Takayasu's Arteritis Presenting as Heart Failure in a 19-Year-Old Female

Andrew R. Benck, MD,a Shivani Patel, MD,b Emily Zern, MD, Kevin S. Shah, MD, Lillian R. Benck, MD, David Chang, MD, Chelsey J.F. Smith, MD, Michele A. Hamilton, MD

ABSTRACT

This report presents the case of this atypical presentation of a rare disease in a 19-year-old female with cardiomyopathy and hypertension. Investigation revealed renovascular stenosis, infarcts, and active vasculitis pathognomonic for Takayasu arteritis (TA). Cardiac magnetic resonance imaging demonstrated mild pericardial inflammation and epicardial edema. Vasculitis-induced renovascular secondary hypertension resulted in myocardial dysfunction, which recovered with treatment of hypertension and TA. (Level of Difficulty: Beginner.) (J Am Coll Cardiol Case Rep 2019;1:355–9) © 2019 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 19-year-old previously healthy Asian female was admitted for newly diagnosed heart failure with reduced ejection fraction (HFrEF). Two months prior to admission, she developed a persistent, dry cough followed by fatigue, anorexia, muscle cramps, and orthopnea. She denied chest pain, abdominal pain, fevers, night sweats, hemoptysis, joint pains, rash, hair loss, weight loss, oral or vaginal ulcers, visual changes, eye pain or redness, headaches, or syncope.

On initial examination, she was afebrile with blood pressure 172/106 mm Hg, heart rate of 98 beats per min, oxygen saturation of 100% without supplemental oxygen, respiratory rate of 21 breaths/min, and body mass index of 19 kg/m². She appeared fatigued. She had no tenderness to palpation over the forehead, and her conjunctiva were clear. There were no oral ulcerations or cervical lymphadenopathy. The jugular venous pulse was elevated to 9 cm of water. The heart rate was regular, with a normal S1 and S2, with no murmurs or S3 gallop. There were bibasilar lung crackles. There were symmetrical peripheral pulses, equal blood pressures in both arms, no peripheral edema, and no skin or nail changes.

On initial examination, she was afebrile with blood pressure 172/106 mm Hg, heart rate of 98 beats per

LEARNING OBJECTIVES

- To consider Takayasu Arteritis in young women with new onset heart failure and secondary hypertension.
- To relate the pathophysiology of Takayasu’s Arteritis to subsequent end-organ damage.

MEDICAL HISTORY

She denied any significant past medical history, medication use, allergies, travel, substance use, or sexual activity. Family history was negative for cardiovascular, autoimmune, rheumatologic, or thrombotic disease.
DIFFERENTIAL DIAGNOSIS

The initial differential diagnosis included viral myocarditis and cardiomyopathy secondary to severe hypertension. Her history and symptoms were not concerning for substance abuse, genetic cardiomyopathy, or ischemic heart disease.

INVESTIGATIONS

Initial laboratory evaluation was notable for a troponin-I concentration elevated to 0.11 ng/ml, which peaked at 1.87 ng/ml over 48 h, brain natriuretic peptide concentration of 493 pg/ml, white blood cell count of 11.5 (1,000 U/l), and concentrations of hemoglobin at 9.9 g/dl, potassium at 3.0 mEq/l, and creatinine at 1.3 mg/dl, and an elevated erythrocyte sedimentation rate and C-reactive protein at 55 mm/h and 12.7 mg/l, respectively (Table 1). Chest radiography revealed pulmonary edema with bilateral pleural effusions. Transthoracic echocardiography revealed a left ventricular ejection fraction (LVEF) of 15% and left ventricular dilatation with end-diastolic dimension of 5.5 cm (reference range 3.9 to 5.3 cm) and multiple calcified apical mural thrombi. There was no left ventricular hypertrophy. The right ventricle demonstrated normal function, and there was no significant valvular disease.

Cardiac magnetic resonance (CMR) imaging was notable for possible perimyocarditis with only epicardial edema and minimal late gadolinium enhancement. Clinical presentation, imaging, and elevated inflammatory markers prompted rheumatologic serological studies and hypercoagulable workup, which were unrevealing (Table 2).

