Journal of Zhejiang University SCIENCE B
ISSN 1673-1581 (Print); ISSN 1862-1783 (Online)
www.zju.edu.cn/jzus; www.springerlink.com
E-mail: jzus@zju.edu.cn

Case Report:

Takayasu's arteritis associated with Crohn's disease

You-shi LIU[†1], You-hong FANG[2], Ling-xiang RUAN[3], You-ming LI[1], Lin LI[1], Ling-ling JIANG[†‡1]

([1]*Department of Gastroenterology, the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China*)

([2]*Children's Hospital of Zhejiang University, Hangzhou 310003, China*)

([3]*Department of Radiology, the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China*)

[†]E-mail: lys_2002cn@yahoo.com.cn; jll-03@hotmail.com

Received Dec. 11, 2008; Revision accepted June 9, 2009; Crosschecked July 1, 2009

Abstract: Takayasu's arteritis (TA), also known as the "pulseless disease," is a chronic vasculitis of the aorta and aortic branches. TA with Crohn's disease is rare and has not been documented in China before. In this paper we report on a case of Takayasu's arteritis associated with concurrent Crohn's disease. A 17-year-old Chinese male developed upper limb sourness and a sensation of fatigue, and his upper limb pulses were absent. He was diagnosed with TA and underwent an axillary artery bypass with autologous great saphenous vein on the left subclavian artery. After the surgery, he regained the normal blood pressure. This patient also had years of diarrhea and developed an anal canal ulcer, and was diagnosed with inflammatory bowel disease and ulcerative colitis before. Five months after the TA surgery, he was hospitalized for severe stomachache and diarrhea and was finally diagnosed with Crohn's disease. The possible pathophysiological mechanisms responsible for concurrent existence of TA and Crohn's disease may be associated with immune disorders, especially autoimmunity.

Key words: Takayasu's arteritis, Crohn's disease, Inflammatory bowel disease, Immune disorders
doi:10.1631/jzus.B0820391 **Document code:** A **CLC number:** R543

INTRODUCTION

Takayasu's arteritis (TA) (Tann *et al*., 2008), also known as the "pulseless disease," is a chronic vasculitis of the aorta and aortic branches. Crohn's disease (CD) (Sands, 2007), one of inflammatory bowel diseases, is characterized by transmural inflammation and can involve any part of the gastrointestinal tract, resulting in significant complications such as abscesses, fistulas, and strictures. TA combined with CD is rare and has not been documented in China before. Here we report on a rare case of TA associated with Crohn's disease.

CASE REPORT

A 17-year-old Chinese male developed upper limb sourness and a sensation of fatigue, and increased sweating in the armpits. The symptoms improved with rest, and no pain and numbness were present. He was admitted to a local hospital in August 2004. One week prior to his hospitalization, a physical examination revealed the absence of pulses in his armpits, forearms, and radial areas, and the patient was diagnosed with TA of the upper limbs. The result of magnetic resonance angiography (MRA) from another hospital indicated normal carotid arteries on both sides, although the subclavian arteries were narrowed. Upon admission, physical findings were as follows: body temperature (*T*), 36.7 °C; pulse (*P*), 80 min^{-1}; respiratory rate (*R*), 20 min^{-1}; blood pressure (BP), absent in upper limbs; no bruits below the clavicles; absence of pulse at armpits, forearms, and radials; warm fingers; and no atrophic skin on forearms. Lab results showed the erythrocyte sedimentation rate (ESR) 28 mm/h, plasma-albumin 23.1 g/L, blood routine indicating white blood counter (WBC) at 11×10^9 L^{-1}, hemoglobin (Hb) 122 g/L, and platelet (PLT) 352×10^9 L^{-1}. He was negative for complement,

‡ Corresponding author

human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). Digital subtraction angiography (DSA) indicated occlusion at the distal end of the left subclavian artery, whereas the armpit, forearm and radial arteries were normal. Similar findings were obtained from the right side (Fig.1). Magnetic resonance pulmonary angiography (MRPA) exhibited normal common carotid arteries, internal and external carotid arteries, and spinal arteries on both sides associated with fine subclavian arteries. Line feed was normal with smooth borderlines. The patient was prescribed oral prednisone 5 mg/d; however, no significant improvement was achieved. Since the symptoms of the left upper limb were more problematic, an axillary artery bypass with autologous great saphenous vein was performed on the left subclavian artery. After the surgical treatment, his blood pressure was restored to a normal range.

