Rare Case of Takayasu's Arteritis Associated with Crohn's Disease

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Abstract

Takayasu's arteritis (TA) and Crohn's disease (CD) are chronic inflammatory diseases of uncertain etiology. Although co-existence of these rare diseases is estimated to occur in 1 in 10 billion individuals, a theoretically unexpected association has been reported in several patients and it is suggested that those associations may have been more than an unusual coincidence. Herein, we report a case of TA associated with clinically inactive CD. A Japanese woman was diagnosed with colonic CD at the age of 15, developed aortic valve regurgitation at 19, and then presented with general fatigue, low grade fever, and painful sensations in her left arm at 25. She was diagnosed with TA based on computed tomography scanning and magnetic resonance angiography findings, and treatments with prednisolone and cyclosporine were started. Thereafter, valve replacement and right coronary artery bypass graft surgery were performed. The possible pathophysiological mechanism responsible for concurrent existence of TA and CD may be associated with immune disorders. Early diagnosis of vascular lesions for patients with inflammatory bowel disease is highly encouraged.

Key words: Crohn's disease, Takayasu's arteritis

(Intern Med 50: 1581-1585, 2011)

(DOI: 10.2169/internalmedicine.50.5406)

Introduction

Crohn's disease (CD) is often associated with extraintestinal complications and is manifested in various organs such as the skin, eyes, joints, and cardiovascular system. Takayasu's arteritis (TA), also known as pulseless disease, is an autoimmune-mediated disorder that develops into chronic vasculitis, which mainly involves the aorta and its branches, though it has an uncertain etiology. Several case reports have noted TA and CD in the same patient, though such co-existence has been theoretically estimated to occur in only 1 in 10 billion individuals (1-28). Thus, there may be a pathophysiological link between these diseases. Herein, we report a rare case of TA associated with clinically inactive CD.

Case Report

A 15-year-old Japanese female first came to our hospital in 1998 complaining of low grade fever and upper abdominal pain. Colonic CD was diagnosed by colonoscopy findings, which showed patchy and longitudinal mucosal ulcerations, cobblestone areas, and strictures in the transverse colon (Fig. 1). Barium enema X-ray results indicated no extension of the disease into the small intestine. Fecal culture results showed normal bacterial microflora. Although a colonic histological examination revealed marked infiltration of inflammatory cells, non-caseating epithelioid cell granulomas were not observed. The diagnosis of CD in this patient was based on typical endoscopic findings, as noted above. Physical examinations, including blood pressure, pulse, and

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Received for publication February 25, 2011; Accepted for publication March 29, 2011

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Figure 1. Colonoscopy image showing characteristic findings of CD, including patchy and longitudinal ulcerations with pseudopolyps and stenosis.

heart sounds, were normal at the onset of CD. Over the next 10 years, her abdominal symptoms were well controlled by treatment with mesalazine. However, she intermittently complained of general fatigue, low grade fever, arthralgia, and headache, though no specific CD symptoms were noted. In 2002, the patient underwent surgery for arthritis in the bilateral wrists and aortic valve regurgitation was incidentally discovered.

In 2008, at the age of 25 years old, the patient reported general malaise, recurrent fever, and a sense of numbness in the left arm during exercise. In a physical examination, a systolic ejection murmur was heard along the left upper sternal border, and the left humeral and radial pulses were markedly diminished. Blood pressure in the right upper limb was 92/70 mmHg, while it was 70/50 mmHg on the left side. Bruits were audible over the bilateral carotid arteries. On the other hand, her abdomen was flat and soft, with no tenderness to palpation. Laboratory test results at that time showed an erythrocyte sedimentation rate (ESR) of 131 mm/hour, white blood cell count at 6,980/ μ L, red blood cell count at 3.8 million/ μ L, hemoglobin at 9.2 g/dL, hematocrit at 29.4%, platelet count of 460,000/ μ L, total protein at 7.9 g/dL, albumin at 3.1 g/dL, and C-reactive protein (CRP) at 8.4 mg/dL. A colonoscopy examination revealed only a few superficial aphthous lesions in the proximal colon. Although computed tomography (CT) scanning did not show any intestinal inflammation or abdominal abscesses, thickening of the wall of the aorta was detected, while magnetic resonance angiography (MRA) also revealed thickness of the aortic wall and periaortic soft tissues from the aortic arch to thoracic aorta. The vascular branches of the aorta were stenotic, with the left subclavian artery markedly narrowed. Echocardiography showed a dilated left ventricle and severe aortic incompetence. Results of cardiac catheterization and coronary angiography also confirmed severe aortic regurgitation and marked narrowing of the right coronary ostium (Fig. 2).