A secondary hypertension investigation was pursued, given her young age, new onset severe hypertension, and end-organ dysfunction. Laboratory study results were pertinent for urine and plasma metanephrines of 287 µg/24 h and <0.20 nmol/l, respectively, both within normal ranges, and an elevated serum aldosterone and renin activity (115 ng/dl and 26.1 ng/ml/h, respectively) but with a normal ratio of 4.40. The presence of renal dysfunction prompted a vascular ultrasonography examination which demonstrated no perfusion to the left kidney. Computed tomography angiography results demonstrated embolic infarcts in the right kidney and complete occlusion of the left renal artery with an atrophic left kidney suggestive of chronic ischemic change (Figure 1), a narrowed aorta (0.7 cm) at the level of the diaphragm with post-stenotic dilation (Figures 2 and 3), and stenosis of the celiac artery with post-stenotic dilation (Figure 3). CMR revealed 50% stenosis of the proximal right renal artery and superior mesenteric artery and mural enhancement of the mid-abdominal aorta and renal arteries consistent with active vasculitis. Invasive coronary angiography demonstrated normal epicardial coronary arteries.

MANAGEMENT

TA was diagnosed based on imaging. The diagnosis of TA is rarely made by biopsy, given the impracticality...
of large vessel biopsy in the absence of planned vascular intervention. It was postulated that profound hypertension from TA led to the patient’s severe myocardial dysfunction. She was treated with anticoagulant agents for the ventricular thrombi, and diuresis resulted in improvement in cough and orthopnea. For treatment of hypertension and initiation of guideline-directed therapy for HFrEF, an angiotensin-converting enzyme inhibitor and beta-blocker therapy was initiated. Intravenous pulsed solumedrol was given for induction of remission followed by high-dose prednisone at 1 mg/kg daily according to European League Against Rheumatism recommendations (1).

### DISCUSSION

This case represents an atypical presentation of TA in a young Asian woman with HFrEF and severe hypertension. Left ventricular dilation, ventricular

| TABLE 2 Rheumatologic Serologic Studies and Hypercoagulability Studies |
|-------------------------------|
| Laboratory Study           | Value     | Reference Range |
| ANA                          | 1:40      | <1:40 titer     |
| RF                           | <15       | <20 IU/ml       |
| CCP                          | <20       | <20 U           |
| dsDNA                        | <10       | <10 titer       |
| RNP                          | 2         | <20 U           |
| Smith Ab                     | 3         | <20 U           |
| SSA Ab                       | 1         | <20 U           |
| SSB Ab                       | 2         | <20 U           |
| MPO                          | <1        | <1 Al           |
| PR3                          | <1        | <1 Al           |
| ANCA                         | <10       | <10 titer       |
| Scl-70                       | 2         | <20 U           |
| Transglutaminase IgA         | <1        | <1 U/ml         |
| C3C                          | 133       | 83-193 mg/dl    |
| C4C                          | 31        | 15-57 mg/dl     |
| IgA                          | 296       | 65-421 mg/dl    |
| IgG serum                    | 1,031     | 552-1,631 mg/dl |
| IgM                          | 66        | 33-293 mg/dl    |
| Lupus anticoagulant (hexagonal) | 3.1          | <12 s          |
| Factor V Leiden              | Negative  | Negative        |
| Cardiolipin Ab IgG           | <10       | <20 GPL         |
| Cardiolipin Ab IgM           | <10       | <20 MPL         |
| Cardiolipin Ab IgA           | <10       | <20 APL         |
| Beta 2-glycoprotein 1 IgG    | <10       | 0-20 SGU        |
| Beta 2-glycoprotein 1 IgM    | <10       | 0-20 SMU        |
| Beta 2-glycoprotein 1 IgA    | <10       | 0-20 SAU        |
| Cryoglobulins                | Negative  | Negative        |
| Protein C activity           | 87        | 70%-130%        |
| Protein S activity           | 73        | 65%-140%        |

Al = antibody index units; ANA = anti-nuclear antibodies; ANCA = anti-neutrophil cytoplasmic antibodies; APL = anti-phospholipid antibodies; C3C = complement component 3; C4C = complement component 4; CCP = cyclic citrullinated peptide; dsDNA = double-stranded DNA; GPL = IgG phospholipid units; MPL = IgM phospholipid units; MPO = myeloperoxidase; PR3 = proteinase 3; RF = rheumatoid factor; RNP = ribonucleoprotein; SAU = standard IgA beta-2 glycoprotein unit; Scl-70 = sclero-70; SGU = standard IgG beta-2 glycoprotein unit; Smith Ab = Smith antibody; SMU = standard IgM beta-2 glycoprotein unit; SSA Ab = Sjogren’s Syndrome related antigen A antibodies; SSB Ab = Sjogren’s Syndrome related antigen B antibodies.

Global hypoperfusion of the left kidney without focal area of infarct. The right kidney has several areas of peripheral cortical hypoperfusion. CTA = computed tomography angiography.
thrombi, and atrophic left kidney suggested disease chronicity, and imaging was consistent with TA. TA is a rare disease, presenting typically in Japanese females in the second or third decade of life (2,3). TA damages vasculature through transmural infiltration of arterial walls by inflammatory cells, causing granuloma formation. In the sclerotic phase, intimal fibroplasia and medial scarring forms stenotic regions, and degeneration of elastic fibers forms dilated regions (4). Classically, TA affects large vessels, specifically the aortic arch and its major branches (2), although coronary artery involvement occurs in 5% to 10% of patients (5).

