Ultrasound diagnosis and follow-up of Takayasu arteritis with femoral vein involvement

Xinping Jiang, PhD,[a] Jinxiang Liu, MD,[b] Yang Zhang, MD,[c] *and* Xiaofeng Sun, PhD,[a] *Changchun, China*

ABSTRACT

Takayasu arteritis (TA) is a form of chronic vasculitis that mainly affects the aorta and its main branches, most commonly in young female patients. The pathogenesis of the disease remains unclear, and the clinical manifestations are nonspecific. Therefore, misdiagnosis of the disease is considered to be common. Moreover, to the best of our knowledge, TA affecting veins has not been reported. Here we report a case of an adolescent with TA affecting the femoral vein as diagnosed by ultrasound. (J Vasc Surg: Venous and Lym Dis 2019;7:587-90.)

Keywords: Ultrasound; Takayasu arteritis; Femoral vein

Takayasu arteritis (TA) is a form of chronic vasculitis that mainly affects the aorta and its main branches, most commonly in young female patients. The pathogenesis of the disease remains unclear, and the clinical manifestations are nonspecific. Therefore, misdiagnosis of the disease is considered to be common. Moreover, to the best of our knowledge, TA affecting veins has not been reported. Here we report a case of an adolescent with TA affecting the femoral veins as diagnosed by ultrasound. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

CASE REPORT

A 13-year-old girl came to our hospital complaining of high fever and pain throughout both lower extremities and an ankle joint starting 1 month previously. The patient had symptoms of mild cough, fatigue, and myalgia of the lower extremities. The highest body temperature recorded during the progression of the disease was 40°C. Before admission to our hospital, the patient received antibiotics in another hospital. However, it showed no efficacy. Within 1 month before admission, the patient suffered from numbness after walking and had lost 5 kg of body weight. Physical examination on admission revealed systolic murmur of the abdominal aorta around the umbilicus, nonpalpable pulse of the dorsalis pedis artery, and tenderness in the lower extremities and both ankle joints. No other abnormality was detected on physical examination. Laboratory tests showed a white blood cell count of 9.95 $\times$ 10^3/μL, hemoglobin level of 9.2 g/dL, platelet count of 643 $\times$ 10^3/μL, erythrocyte sedimentation rate of 120 mm/h, high-sensitivity C-reactive protein level of 121 mg/L, negative results for T-SPOT (Oxford Immunotec Ltd, Milton, Abingdon, United Kingdom) and purified protein derivative, and increased C3 and C4 levels. The results of blood tests for serum myocardial enzyme levels, liver and renal function, and levels of immunoglobulin (Ig) G, IgA, IgM, antistreptolysin O, antinuclear antibody, and rheumatoid factors were normal. Ultrasound evaluation revealed markedly thickened walls of multiple arteries, including the common carotid artery, bilateral subclavian artery, bilateral upper limb arteries (axillary artery, brachial artery, radial artery, and ulnar artery), bilateral lower limb arteries (femoral artery, anterior tibial artery, posterior tibial artery, and peroneal artery), abdominal aorta, and superior mesenteric artery, with considerable stenosis. Moreover, the walls of lower limb deep veins, especially the femoral vein, were diffusely, circumferentially, and concentrically thickened (1.9 mm; Videos 1 and 2, online only). The lumen was unobstructed, and there was no thrombus. The femoral vein valvular anatomy was normal, and the venous reflux time was <1 second.