Based on these findings, the patient was diagnosed with TA and treatments with aspirin (100 mg/day), warfarin (3.5

mg/day), and prednisolone (60 mg/day) were started. Her symptoms improved substantially, with decreases in CRP and ESR. However, when prednisolone was reduced to 20 mg/day, inflammatory levels took a turn for the worse and 150 mg of cyclosporine was added, which resulted in gradual improvements in laboratory data. After the inflammation had subsided, the patient underwent aortic valve replacement and right coronary artery bypass graft surgery for severe aortic regurgitation and stenosis of the coronary artery, which were performed without complications. At the time of writing, she is doing well and continuing treatment with prednisolone, cyclosporine, aspirin, and warfarin.

Discussion

CD is a chronic inflammatory disorder of the gastrointestinal tract, with onset typically occurring in the second and third decades of life, and the majority of affected individuals progressing to relapsing and chronic disease. According to large epidemiological studies, CD is most common in Scandinavia, Great Britain, and North America, with lower rates reported in southern Europe, Africa, and Asia. The incidence and prevalence of CD could be as high as 14.6/100,000 per year and 199/100,000, respectively (29).

In 1905, Takayasu described a 21-year old woman with a peculiar arteriovenous malformation of the optic fundus (30), while Onishi (31) and Kagoshima (32) described similar ocular findings along with absence of radial pulse in the same year. Thereafter in 1951, the clinical features of TA were summarized by Shimizu and Sano in an English language journal under the name "pulseless disease (33)." TA is known to be a type of chronic vasculitis mainly involving the aorta and its main branches, with adolescent girls and women in their second and third decades of life at higher risk. TA is rare and it is most commonly reported in Japan, Southeast Asia, India, and Mexico. In 1990, the Japanese government added TA to the list of intractable diseases, with 5,000 patients included in the list over the subsequent

Figure 2. (A) CT scan showing thickening of the aorta wall. (B) MRA image revealing stenotic vascular branches of the aorta, with the left subclavian artery markedly narrowed. (C) Echocardiography image showing a dilated left ventricle and severe aortic regurgitation. (D) CT coronary angiography image revealing serious narrowing of the right coronary ostium.

decade. On the other hand, a study of North American patients found the incidence to be 2.6/1 million/year (7), though the true extent of the disease in western countries is not known.

TA and CD are both rare diseases, and the chance of their co-existence has been estimated to be 1 in 10 billion individuals (1). On the other hand, theoretically unexpected associations have been reported by several authors, with the first case of TA associated with CD described by Yassinger et al (1). In a North American study of 32 TA patients, 2 also had CD (7). Kerr et al found that 2 of 64 TA patients had CD and 2 other cases had ulcerative colitis (UC) (10). In addition, Reny et al reported that CD was present in 9% of a group of 44 TA patients (14). In Table 1, including the present case, we have listed 37 cases of CD and TA in the same individual, reported in literature (1-28). For those 37 patients, the age at diagnosis was noted for 32 cases, of whom the onset of TA symptoms was simultaneous or later than that of CD in 78% (25/32) of the affected patients, suggesting that CD may be a trigger of TA, though it is diffi-

cult to accurately determine its onset. The activities of both diseases were reported in 14 and occurred in parallel in 43% (6/14) of those cases. The present patient had followed a good course for controlling CD, even though her drug compliance was poor.

Four cases of surgery for CD have been reported among patients with co-existing TA. However, the long term prognosis of each disease in patients with both is unknown. Reny et al reported that patients with coexistent TA and CD tended to be younger at the time of diagnosis, and also tended to have systemic symptoms more frequently than those with TA alone. On the other hand, the distribution of vascular lesions in patients with both diseases does not seem to be different from that of patients with TA alone (14). No evidence of a genetic link between TA and CD has been reported, while UC, another major form of IBD, has been reported to be complicated with TA in some cases, with the HLA-B52 and -DR2 antigens known to have common associations with UC and TA (35).

