Takayasu Arteritis

Mark A. Creager, MD

Cardiovascular Division, Brigham and Women's Hospital, Boston, MA

Takayasu arteritis is a severe inflammatory vascular disorder that can involve the thoracic or abdominal aorta and their branches as well as the pulmonary artery. It has a much higher incidence in women than in men, and is most frequently found in Asia, although known in North America, Europe, Africa, and the Middle East. Clinical presentation depends on the location and severity of the aortic branch lesions. Diagnosis is difficult, and treatment options include corticosteroids, percutaneous transluminal angioplasty, or surgical bypass. The case of an Indian woman requiring bypass surgery is presented here, with indications for diagnostic and treatment strategy in other patients.
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A 53-year-old woman, a native of India, presented with complaints of right and left calf discomfort when walking. An ache and feeling of fatigue developed in each calf after she walked 100 yards. The symptoms had been present for several months. She denied pain or numbness in either foot.

History

The patient had an extensive history of cardiovascular disease. At age 38, she had an inferior myocardial infarction. Coronary angiography shortly thereafter demonstrated 60% stenosis of the ostium of the right coronary artery. There were no other coronary artery stenoses. The left main, left anterior descending, and left circumflex coronary arteries had no evidence of atherosclerosis. At age 45, she had several

episodes of amaurosis fugax associated with right arm and leg weakness. Angiography demonstrated a 95% stenosis at the origin of the left internal carotid artery. Also noted on the angiogram was occlusion of the left subclavian artery. She underwent left carotid endarterectomy. At age 52, she was hospitalized for congestive heart failure, and she responded to diuretic and angiotensin-converting enzyme (ACE) inhibitor therapy.

She had several risk factors for atherosclerosis. For the past several years, she had been treated for systolic hypertension. She had been told that her high density lipoprotein (HDL) cholesterol was low. She had never smoked cigarettes. She had no history of diabetes. She denied a family history of premature coronary artery disease. Her medications include enalapril, isosorbide dinitrate, gemfibrozil, niacin, and aspirin.

Physical Examination

At the initial office visit, the patient appeared well and was in no distress. Her height was 5'3" and her weight was 58 kg (128 lb). Her blood pressure was 180/80 mm Hg, and her heart rate was 70 beats per minute. The carotid pulse contour was notable for its increased amplitude. There were bilateral carotid bruits and also a left subclavian bruit. The jugular venous pulse was approximately 7 cm above the mid-right atrium. Her lungs were resonant to percussion and clear to auscultation. Her cardiac exam included a grade 2/6 early peaking systolic ejection murmur best heard at the left sternal border, and radiating to the neck, and also a grade 2/4 diastolic decrescendo murmur along the left sternal border. Her abdominal examination was unremarkable. No bruits were audible. The aorta was not palpable. There were no abdominal masses. Peripheral pulse examination included normal right brachial, radial, and ulnar pulses but trace left brachial, radial, and ulnar pulses. Her right femoral, popliteal, dorsalis pedis, and posterior tibial pulses were diminished, and the left femoral, popliteal, dorsalis pedis, and posterior tibial pulses were absent. Her skin examination included multiple erythematous nodular lesions on the left leg, each approximating 2 to 3 cm in diameter.

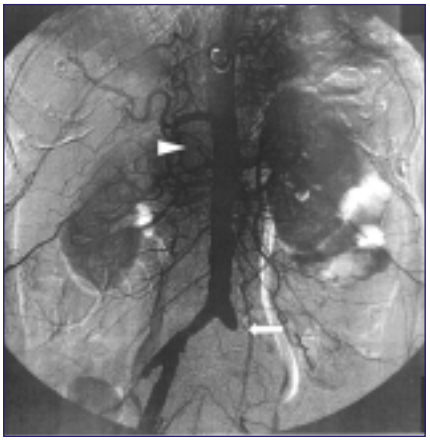

Figure 1. *Abdominal aortogram demonstrating occlusion of the superior mesenteric artery and inferior mesenteric artery. The superior mesenteric artery (arrowhead) reconstitutes via collateral vessels. The left iliac artery is also occluded (arrow).*