The patient was diagnosed with TA on the basis of ultrasound evidence (Fig 1), clinical manifestations, and laboratory tests. The symptoms of fever and muscle pain did not improve despite antimycoplasma and antiviral therapy for 1 week. Methylprednisolone pulse therapy (1000 mg/d intravenously for 3 days) was then given from the ninth day to when the temperature gradually decreased to normal. Myalgia and joint pain were relieved after six applications of methylprednisolone pulse therapy. Prednisone acetate was prescribed at 10 mg/d orally at the interval of pulse therapy. Meanwhile, calcium and vitamin D were also prescribed. Methotrexate was intolerable for the patient because of gastrointestinal side effects, such as severe vomiting, loss of appetite, and liver damage after first use. Thus, oral mycophenolate mofetil was prescribed at 0.75 mg twice daily. Serial blood tests showed that C-reactive protein level declined to normal by week 1; sedimentation rate declined to normal by

From the Department of Ultrasound,[a] Department of Pediatric Rheumatology,[b] and Department of Vascular Surgery,[c] The First Hospital of Jilin University.

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Correspondence: Xiaofeng Sun, PhD, Department of Ultrasound, The First Hospital of Jilin University, 71 Xinmin Street, Changchun 130021, China (e-mail: 843276182@qq.com).

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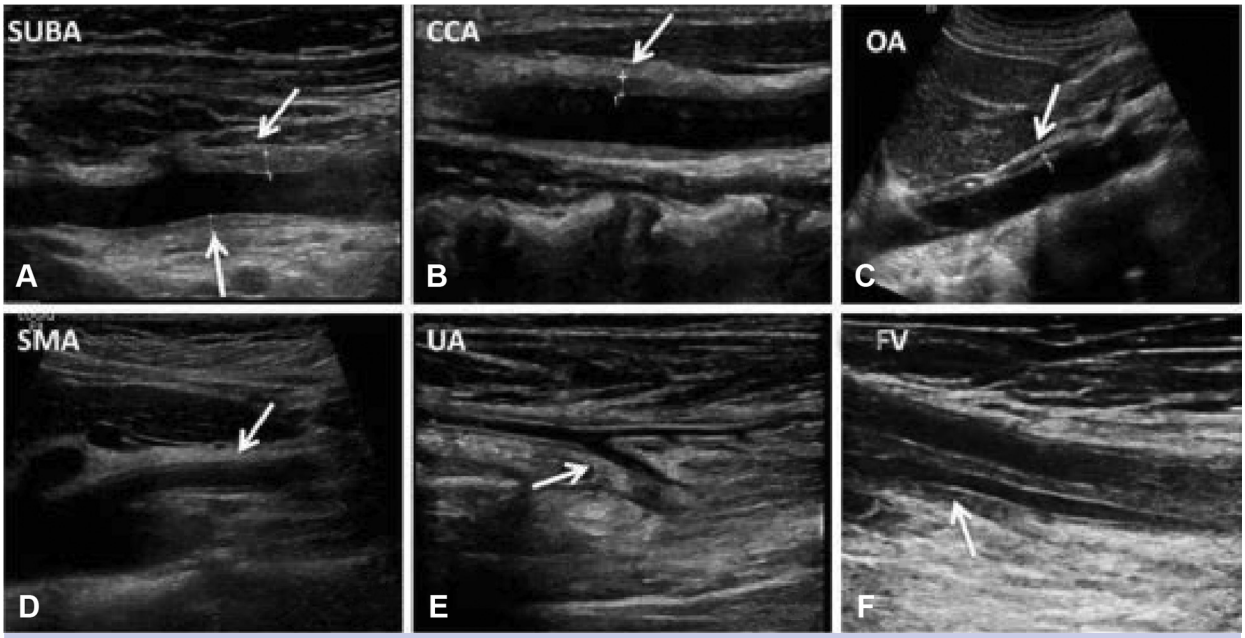

Fig 1. Vascular lesions on longitudinal ultrasound image. Diffuse thickening of arterial wall and stenosis of the lumen. **A,** The wall thickness of the subclavian artery (*SUBA*) was 2.2 mm. **B,** The wall thickness of the common carotid artery (*CCA*) was 1.45 mm. **C,** The wall thickness of the upper segment abdominal aorta (*OA*) was 3.3 mm. **D,** The wall thickness of the superior mesenteric artery (*SMA*) was 1.8 mm. **E,** The wall thickness of the ulnar artery (*UA*) was 1.1 mm. **F,** Thickening of the wall of the deep veins in the lower limbs. The wall thickness of the femoral vein (*FV*) was significantly increased (1.9 mm).