Early diagnosis and treatment are very important for pa-

Table 1. 37 Case Reports of Takayasu's Arteritis Associated with Crohn's Disease

No	Author	Year	Sex	Age at diag.		Type		Activity	Therapy	Reference
				CD	TA	CD	TA			
1	Yassinger	1976	F	12	15	NA	V	NA	PSL	1
2	Reimund	1977	F	21	33	NA	NA	NA	NA	2
3	Friedman	1979	F	24	21	IC	NA	CD>TA	PSL, Sulfasalazine, TA ope	3
4	Owyang	1979	F	15	19	C	NA	CD=TA	PSL	4
5	Beau	1980	F	17	17	NA	V	NA	NA	5
6	Lenhoff	1982	F	24	24	C	V	CD=TA	PSL	6
7	Hall	1985	NA	NA	NA	NA	NA	NA	NA	7
8			NA	NA	NA	NA	NA	NA	NA	
9	Elburg	1992	F	14	14	C	V	CD=TA	PSL	8
10	Bentineb	1992	F	31	23	NA	NA	NA	NA	9
11	Kerr	1994	NA	NA	NA	NA	NA	NA	NA	10
12			NA	NA	NA	NA	NA	NA	NA	
13	Houman	1995	M	19	19	NA	I	NA	NA	11
14	Hilario	1998	M	10	14	I	IIb	CD<TA	PSL, AZA, Sulfasalazine	12
15	Todini	1999	F	10	23	NA	NA	NA	NA	13
16			F	22	24	NA	NA	NA	NA	
17	Reny	2000	F	16	20	NA	I	NA	PSL	14
18			F	23	34	NA	I	NA	PSL	
19			F	30	20	NA	I	NA	PSL, CD ope	
20			F	24	26	NA	V	NA	PSL	
21	Goldman	2000	M	13	33	NA	NA	NA	PSL, MTX, TA ope	15
22	Biagi	2001	F	15	22	C	V	CD<TA	PSL, Mesalazine	16
23			F	39	35	IC	I	CD=TA	PSL, Mesalazine, CD ope	
24	Levitsky	2002	F	12	20	NA	V	NA	PSL	17
25	Ohta	2003	F	20	16	NA	III	NA	PSL	18
26	Kettaneh	2003	F	16	16	NA	NA	NA	PSL, AZA, CD ope	19
27			F	29	29	NA	NA	NA	PSL	
28	Ozsoyler	2005	M	34	40	NA	NA	CD<TA	Anticoagulation, TA ope	20
29	Domenech	2005	F	20	27	IC	NA	CD=TA	PSL, Infliximab, G-CAP, CD ope	21
30	Cheema	2005	F	28	45	NA	NA	CD<TA	TA ope	22
31	Dumarey	2007	F	18	18	NA	NA	CD<TA	PSL	23
32	Baqir	2007	F	<20	20	NA	IV	NA	NA	24
33	Burke	2008	NA	NA	NA	NA	NA	NA	NA	25
34	Kellermayer	2008	F	12	17	C	V	CD=TA	PSL, Mesalamine, 6-MP, Infliximab	26
35	Farrant	2008	F	25	24	I	I	CD>TA	CD ope	27
36	Liu	2009	M	18	17	IC	I	NA	PSL	28
37	This case	2010	F	15	25	C	IIb	CD<TA	PSL, Cyclosporine, TA ope	

NA: not available, I: ileum, C: colon, PSL: prednisolone, AZA: azathioprine,

MTX: methotrexate, G-CAP: granulocyteapheresis, 6-MP: 6-mercaptopurine

tients with TA to prevent renal hypertension, aortic regurgitation, congestive heart failure, and cerebrovascular accident. A delay between symptoms and diagnosis ranging from 2 to 11 years has been reported in western countries (36). On the other hand, a study in India reported delays of only 2.5 to 5.5 months (37). This discrepancy likely reflects the difference in disease incidence between the two populations, which results in different levels of awareness (34). The present patient was found to have TA 6 years after being diagnosed with aortic regurgitation. Since her CD symptoms were well controlled and she did not complain of other symptoms, it was difficult to make an early diagnosis of TA.

When there is a discrepancy between clinical inflamma-

tory markers and gastrointestinal symptoms in IBD patients, attention should be paid to extraintestinal complications including TA. Physical examinations, including measuring of bilateral blood pressure and pulses, and detection of systolic heart sound murmur, are important for early diagnosis of TA. A recent study suggested that non-invasive modalities including ultrasonography (US), CT, MRI, and fluoro-D-glucose-positron emission tomography (FDG-PET) can provide a diagnosis of TA early in the course of the disease (38). When such modalities are used for patients with IBD based on their symptoms, careful evaluation of the results for diagnosis of cardiovascular diseases including TA is important.

The authors state that they have no Conflict of Interest (COI).

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