Noninvasive studies of the legs included segmental pressure measurements and pulse volume recordings. These were abnormal. Pressure gradients were present in each leg consistent with aortoiliac and superficial femoral/popliteal artery stenoses. The right ankle/brachial index was 0.57, and the left ankle/brachial index was 0.33. A carotid ultrasonographic examination demonstrated complete occlusion of the right internal carotid artery and 60% stenosis of the left internal carotid artery. Aortofemoral arteriography demonstrated a diseased abdominal aorta and occluded superior and inferior mesenteric arteries Figure 1). No stenotic lesions were found in either renal artery. The aortic bifurcation was patent. Of the arteries supplying the right leg, the external iliac artery was occluded, and there were collaterals supplying a patent right common femoral artery. Of the arteries supplying the left leg, the external iliac, internal iliac, common femoral, and superficial femoral arteries were occluded (Figure 2). The ECG demonstrated sinus rhythm and met criteria for left atrial enlargement and left ventricular hypertrophy. An echocardiogram found the size of the left ventricle to be at the upper limits of normal. There was a hypokinesis of the inferior wall. The left ventricle ejection fraction was 60%. The aortic valve was slightly thickened, and there was evidence of moderate aortic regurgitation.

Laboratory Data

The total cholesterol was 184 mg/dL; low density lipoprotein (LDL) cholesterol, 131 mg/dL; HDL cholesterol, 28 mg/dL; and triglyceride level, 124 mg/dL. Hematocrit was 37%. The erythrocyte sedimentation rate was 117 mm/h.

The patient underwent aortobifemoral bypass surgery. At that time, a biopsy was taken from the aortic

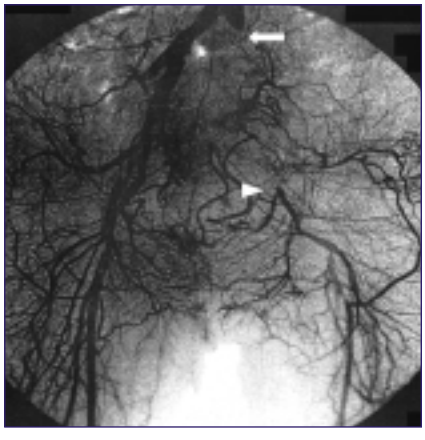

Figure 2. *Pelvic arteriogram. The left iliac, common femoral, and superficial femoral arteries are occluded (arrow). The left superficial femoral artery is reconstituted via collateral vessels (arrowhead).*

wall and also from a left leg skin lesion. The arterial wall biopsy demonstrated extensive medial and adventitial fibrosis. There were no inflammatory cells. The skin biopsy demonstrated dermal and subcutaneous inflammation and fibrosis. The findings were considered nonspecific, but consistent with erythema nodosum. She recovered uneventfully from her surgery, and her symptoms of claudication resolved.

Discussion

The salient features of this patient's presentation included disabling claudication secondary to obstruction of the peripheral arteries; coronary artery disease with prior inferior myocardial infarction; aortic regurgitation; carotid artery disease with previous left carotid endarterectomy; and now total occlusion of the right internal carotid artery. There are two principal scenarios that would explain most, if not all, of these findings. The first would be diffuse atherosclerosis affecting coronary, carotid, and extremity arteries. Severe premature atherosclerosis could be explained potentially by her dyslipidemia, characterized by a very low HDL cholesterol despite therapy. The second explanation for her symptoms is vasculitis—specifically, Takayasu arteritis.

Takayasu arteritis is an inflammatory vascular disorder that primarily involves the aorta and its major branches, typically in a focal manner. The incidence of Takayasu arteritis is much greater in women than in men. It occurs most commonly in Asia, yet it also is known to affect persons in North America, Europe, the Middle East, and Africa.[1,2] In the initial inflammatory stage, the vascular wall shows infiltration of plasma cells, lymphocytes, and, occasionally, giant cells. The entire vessel wall is involved, particularly the adventitia and media, and there is destruction of the internal elastic lamina. In the chronic stage, the vascular wall is characterized by fibrosis of the media and adventitia, and intimal thickening, often leading to severe stenosis or complete obstruction of the vascular lumen. The location of the arteritis varies among patients. The thoracic aorta and its branches are most commonly affected, but the abdominal aorta and branches as well as the pulmonary artery may be affected. Classification schemes based on the location of the vascular lesions have been described.[2,3,4] Involvement of the abdominal aorta appears to occur more commonly in Indian patients.