A year ago, this patient had a chief complaint of recurrent watery diarrhea, occasionally with bloody mucus, 5 to 6 times daily without obvious provocation. He had displayed paroxysmal stomachache and fever since he was 16 years old. His body temperature fluctuated between 38 and 40 °C without nausea, vomiting, sensations of suppression in the chest area, or shortness of breath. He was diagnosed with inflammatory bowel disease by using colonoscopy. The pathological report revealed "chronic inflammation of colon mucous membrane associated with inflammatory granulation tumor formation." He was prescribed oral prednisone 25 mg/d. The dosage was reduced to 5 mg/week. Meanwhile, he was given oral sulfasalazine (SASP) 1.0 g tid. After one month of treatment, his stomachache disappeared. The frequency and consistency of bowel movements were normalized (i.e., daily solid stools). After that, the SASP dose was reduced to 0.75 g tid to maintain the therapeutic effect. Sometimes he replaced SASP with olsalazine sodium.

During the surgical procedure for TA, the patient stopped taking olsalazine sodium, and defecation became more frequent, about 4 to 5 times a day (watery and mucous bowel). After the surgery, stomachache and diarrhea occurred, which were difficult to manage. Five months following operation, he was hospitalized in the Internal Medicine Department, Division of Digestive Diseases, at our hospital. The colonscopic examination revealed ileocecal junction

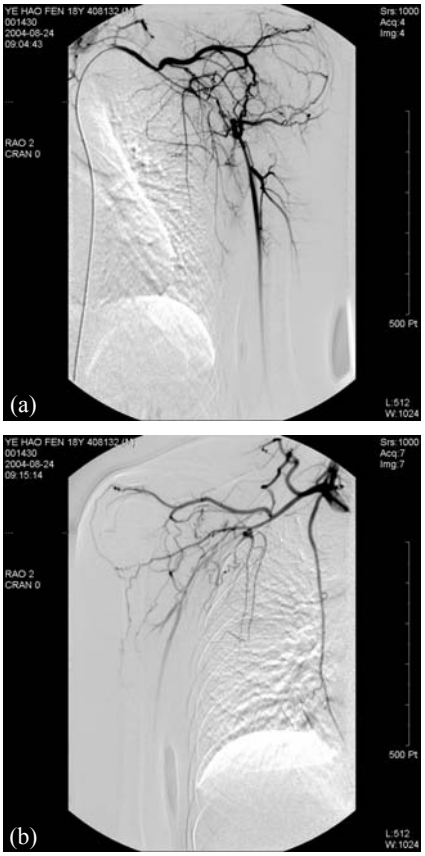

Fig.1 (a) Left subclavian arterial angiography (DSA) showed severe constriction of the dosal left subclavian and axillary arteries, especially the left axillary artery where extensive lateral circulation developed. Some vessels were tortuous and dilated. The trunk of the brachial artery was normal; (b) Right subclavian arterial angiography (DSA) showed occlusion of right subclavian and axillary arteries where extensive lateral circulation developed. Some vessels were tortuous and dilated. Internal mammary artery was dilated and anastomosed with the vascular network of the right chest wall. The trunk of the right brachial artery was normal

malformation with pseudopolyps, surface ulcer, colon segmental changes, and barium enema tomography with characteristic "intestine inflammatory change." No abnormities were found from bone marrow aspiration. He was diagnosed with Crohn's disease and was prescribed methylprednisolone and Etiasa. He was discharged upon significant improvement of his condition following treatment. The patient was subsequently hospitalized three times due to recurrent stomachache and diarrhea with mucous and bloody stools. During hospitalization, C-reactive protein (CRP) was 68.6 mg/L, ESR was 47~52 mm/h, IgH