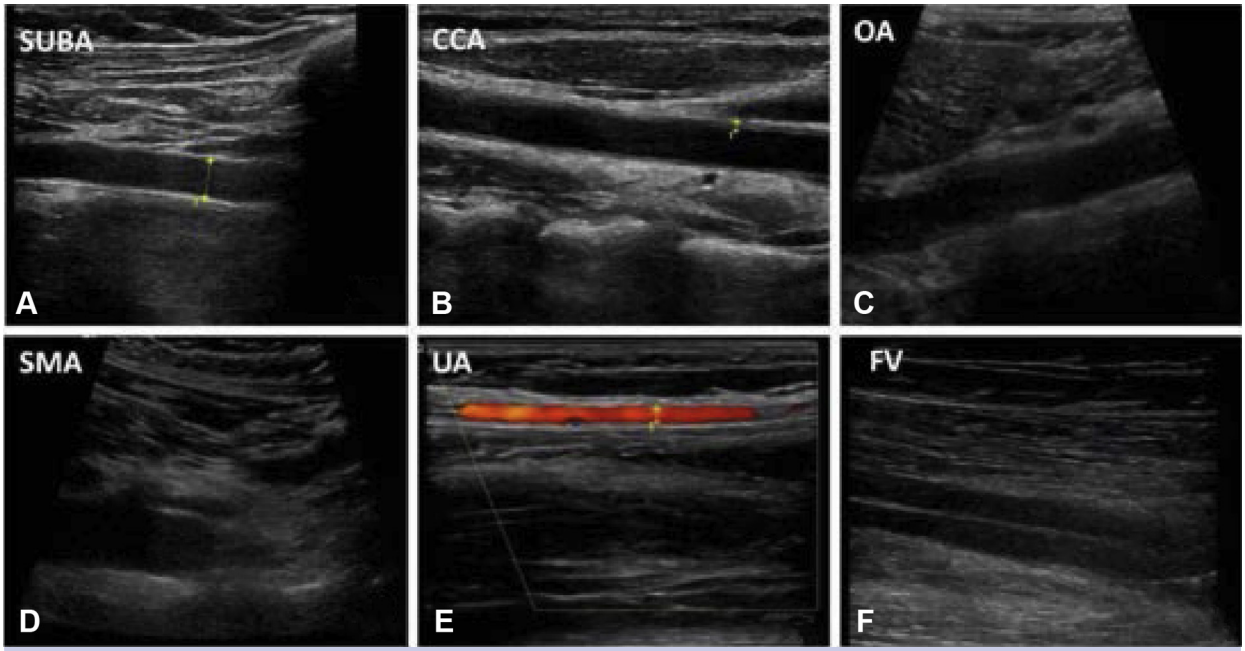

Fig 2. Ultrasound examination images after glucocorticoid impulse therapy for 4 months. The wall thickening of the involved vasculature was alleviated. **A,** The wall thickness of the subclavian artery (*SUBA*) was 0.8 mm. **B,** The wall thickness of the common carotid artery (*CCA*) was 0.9 mm. **C,** The thickening of the upper segment abdominal aorta (*OA*) was 1.0 mm. **D,** The wall thickness of the superior mesenteric artery (*SMA*) was 0.9 mm. **E,** The wall thickness of the ulnar artery (*UA*) was 0.7 mm. **F,** Thickening of the wall of the deep veins in the lower limbs. The wall thickness of the femoral vein (*FV*) was 0.5 mm.

