CASE REPORTS

Severe Chronic Aortic Insufficiency Requiring Valve Replacement: An Infrequent Complication of Takayasu's Disease

Jennifer Brady, M.D., Barry C. Esrig, M.D.,* Kamran Hamirani, M.D., Ada Baisre, M.D.,† and Muhamed Saric, M.D., Ph.D., F.A.C.C., F.A.S.E.

Department of Medicine, *Department of Cardiothoracic Surgery, and †Department of Pathology & Laboratory Medicine, New Jersey Medical School, Newark, New Jersey

Takayasu's arteritis (TA) is a granulomatous vasculitis of medium and large arteries, which most often presents as pulseless disease due to widespread arterial stenoses. Only the minority of TA patients have aortic valve insufficiency, which is due to aortic root dilatation following aortitis and aneurysm formation. No other cardiac valve is involved. We report a case of Takayasu's disease-related severe aortic insufficiency (AI) in a Filipino woman, which necessitated aortic valve replacement. It is important to consider TA in the differential diagnosis of AI in young women, particularly those with early-onset systemic hypertension and pulse deficits. Early diagnosis and therapy of TA can improve outcomes. (ECHOCARDIOGRAPHY, Volume 23, July 2006)

Takayasu's, *pulseless disease*, *aortic insufficiency*

Case Report

A 31-year-old woman originally from the Philippines presented with progressive dyspnea on exertion and a presyncopal episode 3 years after immigrating to the United States. At age 26, she had been diagnosed with systemic hypertension and was treated with two antihypertensive medications. In addition, a murmur of aortic insufficiency (AI) was noted on physical exam; no further workup was performed at that time.

On admission, she was noted to have a blood pressure of 120/54 mmHg in the right arm and a regular heart rate of 82 beats/min. Lungs were clear to auscultation bilaterally. Heart exam revealed a 3/6 systolic ejection murmur at the base, and a 2/4 decrescendo diastolic murmur at the left lower sternal border. Lower extremities had no edema. Left radial and both femoral pulses were absent. Laboratory examination was notable only for a mildly elevated erythrocyte sedimentation rate (ESR) of 31 mm/hour (normal 0–20 mm/hour).

Transthoracic echocardiogram revealed severe AI with left ventricular (LV) dilatation (end-diastolic diameter 6.2 cm; end-systolic diameter 4.5 cm), and borderline LV systolic function (Table I). There was no left atrial enlargement and the mitral valve was normal.

Transesophageal echocardiography was performed to better elucidate the mechanism of AI. Neither annuloaortic ectasia nor significant primary leaflet pathology was seen. However, there was dilatation of the sinotubular junction (3.9 cm) and aortic sinuses (maximum diameter of 5.4 cm; Fig. 1A). This resulted in pulling apart of the aortic cusps and creation of a central regurgitant orifice of about 0.6 cm^2 (Fig. 1B). The distal aortic arch, the descending thoracic aorta, and the very proximal abdominal aorta were normal in diameter.

Pulsed wave Doppler recordings from the descending thoracic aorta showed holodiastolic flow reversal consistent with severe AI (Fig. 1C).

Cardiac catheterization was performed via the right radial artery with the primary goal

Address for correspondence and reprint requests: Muhamed Saric, M.D., Ph.D., F.A.C.C., F.A.S.E., Director, Echocardiography Lab, Division of Cardiovascular Diseases, New Jersey Medical School, 185 South Orange Avenue I-538, University Heights, Newark, NJ 07103. Fax: (973)-972-4737; E-mail: saricmu@umdnj.edu

TABLE I

Echocardiographic and Cardiac Catheterization Volume, Fraction and Flow Data

	Echocardiography	Cardiac Catheterization	Both Methods Combined
LV end-diastolic volume (ml)	190		
LV end-systolic volume (ml)	90		
LV total stroke volume (ml)	100		
LV ejection fraction	53%		
Cardiac output (l/min)		5.4	
Heart rate (beats/min)		98	
Effective antegrade stroke volume (ml)		55	
Regurgitant volume (ml/beat)			45
Regurgitant fraction			45%

Echocardiography data were obtained using biplane Simpson's rule. Cardiac output was measured using Fick principle. Total stroke volume refers to the sum of effective and regurgitant volumes. LV = left ventricle.

of excluding associated coronary artery disease. Coronary angiography revealed no coronary stenoses; hemodynamic data are shown in Table I.

Subsequently, she underwent valve-conduit surgery with a 23-mm St. Jude mechanical aortic valve and a 30-mm Hemashield graft placement in the proximal ascending aorta.

Because of peripheral pulse deficits, she underwent duplex ultrasound imaging of major arterial beds, which demonstrated widespread nonatherosclerotic stenoses (Table II and Fig. 2). Ultrasound and magnetic resonance imaging of renal arteries was also ordered to exclude renal artery stenosis as the cause of early-onset hypertension. However, the patient refused these studies, based on her perception as a registered nurse, that they were unwarranted.