Secondary hypertension has been reported in 33% to 83% of TA patients (6) and is one of its most common clinical manifestations (3,4). The mechanism of hypertension in TA is not well defined but likely involves mechanical vascular obstruction, neural activation of baroreceptors from aortic arch involvement, and hormonal factors (3). TA involves the renal arteries, resulting in stenosis in 23% to 31% of cases (7), which likely leads to activation of the renin-angiotensin-aldosterone-system (RAAS), contributing to severe hypertension.

Heart failure has been described as a comorbidity in 13.2% of TA patients (8). In a cohort of 54 Japanese patients, secondary hypertension was prevalent in 37% of patients, and the cause of death in 7 of 8 patients was heart failure or stroke (9). TA can cause heart failure through inflammatory myocarditis, but more commonly, it is caused by renovascular secondary hypertension (10).

In the present case, subacute cardiomyopathy and elevated inflammatory markers and troponin initially suggested a primary pathology of myocarditis. However, cardiac CMR demonstrated only minimal myocardial inflammation. Severe hypertension and renal dysfunction led to a secondary hypertension evaluation and vascular imaging, which demonstrated mural enhancement consistent with an active vasculitic process as well as the pathognomonic stenotic and aneurysmal lesions of TA.

**FOLLOW-UP**

After 3 months of steroid therapy, the patient was slowly transitioned to methotrexate therapy as a steroid-sparing agent. Repeated echocardiograms at 3 months demonstrated LVEF of 42% with resolved apical thrombi, followed by complete myocardial recovery at 6 months. Repeated magnetic resonance angiography showed no evidence of active vasculitis.

**CONCLUSIONS**

This case demonstrates HFrEF as the initial presentation of TA. This patient’s cardiomyopathy was precipitated predominantly by secondary hypertension, with mild perimyocarditis extending only into the epicardial space. The mechanisms by which TA
results in severe hypertension includes mechanical vascular obstruction, baroreceptor activation, and RAAS activation. In this case, complete myocardial recovery was achieved with guideline-directed medical therapy, adequate blood pressure control, and immunosuppression for TA.

**ADDRESS FOR CORRESPONDENCE:** Dr. Andrew R. Benck, Department of Internal Medicine, Cedars-Sinai Medical Center, 8700 Beverly Boulevard, Room 5512, Los Angeles, California 90069. E-mail: andrew.benck@cshs.org.

**REFERENCES**

1. Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009;68:318-23.
2. Johnston SL, Lock RJ, Gompels MM. Takayasu arteritis: a review. J Clin Pathol 2002;55:481-6.
3. Sadurska E, Jawniak R, Majewski M, Czekajski-Chehab E. Takayasu arteritis as a cause of arterial hypertension. Case report and literature review. Eur J Pediatr 2012;171:863-9.
4. Serra R, Butrico L, Fugetto F, et al. Updates in pathophysiology, diagnosis and management of Takayasu arteritis. Ann Vasc Surg 2016;35:210-25.
5. Lie J. Pathology of isolated nonclassical and catastrophic manifestations of Takayasu arteritis. Int J Cardiol 1998;66:511-21.
6. Valente ES, Almeida RD, Sacco AG, Lazzarin MC, Silva AMd, Andreazza M. Takayasu's arteritis with renal artery stenosis diagnosed in a patient with 65 years old. J Bras Nefrol 2015;37:501-4.
7. Braga NTM, Carneiro AB, Zuntini KLDCR, Araújo FB, Daher EF. Takayasu arteritis: differential diagnosis in a teenager with severe acute kidney injury: a case report. J Bras Nefrol 2019 Jan 10 [E-pub ahead of print].
8. Lee GY, Jang SY, Ko SM, et al. Cardiovascular manifestations of Takayasu arteritis and their relationship to the disease activity: analysis of 204 Korean patients at a single center. Int J Cardiol 2012;159:14-20.
9. Ishikawa K. Natural history and classification of occlusive thromboarteropathy (Takayasu’s disease). Circulation 1978;57:27-35.
10. Talwar K, Kumar K, Chopra P, et al. Cardiac involvement in nonspecific aortoarteritis (Takayasu’s arteritis). Am Heart J 1991;122:1666-70.

**KEY WORDS** autoimmune, cardiac magnetic resonance, cardiomyopathy, hypertension, systolic heart failure, vascular disease.