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CASE REPORT

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Vasculo–Behçet's syndrome with widespread arterial involvement

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Abstract An 18-year-old woman with a history of multiple oral ulcers followed by erythema nodosum was admitted to our hospital because of the lack of a pulse in her upper left extremity and occasional dizziness. High C-reactive protein (CRP) levels were detected in her serum. Arterial angiography showed a widespread narrowing of the major arteries, including both carotid arteries, the left vertebral artery, the left subclavian artery (branches of the aortic arch), the abdominal aorta, and left renal arteries. However, no involvement in the circle of Willis was noted, and this was confirmed by magnetic resonance angiography. Pulmonary scintigraphy showed no perfusion defect. The distribution of the arterial involvement, her youth, and negative human leukocyte antigen (HLA) B51 were consistent with Takayasu arteritis, although the presence of mucocutaneous involvement favored a diagnosis of vasculo-Behçet's syndrome. We treated the patient with prednisolone and warfarin, which resulted in an improvement in CRP levels and no thrombosis-related complications.

Key words Angiography · Multiple arterial involvement · Vasculo–Behçet's syndrome

Introduction

Behçet's syndrome is an intractable disease characterized by inflammation of the systemic organs, including the oral mucosa, skin, eye, and external genital region. The main pathological lesion is widespread vasculitis. The involvement of large vessels in Behçet's syndrome is often referred to as vasculo-Behçet's syndrome. The vascular involvement is often observed in the venous system rather than the arteries. Venous involvement sometimes causes Budd–Chiari syndrome or thrombophlebitis.[1] With regard to the arterial system, the whole arterial tree can be affected by occlusion or the formation of an aneurysm.[2] The prevalence of arterial lesions in patients with Behçet's syndrome is about 2%. These lesions usually affect the aorta or its branches, and can cause serious complications such as renal hypertension, pulseless syndrome,[3] syncopal attacks, aortic arch syndrome, stroke, and pulmonary hemorrhage. We present a case of Behçet's syndrome with multiple arterial involvement identified by arteriography.

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Case report

An 18-year-old Japanese woman visited a medical practitioner in August 1999 because of multiple oral aphthus ulcers, and was admitted to a regional hospital for a few weeks. The oral aphthus ulcers were observed as many painful lesions, each of which had a diameter of 2–3 mm. Although her oral lesions improved, she subsequently suffered from erythema nodosum in November 1999. In August 2000, she visited the hospital again because of occasional attacks of dizziness. During hospitalization, she was noted to have no pulse in her left arm, and to have high serum C-reactive protein (CRP) levels. The patient was then referred to our hospital and admitted on September 4, 2000, for further management.

On admission, she was afebrile with a pulse rate of 68 beats/min. Arterial blood pressure measured in the right arm was 106/50 mmHg, but no reading could be obtained measured in the left arm. There was no lymphadenopathy, mucocutaneous lesions, or cardiac murmurs. A chest examination was normal, including a normal breath sound. However, auscultation of the abdomen identified an abdominal bruit. Chest X-ray, abdominal X-ray, and electrocardiography were normal.