Based on the combination of elevated ESR, severe AI due to aortic root dilatation, and extensive arterial nonatherosclerotic occlusive disease, a clinical diagnosis of Takayasu's syndrome was established. This diagnosis was confirmed by surgical pathology of the aortic specimen (Fig. 3). Because there were no giant cells present, the findings were consistent with healed Takayasu's arteritis (TA).

TABLE II

Peripheral Arterial Ultrasound Data

Artery	Degree of Stenosis
Right internal carotid	50–59%
Left internal carotid	70–99%
Left subclavian	50%
Left radial	Total occlusion
Left & right common femoral	Total occlusion
Left & right superficial femoral	Total occlusion
Left & right popliteal & posterior tibialis	Severely diminished flow

Discussion

TA is a granulomatous vasculitis of medium and large arteries, with the aorta and its main branches being the primary sites. The cause and pathogenesis are unknown, although immune mechanisms are suspected. Histologically, the earliest change seems to be an adventitial mononuclear infiltrate, eventually accompanied by granulomatous changes and gradual progression to a panarteritis.[1]

TA often begins with constitutional symptoms, such as fever, night sweats, fatigue, malaise, myalgias, arthralgias, and weight loss, but these may be absent in 13% to 80% of patients.[2,3]

Figure 1. *Echocardiography of aortic valve in Takayasu's aortitis.* ***A.*** *Transesophageal color Doppler image of aneurysmal aortic root (5.4 cm at the widest diameter of sinuses of Valsalva) showing severe aortic regurgitation (**asterisk**). LA = left atrium.* ***B.*** *Transesophageal short-axis view of aortic valve at end-diastole showing a very large central regurgitant orifice (**asterisk**) of 0.6 cm^2 as a consequence of aortic root dilatation and pulling apart of the aortic cusps. LA = left atrium; RA = right atrium.* ***C.*** *Spectral Doppler image showing holodiastolic flow reversal (**asterisk**) in the descending thoracic aorta, a finding consistent with severe aortic valve insufficiency.*