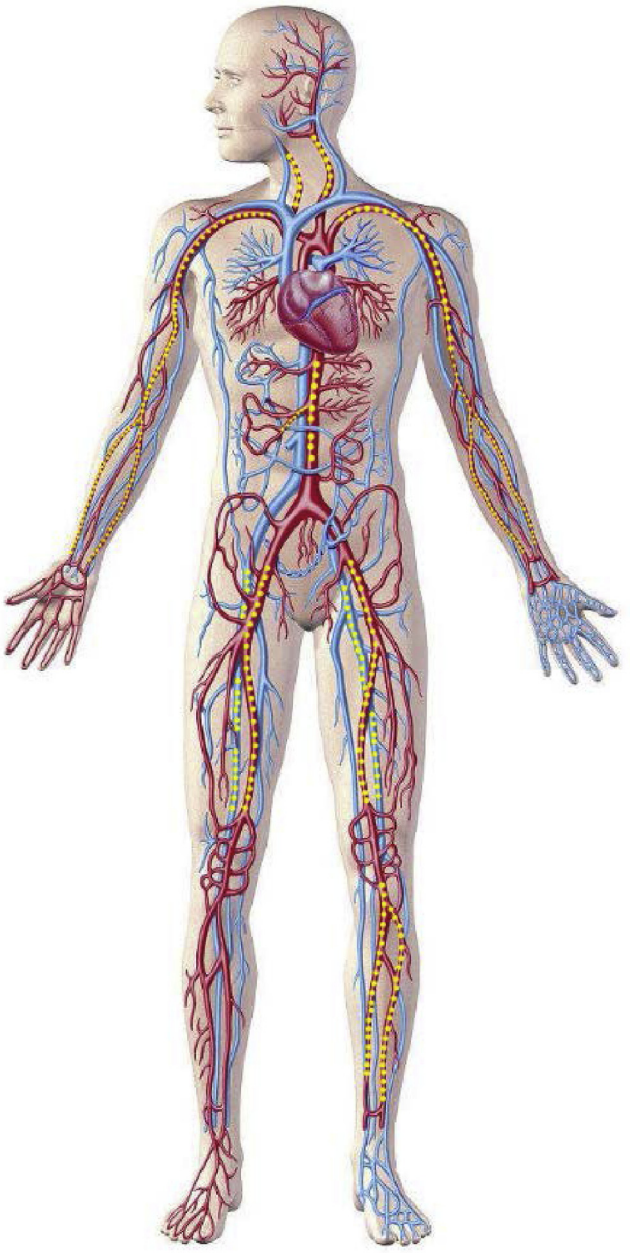

Fig 3. Anatomic diagram to document the clinically affected arteries and veins (marked by *yellow dots*), including the bilateral common carotid artery, bilateral subclavian artery, bilateral upper limb arteries (axillary artery, brachial artery, radial artery, and ulnar artery), bilateral lower limb arteries (femoral artery, anterior tibial artery, posterior tibial artery, and peroneal artery), abdominal aorta, superior mesenteric artery, and femoral vein.

week 9; platelet count and hemoglobin level declined to normal by week 3. The diffuse thicknesses of the involved arterial and venous walls were also significantly reduced as detected by vascular ultrasound (Fig 2). There were no abnormalities in the bilateral lower extremity veins that presented diffuse thickness previously. Relapse did not occur during follow-up.

DISCUSSION

TA is a type of chronic vasculitis that primarily affects the aorta and its main branches.[1] However, the etiology of TA remains unclear. The typical pathologic characteristic of TA is arterial wall vasculitis; the lesion often invades from the intima or adventitia to the intima. Interestingly, no previous case of TA affecting veins was found in a search of the literature or in our experience in clinical practice.[2] In our case, the results of vascular ultrasound indicated that TA in this patient affected the bilateral upper limb arteries (axillary artery, brachial artery, radial artery, and ulnar artery) and bilateral lower extremity arteries (femoral artery, anterior tibial artery, posterior tibial artery, and peroneal artery) and caused diffuse thickening of the venous canal wall (Fig 3).