Table 1. Laboratory findings on admission

WBC	6500/mm^3	TP	7.6 g/dl	CRP	2.5 mg/dl
Seg	62.8%	Alb	4.3 g/dl	IgG	1450 mg/dl
Lymph	34.3%	Na	140.1 mEq/l	IgA	257 mg/dl
Mono	5.7%	K	4.2 mEq/l	IgM	111 mg/dl
Eosino	4.4%	Cl	103 mEq/l	IgD	6.9 mg/dl
Baso	0.2%	Ca	9.8 mg/dl		
RBC	463 × 10^4/mm^3	BUN	10.0 mg/dl	ANA	<40
Hb	12.1 g/dl	Crea	0.54 mg/dl	anti-DNA Ab	1.9 IU/ml
Hct	37.7%	BS	84 mg/dl	anti-RNP Ab	2.2 IU/ml
Plt	40 × 10^4/mm^3	GOT	7 IU/l	anti-Sm Ab	0.1 IU/ml
ESR	64 mm/h	GPT	8 IU/l	anti-SS-A Ab	2.4 IU/ml
PT	13.3 s	LDH	119 IU/l	anti-SS-B Ab	0.9 IU/ml
INR	1.21	CPK	48 IU/l		
		T. Bil	0.3 mg/dl	HLA A locus	A24
Urinalysis		ALP	343 IU/l	B locus	B52
Sugar	(−)	γ-GTP	16 IU/l	C locus	(−)
Protein	(−)	T. chol	162 mg/dl	P-ANCA	<10 EU
Sediment	(−)	TG	60 mg/dl	C-ANCA	<10 EU

ANA, antinuclear antibody; P-ANCA, perinuclear antineutrophil cytoplasmic antibody; C-ANCA, cytoplasmic antineutrophil cytoplasmic antibody

Laboratory findings (Table 1) showed a hemoglobin level of 12.1 g/dl, a total leukocyte count of 6500/mm^3, and a platelet count of 40.0 × 10^4/mm^3. Urinalysis revealed no protein and no occult blood. Blood chemistry showed normal total protein (TP), blood urea nitrogen, creatinine, serum transaminases, lactate dehydrogenase (LDH), and alkaline phosphatase (ALP). Serological tests showed IgG, IgA, and IgM of 1450, 257, and 111 mg/ml, respectively. Her rheumatoid factor was 2.4 IU/ml and antinuclear antibody was negative. Furthermore, anti-DNA antibody, anti-RNP antibody, anti-Sm antibody, and anti-SS-A/SS-B antibody were negative. Serum CRP level was elevated at 2.5 mg/dl. As for human leukocyte antigen (HLA) A, B, and C locuses, we only detected HLA type A24 and B52, and type B51 was negative.

Although we consulted an ophthalmologist to check whether the eyes were involved, there was no evidence of inflammatory exudate in the anterior chambers of both eyes. Furthermore, there were no signs of uveitis or inflammation of the vitreous body.

Arteriography, including digital subtraction angiography (DSA),[4] was performed to confirm vascular involvement (Fig. 1). Widespread arterial narrowing was noted, including the bilateral carotid arteries, the left vertebral artery, and the left subclavian artery (all branches of the aortic arch). The most severely affected vessel was the left subclavian artery. Therefore, subclavian artery stenosis was thought to be the cause of the lack of pulse in the left radial artery. In addition to arterial stenosis, a rich collateral vascular network was evident around the areas of stenosis. In addition to the abnormalities in the upper thoracic/cervical region, arteriography revealed stenosis of the abdominal aorta, left renal artery, and supramesenteric artery. However, both the left and right femoral arteries were free of stenosis. As well as the arteries, we checked venous involvement in the late phase of the angiography, but found no serious stenosis of the pulmonary veins or renal veins, Based on the widespread stenosis of the aortic branches, we performed magnetic resonance angiography (MRA) to examine the involvement of the circuit of Willis (Fig. 2). However, the circle of Willis was intact and there was no focal lesion in the brain. We also conducted pulmonary scintigraphy using ^{99m}technetium to determine any pulmonary involvement, but no perfusion defect was noted in her lungs. Moreover, we performed single-photon emission computed tomography (SPECT), with and without acetazolamide loading, to determine brain blood flow. Without loading, SPECT revealed a slight bilateral reduction of blood flow in the basal ganglia and parietal/temporal lobes. However, blood flow improved with acetazolamide loading. These findings suggested Takayasu arteritis or vascular-Behçet's disease, owing to the youth of the patient and her history of mucocutaneous lesions. A final diagnosis of vasculo-Behçet's syndrome was made based on the presence of oral aphthus ulceration and erythema nodosum. Accordingly, treatment with prednisolone and warfarin potassium was started in order to control vascular inflammation and thrombosis.

