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CASE REPORT

A case of Crohn's disease associated with Takayasu's arteritis and Henoch-Schönlein purpura

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Abstract A 14-year-old Japanese man was diagnosed with Crohn's disease in October 2001. Four years later, the patient was referred to our institution because of neck pain, fever and asymmetrical blood pressure. Magnetic resonance angiography, computed tomography and ultrasonography revealed findings compatible with Takayasu's arteritis. In March 2006, the patient developed purpura over bilateral hands and lower extremities, arthralgia, lower abdominal pain and microhematuria. The patient was diagnosed with Henoch-Schönlein purpura. This is the first reported case of Crohn's disease associated with two types of vascular complications.

Keywords Crohn's disease · Arteritis · Vasculitis

Introduction

Takayasu's arteritis is one of the major chronic, inflammatory vascular diseases and occurs predominantly in adolescents. It has been reported previously that the prevalence of Crohn's disease is higher in patients with Takayasu's arteritis than in the general population. Henoch-Schönlein purpura (HSP) is an acute and inflammatory vascular syndrome characterized by cutaneous purpura, arthritis, nephritis, abdominal pain and gastrointestinal bleeding, which is caused by immunoglobulin (Ig) A deposition in vessel walls. There have been few reports of HSP complicating the conditions of patients diagnosed with Crohn's disease. We herein describe a case of Crohn's disease associated with both Takayasu's arteritis and HSP.

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Case report

A 14-year-old Japanese man visited a neighboring hospital in October 2001 because of an anal fistula. Colonoscopy and barium enema demonstrated a discrete ulcer of the ileum and aphthoid ulcers of the colon (Fig. 1a, b). Histological examination of the biopsy specimen obtained from the ileum and the colon showed non-caseating epithelioid cell granulomas. Based on these findings, he was diagnosed with Crohn's disease. Since then, he was treated with enteral nutrition, which relieved his symptoms and his colonic lesions. In September 2005, however, the patient was admitted to our hospital because he developed tenderness over the left anterior cervical region and a high fever.

Physical examination revealed a body temperature of 36.7°C, pulse rate 76/min and blood pressure at the brachial artery of 140/56 mmHg on the right and 128/66 mmHg on the left. He had tenderness over the left anterior cervical region, where a bruit of the left carotid artery and left subclavian artery was audible. He was free of any abdominal symptoms with a calculated Crohn's disease activity index (CDAI) of 100.

His white blood cell count was 8,030/μl, hemoglobin value 12.1 g/dl, erythrocyte sedimentation rate (ESR) 78 mm/h, C-reactive protein (CRP) 5.67 mg/dl, prothrombin time 15.5 s (control, 12.1 s), active partial thrombin

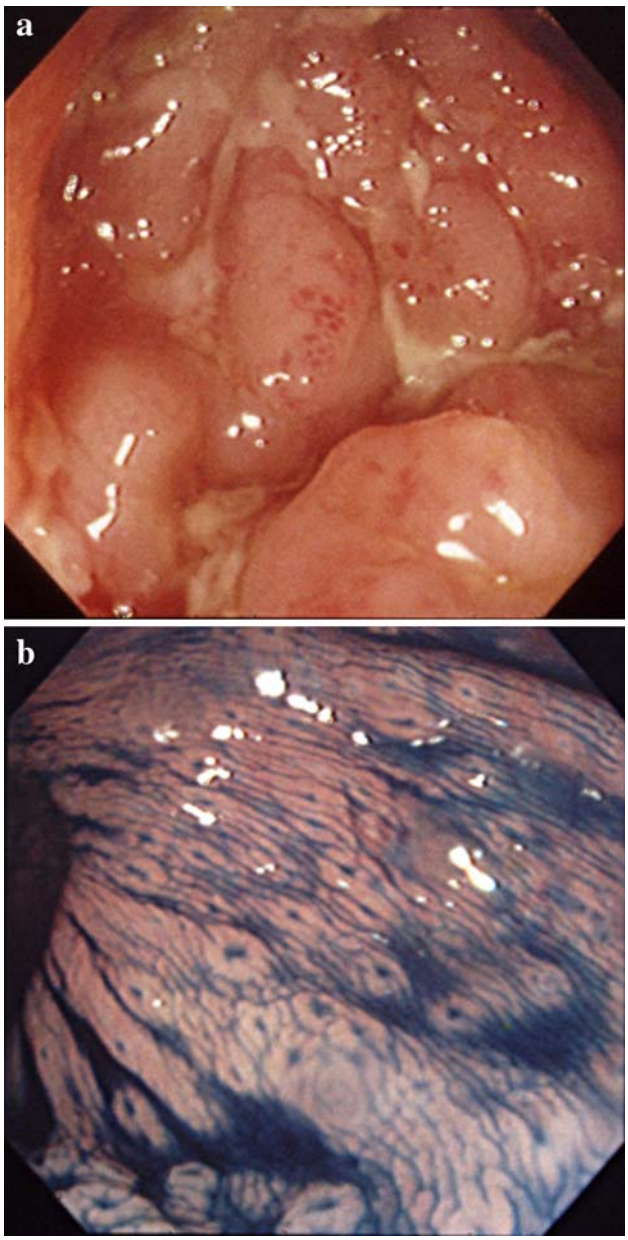

Fig. 1 **a** Ileoscopy at the time of initial diagnosis of Crohn's disease showed the discrete ulcer of the ileum. **b** Colonoscopy showed aphthoid lesions of the colon