According to the 1990 American College of Rheumatology criteria for the classification of TA,[3] a patient aged <40 years with intermittent dyskinesia of the limbs, weakened arterial pulsation of the extremities, abdominal aortic murmur, positive results of laboratory examination, and definite imaging evidence can be definitively diagnosed with TA. Laboratory tests including those for IgG, IgA, IgM, antistreptolysin O, antinuclear antibody, and rheumatoid factor levels were performed, and other inflammatory syndromes were excluded because of the results.

TA diagnosis requires differentiation from Buerger disease because of the lack of specificity of clinical symptoms. Buerger disease is a form of inflammatory disease with obstructed blood vessels. It occurs mostly in young men with a smoking history and mainly affects small and medium-sized vessels, especially those below the knee.[4] Ultrasound manifestations of Buerger disease typically include inset erosion of the roughness of the arterial intima, segmental distribution, and reduced or even completely absent lumen, with or without thrombus.[5] Therefore, Buerger disease could be excluded according to the characteristics and the ultrasound findings in this case.

The etiology of TA is not clear, but accumulating evidence suggests that immune inflammatory reactions play a key role in the pathogenesis of TA.[2] These factors may be the direct cause of the thickening of the venous wall. The typical pathologic change of TA is the whole layer of arterial inflammation, which begins to affect the intima from the middle or outer membrane of the artery, presenting segmental or leaping changes. The pathologic morphology shows diffuse, irregular thickening of the whole artery and thickened intima, resulting in narrowing or obstruction of the arteries, often combined with thrombosis.[1,6] In this case, the arterial wall of the patient was widely affected, even with the lower extremity deep veins showing diffuse thickening. For example, the femoral vein was thickened remarkably to a thickness of

1.9 mm (Fig 1). However, there was no thrombus in the lumen of the veins involved. Is the specific pathogenesis of the thickening of the vein wall the same as TA? Do the lesions begin from the outer membrane to nourish the blood vessels and then gradually spread to the inner lining, finally even causing endothelial cell damage? These questions should be answered in future studies.

In this case, only the diffuse thickening of the vein wall was detected by ultrasound examination, whereas no damage to the valve or limb swelling was shown. TA is a chronic systemic inflammatory disease that can be activated by inflammatory factors, cell adhesion factors, and endothelial cells, even causing thrombus.[7] It is reported that TA can induce venous thrombosis and therefore may be a risk factor for deep venous thrombosis.[8] Moreover, the damage to endothelial cells is the key to thrombosis, and even without vascular wall injury, inflammatory vein thrombosis could occur. Therefore, the treatment of inflammatory thrombosis induced by TA should be mainly immunosuppressive.

Also, in view of the fact that the vascular lesions of TA tend to be segmental or jumping changes, they may also be determined genetically. Indeed, a previous study showed that Toll-like receptors are differentially expressed in the affected segmental artery of TA.[9] Specific genes, such as Toll-like receptors, may be expressed in the affected venous segment of TA for our patient. However, further research is needed to determine whether expression of the Toll-like receptor also differs in the veins.

Ultrasound as a noninvasive means of examination is of great importance for the clinical diagnosis and follow-up of TA patients. There are typical ultrasound manifestations of TA: the wall of the affected vessel shows medium or low echo and diffuse, uniform, and concentric thickening.[10] However, ultrasound examination still has some limitations in the aortic arch and thoracic aorta lesion in TA. The incidence of TA is very low, and limb arteries are rarely invaded; even concurrent veins are rare. However, ultrasound could provide important diagnostic information and a favorable basis for timely treatment.

CONCLUSIONS

Based on our case, ultrasound is an easy and feasible method for the diagnosis and follow-up examination of patients with TA. More important, the examination of small and medium-sized arteries and veins cannot be ignored in diagnosis of TA because veins could be affected in patients with TA.

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