitis and ulcerative colitis (UC)

Reference and year	Age* Sex	Preceding disease & years	c-IC†	ANA‡
Soloway <i>et al.</i> ⁵ 1970	33 F	UC 2 years	?	(-)
Sugishita <i>et al.</i> ⁶ 1973	20 F	Aortitis 2 years	?	(-)
Tsuchiya <i>et al.</i> ⁷ 1976	20 F	UC 4 years	?	(-)
Chapman <i>et al.</i> ⁸ 1978	17 F	UC 2 years	(-)	(-)
Miwa <i>et al.</i> ⁹ 1979	40 F	Aortitis 20 years	?	(-)
Achar <i>et al.</i> ¹⁰ 1986	35 F	UC 1 years	(-)	(-)
Yamaguchi <i>et al.</i> ¹¹ 1988	19 M	UC 9 years	?	?
Ichikawa <i>et al.</i> ¹² 1988	12 F	UC 10 years	(-)	(-)
Present case	8 F	UC 15 years	(-)	(-)

*Age at the time when first symptom appeared; †circulating immune complex;

‡ antinuclear antibodies.

improbable that circulating immune complexes might have induced both colitis and vasculitis.

Nevertheless, this does not exclude the possibility that some immunological defect, other than one of immune complexes, might play an important role in the pathogenesis of the two diseases. One possibility is that certain genes may allow augmented antibody responses, as well as auto-antibodies, following a variety of stimuli, and the anti-aortic and anti-colon antibodies are produced independently. Tsuchiya *et*

*al.*⁷ focused their attention on cellular immunity, but this was not examined in our case.

At present, the simultaneous occurrence of Takayasu's aortitis and ulcerative colitis is extremely rare; the aetiologies of the two diseases remain obscure. Further studies will be required to clarify the relationship between these two diseases, especially in terms of immunological background, including gene expression.

References

1. Nasu, T. Autopsy study of aortitis syndrome. Report by the Ministry of Health and Welfare, Japan, 1975, p111 (in Japanese).
2. Lupi-Herrera, E., Sanchez-Torres, G., Marcushamer, J., Mispireta, J., Horwitz, S. & Vela, J.E. Takayasu's arteritis. Clinical study of 107 cases. *Am Heart J* 1977, **93**: 94–103.
3. Cipriano, P.R., Silverman, J.F., Perlroth, M.G., Griep, R.B. & Wexler, L. Coronary arterial narrowing in Takayasu's aortitis. *Am J Cardiol* 1977, **39**: 744–750.
4. Inanami, H., Asaka, T., Yoshida, K. *et al.* Coronary ostial stenosis due to aortitis syndrome (Takayasu's arteritis) in a young female: Report of a case. *J Cardiol* 1983, **13**: 761–768.
5. Soloway, M., Moir, T.W. & Linton, D.S. Takayasu's arteritis. Report of a case with unusual findings. *Am J Cardiol* 1970, **25**: 258–263.
6. Sugishita, T., Kasai, K., Kikuchi, T. *et al.* A case of aortitis syndrome associated with ulcerative colitis. *Naika* 1973, **31**: 517–521 (in Japanese).
7. Tsuchiya, M., Okazaki, I., Mizuno, O., Asakura, H. & Hiramatsu, K. Aortitis syndrome associated with ulcerative colitis. *Vascular Surg* 1976, **10**: 176–181.
8. Chapman, R., Dawe, C., Whorwell, P.J. & Wright, R. Ulcerative colitis in association with Takayasu's disease. *Am J Dig Dis* 1978, **23**: 660–662.
9. Miwa, Y., Nagasako, K., Sasaki, H. *et al.* Aortitis syndrome associated with ulcerative colitis: Report of a case. *Gastroenterol Jap* 1979, **14**: 492–495.
10. Achar, K.N. & Al-Nakib, B. Takayasu's arteritis and ulcerative colitis. *Am J Gastroenterol* 1986, **81**: 1215–1217.
11. Yamaguchi, A., Kitamura, N., Otaki, M., Minoji, T., Tamura, H. & Kurata, A. A case of Bentall's operation for annulo aortic ectasia complicated with ulcerative colitis and aortitis syndrome. *Nippon Kyobu Geka Gakkai Zasshi* 1988, **36**: 578–582 (in Japanese).
12. Ichikawa, M., Onizuka, T., Ichikawa, K., Ohama, A., Takahara, O. & Hoshino, H. A case of ulcerative colitis associated with Takayasu's arteritis. *Nippon Shokakibyo Gakkai Zasshi* 1988, **85**: 1690–1693 (in Japanese).
13. Bigot, R., Gateau, P., Chermet, J., Doyon, D., & Monnier, J.P. Ileite terminale et maladie de Takayasu. *Ann Radiol (Paris)* 1973, **16**: 767–771.
14. Yassinger, S., Adelman, R., Cantor, D., Halstead, C.H. & Bolt, R.J. Association of inflammatory bowel disease and large vascular lesions. *Gastroenterology* 1976, **71**: 844–846.
15. Friedman, C.J. & Tegtmeier, C.J. Crohn's disease associated with Takayasu's arteritis. *Dig Dis Sci* 1979, **24**: 954–958.
16. Owyang, C., Miller, L.J., Lie, J.T. & Fleming, C.T. Takayasu's arteritis in Crohn's disease. *Gastroenterology* 1979, **76**: 825–828.
17. Beau, B., Colasse, W., Le Bihan, G. & Bourreille, J. Association d'une maladie de Takayasu et d'une colite inflammatoire. *Sem Hop Paris* 1980, **56**: 1841–1845.
18. Lenhoff, S.J. & Mee, A.S. Crohn's disease of the colon with Takayasu's arteritis. *Postgrad Med J* 1982, **58**: 386–389.
19. Gray, R. & Newman, H. Arteritis associated with Crohn's disease. *Gastrointest Radiol* 1983, **8**: 53–55.
20. Talbot, R.W., Heppell, J., Dozois, R.R. & Beart, R.W. Vascular complications of inflammatory bowel disease. *Mayo Clin Proc* 1986, **61**: 140–145.
21. Lagercrantz, R., Hammarstorm, S., Perlmann, P. & Gustafsson, B.E. Immunological studies in ulcerative colitis. Origin of autoantibodies. *J Exp Med* 1968, **128**: 1339–1352.
22. Broberger, O. & Perlmann, P. Autoantibodies in human ulcerative colitis. *J Exp Med* 1959, **110**: 657–674.
23. Ito, I., Saito, Y. & Nonaka, Y. Immunological aspects of aortitis syndrome. *Jpn Circ J* 1975, **39**: 459–462.