gene rearrangement and TCR gene rearrangement were both normal, antinuclear antibody (ANA) was negative, C-antineutrophilic cytoplasmic antibodies (ANCA) and P-ANCA were in normal range, rheumatoid factor (RF) was <20 U/ml, human leucocyte antigen (HLA)-B27 was negative, purified protein derivative (PPD) test was negative, and tumor markers were negative. An anal canal ulcer was identified when he was 19 years old, which was responsible for visibly bloody stools. He was considered to have Crohn's disease associated with anal canal ulcer. In the next six months, the patient's condition was stable. In summary, this patient was diagnosed with TA associated with concurrent Crohn's disease. An axillary artery bypass with autologous great saphenous vein was performed on the left subclavian artery, and this surgical treatment restored the patient's blood pressure to a normal range.

DISCUSSION

TA is a clinical condition of aorto-arteritis initially reported in 1908 by Takayasu (Ishikawa, 1978), a Japanese scholar. Given the main involvement of the aorta and aortic branches for the pathological changes, it is also defined as aorto-arteritis. The prevalence of the disease is relatively high in young Asian women in Japan, China, and India. Nevertheless, its incidence has significantly risen in the US, Europe, and Africa over the recent years.

Cases of inflammatory bowel disease associated with TA are rare, and most of the cases were reported to involve ulcerative colitis associated with TA, but very rarely Crohn's disease associated with TA. It was first reported in Yassinger *et al*.(1976) that some patients with Crohn's disease were identified with complicated TA after the initial diagnosis of Crohn's disease. Reny *et al*.(2003) reported in a retrospective analysis of 44 TA patients that the incidence rate of Crohn's disease in TA patients was 9%, coinciding with the previous case reports. The incidence was somewhat greater compared with the normal population. Meanwhile, the discovery and diagnosis of Crohn's disease and TA were earlier compared with the presence of only one of the two diseases. The symptom and pathology of patients with Crohn's disease complicated with TA were somewhat similar to TA patients with higher frequencies in head and arm arteries as well as their branches in forearms. Furthermore, vibration white fingers were more frequent in patients with Crohn's disease and TA. According to the literature, most patients were diagnosed with Crohn's disease several years or a decade prior to the diagnosis of TA (Daryani *et al*., 2008; Levitsky *et al*., 2002).

The patient reported here is the first case of TA associated with Crohn's disease in China. The patient was diagnosed with inflammatory bowel disease in 2003 followed by diagnosis of ulcerative colitis. He was given olsalazine sodium and SASP. TA was confirmed one year later. He was finally confirmed to be afflicted with Crohn's disease based on colonscopic finding.

Various HLA haplotypes (HLA-A24, B52, Dw12 and DR2) are seen in patients with both Crohn's disease and TA. Hokama *et al*.(2003) reported a case with coexistence of UC and TA, in which the patient carried co B5 and B52, although a direct genetic link was not identified.

Inflammatory bowel disease is common in western countries, whereas TA is frequently found in Japan and Southeast Asia. With the increase in inflammatory bowel disease, cases of TA patients also afflicted with inflammatory bowel disease are reported more frequently (Wang *et al*., 2003). A number of reports have demonstrated that TA is usually associated with immune disorders, or granulomatous diseases such as granulomatous hypophysitis, Crohn's disease, ulcerative colitis, systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), rheumatoid arthritis (RA), etc. (Akar *et al*., 2008). Concurrent existence of these diseases seems to indicate that the onset of TA may be related to dysregulation of the immune system. From the reported cases of Crohn's disease associated with TA (Reny *et al*., 2003), it may be concluded that the coexistence of these two diseases is not coincidental. However, the pathophysiological mechanism underscoring the association between these two diseases remains unclear. Meta-analysis has suggested an increase in the incidence of inflammatory bowel disease in TA patients. In addition, although these two diseases are pathogenically associated, the symptoms commonly associated with inflammatory bowel disease develop earlier than those of TA. It is, therefore, possible that TA