time 45.5 s (control, 34.3 s) and fibrinogen 543 mg/dl (normal range, 150–400 mg/dl). Complement 3 was elevated at 172 mg/dl, and CH-50 was higher than 60 U/ml. Anti-nuclear antibody was negative. Both serum immunoglobulin (Ig) A and urinalysis were normal. Computed tomography (CT) scan revealed a thickened wall of the left common carotid artery and left subclavian artery. Magnetic resonance angiography (MRA) showed an irregular wall of the left common carotid artery, the left subclavian artery and the abdominal aorta (Fig. 2). Ultrasonography (US) of the cervical area showed thickness of the bilateral cervical

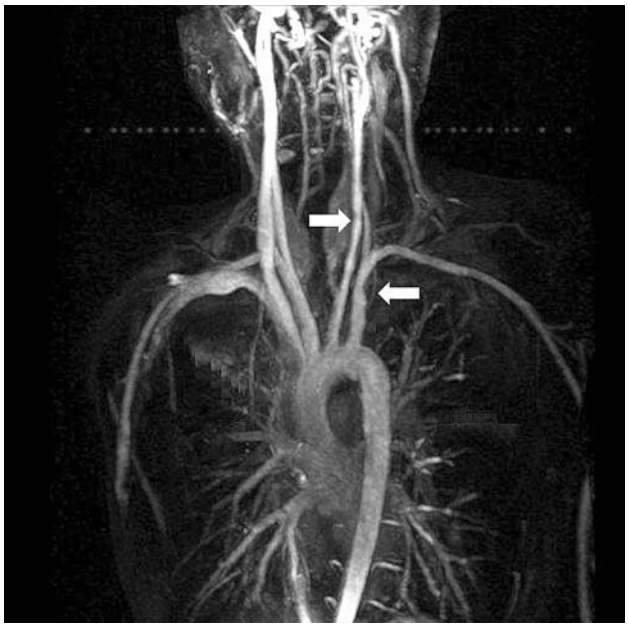

Fig. 2 MRA at the time of initial diagnosis of Takayasu's arteritis showed the rough wall of left common carotid artery and left subclavian artery (*arrows* indicate the rough wall)

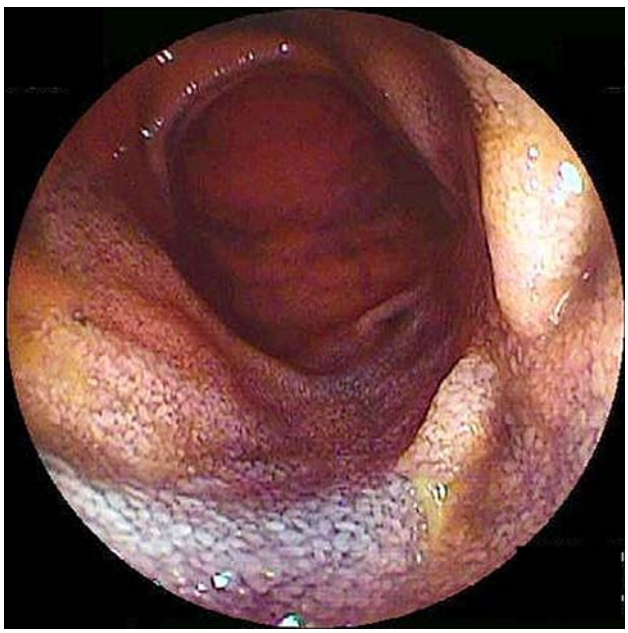

Fig. 3 Double-balloon endoscopy at the time of the diagnosis of Takayasu's arteritis showed scarred ulcers in the ileum

arteries and stenosis of the left carotid artery. Double contrast examination of the small intestine and double balloon endoscopy showed scarred ulcers in the ileum without any evidence of the active phase of Crohn's disease (Fig. 3).