Discussion

In Japan, Behçet's syndrome with vasculitis involving the aorta or vena cava is classified as vasculo-Behçet's syndrome. Concerning arterial lesions in this disease, the entire arterial tree can be involved by general narrowing or a true/pseudo-aneurysm.[2] Arterial lesions are found in about 2% of patients with Behçet's syndrome. These lesions involve the aorta or its branches, and thrombotic obstruction is usually found in medium-sized truncal arteries, especially the subclavian artery and the pulmonary arteries. Histopathologically, typical arterial lesions consist of thickening of the intima, breaks and necrosis of the media, and fibrosis of adventitia. Important pathogenical mechanisms of Behçet's syndrome include chemotaxis and functional acceleration of neutrophils.

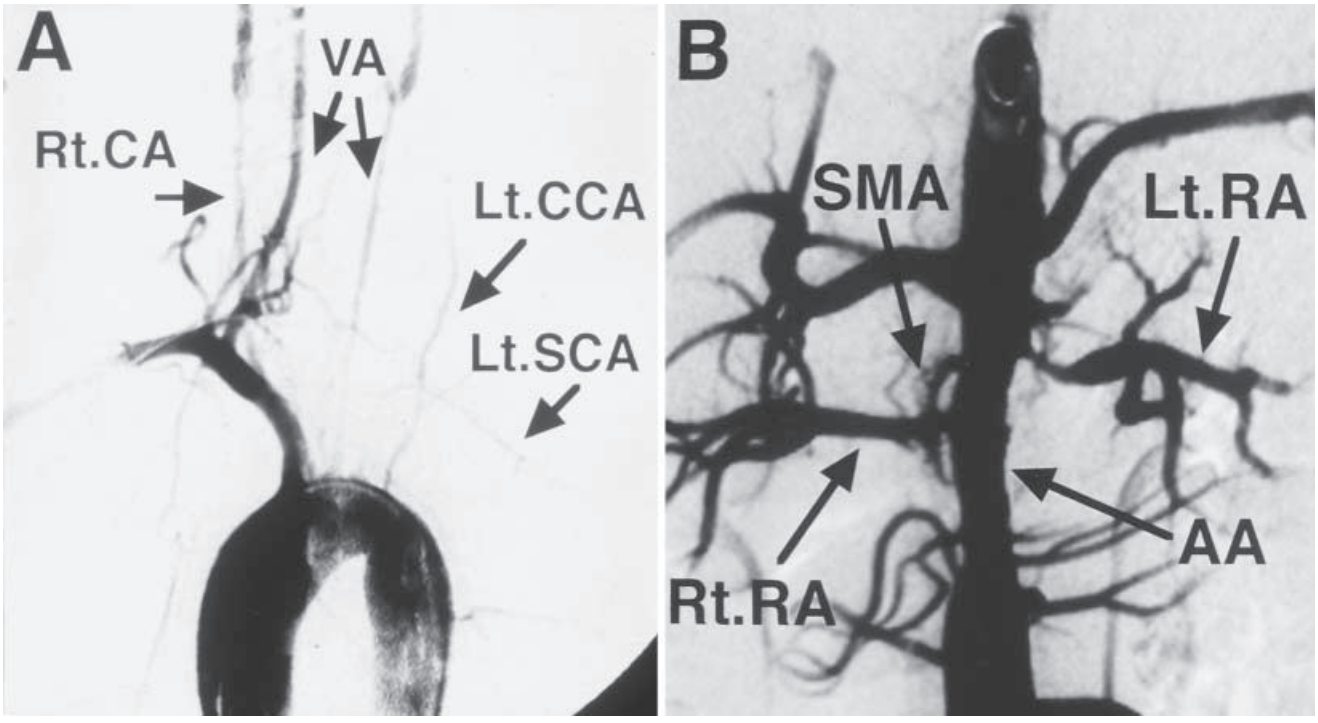

Fig. 1A,B. Arteriograph of aortic arch and abdominal aorta. **A** Multiple arterial narrowing affecting the bilateral carotid arteries, left vertebral artery and, left subclavian artery (branches of the aortic arch). The left subclavian artery showed severe narrowing. **B** The abdominal aorta, left renal artery and supramesenteric artery were stenotic, especially at the origin of the left renal artery. However, both femoral arteries were free of stenosis. *Arrows* indicate main arteries or stenotic lesions.*CA*, carotid artery; *CCA*, common carotid artery; *VA*, vertebral artery; *SCA*, subclavian artery; *AA*, abdominal aorta; *RA*, renal artery; *SMA*, supramesenteric artery

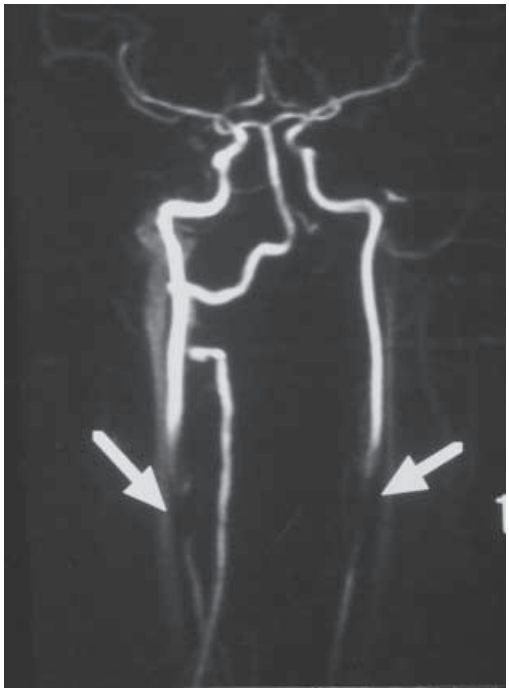

Fig. 2. Magnetic resonance angiography (MRA). MRA was performed to confirm the integrity of the circle of Willis. However, no lesions were detected and no vascular stenosis or ischemic changes were noted in the brain. Note the presence of stenotic carotid arteries and vertebral arteries. *Arrows* indicate areas of stenosis