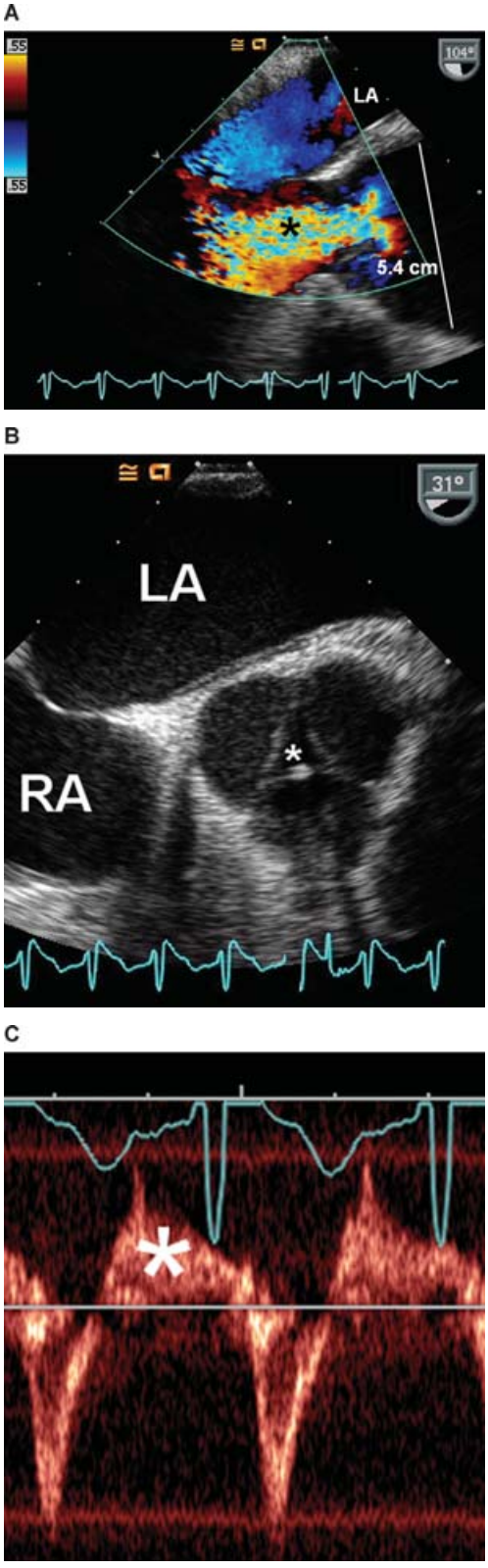

Figure 1. *Continued.*

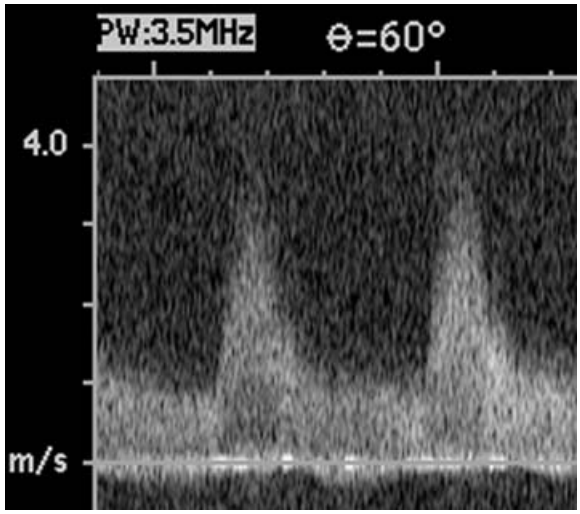

Figure 2. *Spectral Doppler of left subclavian artery very high peak systolic velocity (370 cm/sec) and the presence of abnormal antegrade flow during diastole (end-diastolic velocity of 90 cm/sec) are indicative of significant subclavian artery stenosis. On 2D imaging (not shown), there was a 50%-diameter stenosis.*

In the vast majority of patients, TA is characterized by nonatherosclerotic arterial stenoses and occlusions, leading to diminished or absent pulses as was the case with our patient (Table II). Indeed, TA is often referred to as "pulseless disease." In only 15% of cases, TA leads to vessel dilatation.[4]

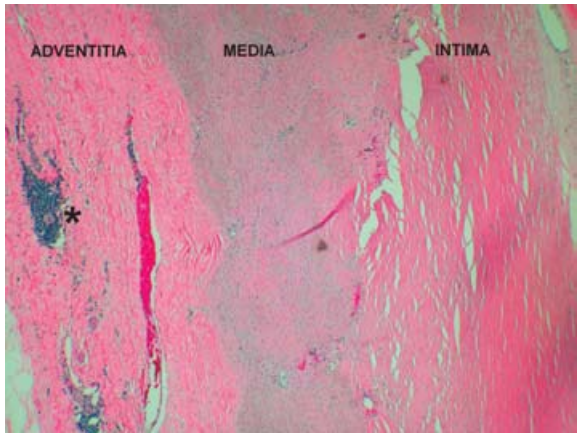

Figure 3. *Histopathology of Takayasu's arteritis ascending aorta with adventitial lymphoplasmacytic infiltrate and perivascular cuffing of the vasa vasorum (**asterisk**) with associated collagenous fibrosis of all layers of the vessel wall, particularly the intima. There are no giant cells present. These findings are consistent with healed Takayasu's arteritis. Hematoxylin/eosin stain; 4× magnification.*

Aortic valve insufficiency is the primary valvular abnormality, and is reported to be present only in the minority (approximately 20%) of TA patients and infrequently requires aortic valve surgery (in one out of six AI patients).[5] AI is usually not due to primary leaflet pathology, but is rather secondary to aortic root dilatation and pulling apart of the aortic cusps in the setting of ascending aortitis and aneurysm formation (Fig. 1).

Behçet's disease may mimic Takayasu's disease. However, the aortic regurgitation secondary to Behçet's disease is due to redundant motion of elongated aortic cusps rather than aortic root dilatation.[6]

The majority of TA cases occur in young (<40 years of age) women of eastern and southern Asian origin. However, TA has been observed throughout the world and may have varying clinical spectrums in different populations. For instance, there is a higher rate of cerebrovascular and cardiac involvement in Japan, whereas abdominal aortic involvement and renovascular hypertension are more prominent in India.[7]

In conclusion, it is important to consider TA in the differential diagnosis of AI in young women, especially in those with early-onset systemic hypertension and pulse deficits. Early diagnosis of TA is essential, since prompt medical and surgical therapy can improve outcomes.

References

1. Cotran: Robbins Pathologic Basis of Disease, 6th Ed. Philadelphia: WB Saunders Company, 1999.
2. Langford CA: Vasculitis. *J Allergy Clin Immunol* 2003;111:S602–S612.
3. Stone JH, Calabrese LH, Hoffman GS, et al: Vasculitis. A collection of pearls and myths. *Rheum Dis Clin North Am* 2001;27:677–728.
4. Isselbacher EM, Eagel KA, Desanctis RW: Diseases of the aorta. In: Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, Vol. 2. Philadelphia: WB Saunders, 1997, pp. 1572.
5. Kerr GS, Hallahan CW, Giordano J, et al: Takayasu arteritis. *Ann Intern Med* 1994;120:919–929.
6. Song JK, Jeong YH, Kang DH, et al: Echocardiographic and clinical characteristics of aortic regurgitation because of systemic vasculitis. *J Am Soc Echocardiogr* 2003;16:850–857.
7. Moriwaki R, Noda M, Yajima M, et al: Clinical manifestations of Takayasu arteritis in India and Japan. *Angiology* 1997;48:369–379.