The clinical presentation depends on the location and severity of the aortic branch lesions. Involvement of the brachiocephalic vessels may cause transient neurologic symptoms or stroke and/or claudication of an upper limb. Ascending aortitis may affect the coronary ostia, causing stenoses and subsequent myocardial

Main Points

- Takayasu arteritis is an inflammatory vascular disorder that often affects the thoracic aorta and its major branches but also affects the abdominal aorta and branches and the pulmonary artery.
- It is seen more commonly in women than in men and principally in Asia, but it also afflicts persons in North America, Europe, the Middle East, and Africa.
- Diagnosis is difficult, involving clinical features of symptom onset at age 40, subclavian and/or carotid artery stenosis; pulse deficit in upper extremity; limb claudication; aortic bruit; angiographic findings of stenosed or occluded aorta or proximal section of a main branch.
- Clinical presentation depends on the location and severity of the aortic branch lesions: bracheocephalic lesions may cause transient neurologic symptoms or stroke and/or claudication of an upper limb.
- Ascending aortitis may affect the coronary ostia, causing stenosis and subsequent myocardial ischemia or infarction.
- Symptoms in the region of the abdominal aorta and branch arteries occur more commonly in Indian patients.
- Treatment is primarily with corticosteroids; about 50% to 60% of patients respond favorably.
- The efficacy of immunotherapy with methotrexate or cyclophosphamide has not been studied in controlled trials.
- Percutaneous transluminal angioplasty (PTA) or surgical reconstruction may treat discrete aortic or branch vessel stenoses affecting limbs or brachiocephalic or coronary arteries.
- Because complications are highest in patients with acute inflammatory lesions, PTA or surgical bypass should be deferred to a quiescent period after corticosteroid treatment.

ischemia or infarction. In addition, aortic root dilatation occurs commonly and is often responsible for aortic regurgitation.[5] Carotid and subclavian bruits are heard frequently, and pulse deficits are common. Patients with involvement of the abdominal aorta and its branch arteries may have symptoms in the affected territory. As with this patient, leg claudication may occur. Occlusion of the mesenteric vessels may lead to intestinal ischemia, and renal artery stenoses may cause hypertension or renal insufficiency. Aortic aneurysms and aortic dissection may have been described in these patients. Erythema nodosum has been reported in patients with Takayasu arteritis.

The diagnosis of Takayasu arteritis is difficult and requires a high index of suspicion. Clinical features of Takayasu arteritis include age 40 years or younger at onset of symptoms and signs; subclavian and/or carotid artery stenosis; pulse deficit in an upper extremity; limb claudication; aortic bruit; and angiographic findings of a stenosed or occluded aorta or proximal section of one of its main branches.[4,6] The erythrocyte sedimentation rate is elevated in a majority of patients. Evidence of arterial disease typical of Takayasu arteritis may be derived from imaging studies, including ultrasonography, computed tomography, magnetic resonance imaging, and conventional contrast angiography.[7,8] Luminal narrowing and thickening of the wall of the aorta or the relevant branch vessels, including the carotid and subclavian arteries, are supportive findings.

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The principal therapeutic intervention is corticosteroids.[9] For example, prednisone could be initiated at a dose of 1 mg/kg/day and maintained at that dose level for 1 to 3 months. Thereafter, the prednisone dose may be tapered gradually, but continued for at least 6 to 12 months. Approximately 50% to 60% of patients will have a favorable response to corticosteroids. Other forms of immunotherapy, such as administration of methotrexate or cyclophosphamide, may be used in patients who fail to respond adequately to corticosteroids, but the efficacy of these drugs has not been studied in controlled trials. Procedures to restore blood flow are indicated in patients with symptomatic flow-limiting stenotic lesions. Percutaneous transluminal angioplasty may be used to treat discrete aortic stenoses or branch vessel stenoses affecting the limbs, or brachiocephalic or coronary arteries.[10] It should be emphasized, however, that complication rates are highest in those patients with acute inflammatory lesions. Such interventions should be deferred, if possible, to a period of disease quiescence following corticosteroid therapy. Similarly, surgical reconstructive procedures may be used to treat flow-limiting stenoses, as was done in this patient. Surgical bypass also should be deferred, if possible, to a period following corticosteroid treatment to reduce the likelihood of graft stenoses.

The principal therapeutic intervention for Takayasu arteritis is corticosteroids.

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