In this case, a widespread involvement of the major arteries was noted, including the carotid artery, the vertebral artery, the subclavian artery, the abdominal aorta, the renal artery, and the supramesenteric artery. Fortunately, however, the circle of Willis and the pulmonary arteries were intact. To our knowledge, widespread involvement of major arteries in Behçet's syndrome has not previously been described. Generally, venous involvement is thought to be frequent rather than arterial involvement, and therefore the differential diagnosis had to include Behçet's syndrome and Takayasu arteritis based on the youth of the patient and the involvement of the arteries. Takayasu arteritis is characterized by the involvement of the arteries and the presence of erythema nodosum.[5–8] However, in addition to these two pathologies, this patient also had multiple oral aphthus ulcers. To our knowledge, there are no reported cases of Takayasu arteritis associated with both oral and skin lesions. Frances et al.[5] reviewed the mucocutaneous manifestations in 80 cases of Takayasu arteritis, but they did not find any oral ulceration. Based on these features, the final diagnosis in this case was vasculo-Behçet's syndrome.

This patient had multiple arterial involvement in spite of her youth. There have been some reports[9,10] of multiple cardiovascular lesions as in this case. Rouguin et al.[9] reported the case of a 26-year-old man with pulmonary artery aneurysms, bilateral renal artery stenosis, and ascending aortic pseudoaneurysm. In this case, the patient died from

massive bleeding from a rupture of the ascending aortic pseudoaneurysm. Another report[10] described a 43-year-old patient who showed bilateral thrombosis of the subclavian arteries, thrombosis of the superior and inferior mesenteric arteries, and an aneurysm of the coeliac trunk all at the same time. It is clear that these patients had a poor prognosis and their condition might be fatal. These reports, as well as the present case, suggest that we must pay attention to such arterial involvement because although it is not common, it is serious.