From these findings, we diagnosed this patient as having both Takayasu's arteritis and Crohn's disease. Treatment with 30 mg/day of prednisolone was initiated. Subsequently,

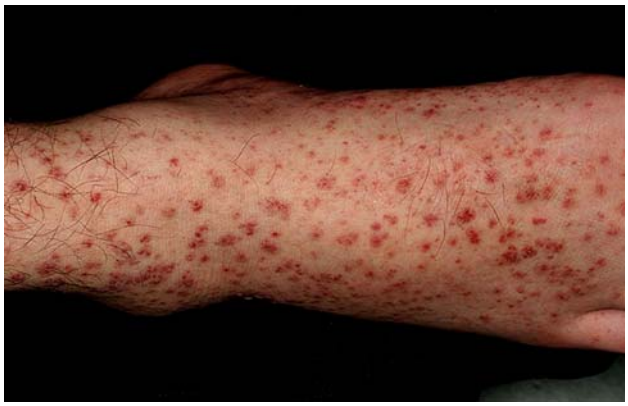

Fig. 4 Bilateral spread of purpura over the lower extremities at the time of diagnosis of HSP

the vascular lesions of the left carotid artery improved along with a gradual decrease in his serum CRP values. The dose of prednisolone was later gradually reduced to 10 mg/day without any relapse of his symptoms.

However, in March 2006, he developed purpura, arthralgia and lower abdominal pain. The purpura was spread through the upper and lower extremities (Fig. 4). At that time, the laboratory data showed a white blood cell count of 9,800/μl, hemoglobin value of 14.4 g/dl, serum creatinine value of 0.81 mg/dl and CRP of 0.71 mg/dl. IgA was elevated to 452 mg/dl. Urinalysis showed microscopic hematuria without any cast. The patient refused a renal biopsy.

From these findings, we diagnosed the patient as having HSP. The dose of oral prednisolone was increased to 15 mg/day. Purpura, arthralgia and abdominal pain immediately improved, while the hematuria persisted. Since then the patient has been maintained with 7.5 mg/day of prednisolone and enteral nutrition, and his skin lesions have resolved. His microscopic hematuria still persists at the time of this writing.

Discussion

The association of Crohn's disease and Takayasu's arteritis was first described by Yassinger et al. [1] in 1976, and since then 32 such cases have been reported in the literature [2, 3]. According to recent epidemiological studies, the incidence of Crohn's disease is approximately 14.6 per 100,000 per year, and the prevalence of the disease is 199 per 100,000 [4]. Previous studies reported that the incidence of Crohn's disease in Takayasu's arteritis ranged between 3.3% and 9.1%, which is far higher than the incidence found in the general population [2, 5]. According to our review of the English and Japanese literature with Medline and Japan Centra Revuo Medicina (Igaku-Chuo-Zasshi), however, there have been only three reported cases of HSP complicating Crohn's disease [6–8]. Furthermore, the coexistence of Takayasu's arteritis and HSP has not been described in the literature.

Recent studies suggest that the HLA haplotype plays an important role in the pathogenesis of both Crohn's disease and Takayasu's arteritis. The human leukocyte antigen (HLA) haplotype DRB1 was reported to be the most frequent in both diseases [9, 10]. Furthermore, increases in interleukin (IL)-12 and IL-6 were noted in the two diseases, suggesting that similar proinflammatory cytokines are commonly involved in the pathogenesis of both diseases [11, 12]. Recently, it has been reported that infliximab, an anti-tumor necrosis factor (TNF)-alpha antibody, was effective in Takayasu's arteritis as well as in Crohn's disease [13]. It thus seems likely that the immunological mechanism that triggered Takayasu's arteritis in our patient is closely associated with the mechanism that triggered his preceding Crohn's disease.

HSP is a vascular disease characterized by cutaneous purpura, arthritis, nephritis, abdominal pain and gastrointestinal bleeding. Such variable symptoms have been shown to be a consequence of widespread leukocytoclastic vasculitis due to IgA deposition in the vessel wall. While IgA or circulating immune complexes have been considered to play pivotal roles in the pathogenesis of HSP, Crohn's disease and Takayasu's arteritis in contrast are thought to be T-cell-mediated diseases. There have been, however, more than nine cases of IgA nephropathy-associated Crohn's disease, and some studies reported that abnormal T-helper lymphocyte function stimulates the production of IgA in IgA nephropathy [14]. It seems possible that the abnormality of T cell function seen in Crohn's disease can stimulate IgA production that results in the occurrence of HSP. Furthermore, previous reports suggest that HLA DRB1 is significant in both Crohn's disease and HSP [15, 16].

Takayasu's arteritis affects the aorta and its main branches, while HSP affects small vessels [17]. Furthermore, the pathogenesis of Takayasu's arteritis is thought to be mediated mainly by Th1 cells [11]. In contrast, HSP is considered to be provoked by immune complex and elevated Th2 response [18]. Thus, these two diseases are presumed to have occurred by chance in our case.

Because Crohn's disease, Takayasu's arteritis and HSP are diseases that manifest gastrointestinal symptoms and arthritis, Takayasu's arteritis and HSP can be easily overlooked in patients with Crohn's disease. Our case suggests that gastroenterologists should pay attention to symptoms indicating Takayasu's arteritis and HSP, such as laterality of blood pressure, bruit of the carotid artery, purpura and arthritis in patients with Crohn's disease.

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