is secondary to chronic inflammatory bowel disease. Aorto-arteritis, a chronic, progressive and nonspecific arteritis, involves immune inflammation mainly in tunica media and the elastic fibers within tunica media. Based on the origin of this disease, it may be categorized into primary aorto-arteritis and secondary aorto-arteritis. Primary aorto-arteritis has no specific identifiable cause while the secondary aorto-arteritis occurs secondary to infection, poisoning, and injury. It is possibly related to immunity, infection, gene or vascular wall structure. The pathophysiological mechanisms of Crohn's disease are closely related to genetic and environmental factors and the development of inflammatory bowel disease (IBD), according to clinical and experimental evidence. The paradoxical reaction of patients' immune system is considered the internal factor responsible for inflammation and tissue damage. Abnormal immune activation and other functional disorders may be essential to the onset and progress of IBD where the immune factors represent the mutual pathogenic basis of disease onset and progression. Coexistence of chronic inflammatory bowel and cardiovascular diseases has been speculated and consolidated. In addition, cross-reactivity between autoantigens in arterial tissues and colonic mucosa could be found in TA patients and associated with Crohn's disease (Rellecke and Strauer, 2006). It may be speculated that the pathogenic mechanisms of these two concurrent diseases are associated with disorders in immunity, especially autoimmunity. Further studies are needed to elucidate the interplay of these immune disorders in the concurrent occurrence of TA and Crohn's disease.

References

Akar, S., Can, G., Binicier, O., Aksu, K., Akinci, B., Solmaz, D., Birlik, M., Keser, G., Akkoc, N., Onen, F., 2008. Quality of life in patients with Takayasu's arteritis is impaired and comparable with rheumatoid arthritis and ankylosing spondylitis patients. *Clin. Rheumatol.*, **27**(7): 859-865. [doi:10.1007/s10067-007-0813-9]

Daryani, N.E., Habibi, A.N., Bashashati, M., Keramati, M.R., Rafiee, M.J., 2008. Takayasu's arteritis associated with Crohn's disease: a case report. *J. Med. Case Rep.*, **2**(1):87. [doi:10.1186/1752-1947-2-87]

Hokama, A., Kinjo, F., Arakaki, T., Matayoshi, R., Yonamine, Y., Tomiyama, R., Sunagawa, T., Makishi, T., Kawane, M., Koja, K., Saito, A., 2003. Pulseless hematochezia: Takayasu's arteritis associated with ulcerative colitis. *Intern. Med.*, **42**(9):897-898. [doi:10.2169/internalmedicine.42.897]

Ishikawa, K., 1978. Takayasu arteritis (occlusive thrombosortopathy)—etiological mechanism and classification. *Nippon Rinsho*, **36**(4):808-814 (in Japanese).

Levitsky, J., Harrison, J.R., Cohen, R.D., 2002. Crohn's disease and Takayasu's arteritis. *J. Clin. Gastroenterol.*, **34**(4):454-456. [doi:10.1097/00004836-200204000-00016]

Rellecke, P., Strauer, B.E., 2006. Chronic inflammatory bowel disease and cardiovascular complications. *Med. Klin. (Munich)*, **11**:56-60.

Reny, J.L., Paul, J.F., Lefebvre, C., 2003. Association of Takayasu's arteritis and Crohn's disease. Results of a study on 44 Takayasu patients and review of the literature. *Ann. Med. Interne*, **54**:75-76.

Sands, B.E., 2007. Inflammatory bowel disease: past, present, and future. *J. Gastroenterol.*, **42**(1):16-25. [doi:10.1007/s00535-006-1995-7]

Tann, O.R., Tulloh, R.M., Hamilton, M.C., 2008. Takayasu's disease: a review. *Cardiol. Young*, **18**(3):250-259. [doi:10.1017/S1047951108002060]

Wang, A.G., Wang, J., Li, B., Tang, H.W., 2003. TA with SLE. One case report. *Clin. J. Rheumatol.*, **7**(5):319.

Yassinger, S., Adelman, R., Cantor, D., Halsted, C.H., Bolt, R.J., 1976. Association of inflammatory bowel disease and large vascular lesions. *Gastroenterology*, **71**(5): 844-846.