An angiographic examination of this patient revealed the involvement of multiple arteries. Control of vasculitis is important, since these lesions can cause additional symptoms such as syncopal attacks, severe abdominal pain, and renovascular hypertension due to progressive arterial stenosis. Therefore, the patient was treated with 10 mg/day of prednisolone and 2 mg/day warfarin potassium. Most rheumatologists outside Japan tend to avoid the use of warfarin potassium, because it may cause fatal hemoptysis. In this case, we used warfarin to prevent serious thromboembolism because we did not detect any perfusion defect by pulmonary scintigraphy. However, the use of warfarin should be avoided except for such a case. This therapy resulted in a lowering of CRP levels below normal limits ($<$0.3mg/dl) and a lack of thrombosis-related complications after 3 months' treatment. We did not select operative treatment[11,12] at this time because of the lack of cardiac symptoms and the absence of arterial aneurysm.

In summary, we have described a case of Behçet's syndrome with multiple arterial involvement presenting with no pulse in the left upper extremity and attacks of dizziness. It is recommended that arteriography should be performed in such patients as soon as possible, and once a diagnosis has been established, treatment with corticosteroids and anticoagulants should commence to inhibit the progression of vascular lesions such as arterial occlusion, and potential thrombosis.

References

1. Shimizu T. Behçet's disease. Semin Arthritis 1979;8:223.
2. Koç Y, Güllü Y, Akpek G. Vascular involvement in Behçet's disease. J Rheumatol 1992;19:402–10.
3. Yamamoto M, Mukai T, Ebara H, Kayama Y, Shida M, Sawada S, et al. Vasculo-Behçet's disease complicated with pulseless features in the upper extremities and panperitonitis: an autopsy case report (in Japanese). Nippon Naika Gakkai Zasshi 1987;76:1114–5.
4. Yamada I, Himeno Y, Suzuki S. Angiography in vasculitis (in Japanese). Nippon Rinsho 1994;52:2041–6.
5. Frances C, Boisnic S, Bletry O, Dallot A, Thomas D, Kieffer E, et al. Cutaneous manifestations of Takayasu arteritis. A retrospective study of 80 cases. Dermatologica 1990;181:266–72.
6. Castresana-Isla CJ, Herrera-Martinez G, Vega-Molina J. Erythema nodosum and Takayasu arteritis after immunization with plasma-derived hepatitis B vaccine. J Rheumatol 1993;20: 1417–8.
7. Sharma BK, Jain S, Sagar S. Systemic manifestations of Takayasu arteritis: the expanding spectrum. Int J Cardiol 1996;54 Suppl:S 149–54.
8. Nikolic J, Peclard N, Deleamont P, Chavaz P, Schifferli J, Bounameaux H. Takayasu arteritis preceded by cardiac and cutaneous lesions. A case report. Vasa 1993;22:347–51.
9. Rouguin A, Edoute Y, Milo S, Shtiwi S, Markiewicz W, Reisner SA. A fatal case of Behçet's disease associated with multiple cardiovascular lesions. Int J Cardiol 1997;59:267–73.
10. Hassen Khodja R, Declemy S, Batt M, Daune B, Avril G, Le Bas P. Behçet's disease with multiple arterial lesions and voluminous hemangioma of the brain. J Mal Vasc 1991;16:383–6.
11. Suzuki A, Amano J, Tanaka H, Sakamoto T, Sunamori M. Surgical consideration of aortitis involving the aortic root. Circulation 1989;80:1222–32.
12. Sasaki SH, Yasuda K, Takigami K, Shiiya N, Matsui Y, Sakuma M. Surgical experiences with peripheral arterial aneurysms due to vasculo-Behçet's disease. J Cardiovasc Surg 1998;39:147–50.