Takayasu Arteritis Presenting as a Pulmonary-Renal Syndrome

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ABSTRACT: Takayasu arteritis is an uncommon disease with a variety of presentations. We report a case of Takayasu arteritis with a presentation of a pulmonary-renal syndrome in a 22-year-old woman. She presented in acute respiratory failure with hemoptysis and acute renal failure; interestingly, however, the renal biopsy was normal. Magnetic resonance angiography (MRA) showed significant narrowing in the distal abdominal aorta with bilateral renal and common iliac artery occlusions. Thoracic and abdominal angiogram confirmed MRA findings of type IV Takayasu arteritis. Percutaneous transluminal angioplasty of the left renal artery normalized kidney function. The initial presentation of Takayasu arteritis as a pulmonary-renal syndrome with severe acute renal failure and diffuse pulmonary hemorrhage is unusual; to our knowledge, this has not been described previously in the literature. We provide a clinical review of Takayasu arteritis and a discussion of systemic manifestations pertinent to the case. **KEY INDEXING TERMS:** Acute renal failure; Vasculitis; Renovascular hypertension. **[Am J Med Sci 2003;325(5): 275–281.]**

Takayasu arteritis is a rare, idiopathic, inflammatory disease that primarily affects large vessels in young women.[1–4] Numerous case reports in the literature demonstrate the wide variety of presentations, depending on the segment of vessels and accompanying organ systems involved. This results in a disorder that provides a significant diagnostic challenge to the clinician. The purpose of this case report is to describe an unusual presentation of Takayasu arteritis initially mimicking a pulmonary-renal syndrome and to provide a clinically relevant review of the disease entity.

Case Report

A 22 year-old woman with a 1-month history of ankle pain and edema presented to a local hospital with 2 days of shortness of breath, midepigastric pain, nausea, and vomiting. History from the family members noted her to have exhibited extreme fatigue over at least the prior month. Past medical history was significant for hyperthyroidism diagnosed 2 years before admission and iron deficiency anemia diagnosed 2 weeks before admission. Medication was limited to propylthiouracil for treatment of hyperthyroidism. She did not smoke tobacco or drink alcohol. She was employed as a telephone operator. Family history was significant for a father with hypercholesterolemia who died of myocardial infarction at age 58 and a mother with hypothyroidism.

At a local hospital a physical examination showed the patient to be tachypneic and tachycardic with a temperature of 35.7°C, respiratory rate of 20 breaths/min, pulse of 141 beats/min, and blood pressure of 181/113 mm Hg. Rales and wheezes were heard diffusely by chest auscultation. Chest radiograph showed diffuse bilateral alveolar infiltrates. Arterial blood gas results included a pH of 7.20, pCO_2 of 33 mm Hg, pO_2 of 47 mm Hg, oxygen saturation of 67% on 3 L of oxygen by nasal cannula. She was intubated and ventilated. Bloody secretions were suctioned from the oral endotracheal tube, believed to be secondary to pulmonary hemorrhage. Other laboratory data are presented in Table 1. She was treated with high-dose steroids, transfused with 2 units of packed red blood cells for worsening anemia, and transferred to the University of Virginia Health System.

On transfer, chest auscultation demonstrated anterolateral rales. Abdominal exam showed mild midepigastric, periumbilical, and right upper quadrant tenderness. Trace ankle edema was present and right foot was cool with mottling. Dorsalis pedis pulses were diminished bilaterally but present by Doppler technique. She was oliguric and her renal function continued to decline, with a serum urea nitrogen of 76 mg/dL and creatinine of 6.4 mg/dL. Urinalysis dipstick showed specific gravity of 1.025, pH 5.0, protein 1+, and large blood, leukocyte esterase negative, and nitrite negative. Urine microscopy showed many red blood cells, many granular casts, few hyaline casts, no cellular casts, and a few calcium oxalate crystals per high-power field. This urine specimen most probably represented acute tubular necrosis, but a glomerular process could not be excluded.

High-dose steroids were continued, and plasmapheresis and hemodialysis were initiated for presumed pulmonary-renal syndrome secondary to a small vessel vasculitis. Renal biopsy was performed and sent for light microscopy, immunofluorescence, and electron microscopy. On light microscopy, a total of 18 glomeruli revealed only a slight increase in cellularity and no inflammation of medium-sized vessels. On immunofluorescence, the specimen had no significant staining, and on electron microscopy, it did not contain electron dense deposits, indicating therefore a normal renal biopsy. Anti-neutrophil cytoplasmic antibody was present in a perinuclear pattern at a

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Table 1. Initial Laboratory Data

Serum	
White blood cells	2.8 $10^3/\mu L$
Hemoglobin	9.5 g/dL
Platelets	186 $10^3/\mu L$
Sedimentation rate	75 mm/hour
Sodium	134 mmol/L
Potassium	3.9 mmol/L
Chloride	96 mmol/L
Bicarbonate	22 mmol/L
Urea nitrogen	45 mg/dL
Creatinine	3.5 mg/dL
Glucose	135 mg/dL
Calcium	9.3 mg/dL
Albumin	2.8 mg/dL
Prothrombin	13.9 seconds
International normalized ratio	1.3
Urinalysis	
Specific gravity	1.025
Protein	100 mg/dL
Blood	Small
Urine fractional excretion of sodium	0.6%

titer >1:160. The test for c–anti-neutrophil cytoplasmic autoantibodies was negative. Other negative serologic studies included anti-glomerular basement membrane antibody, antinuclear antibody, cryoglobulins, anti-human immunodeficiency virus, and hepatitis screen. The erythrocyte sedimentation rate was normal at 20 mm/hour.

Magnetic resonance angiography (MRA) demonstrated a long segment of narrowing in the distal abdominal aorta with bilateral renal and common iliac artery occlusions (Figure 1A). Collateral flow reconstituted the distal renal and external iliac arteries. Thoracic (Figure 1B) and abdominal contrast angiogram (Figure 1C) confirmed MRA findings of type IV Takayasu arteritis (Hata classification).[1] The left renal artery was dilated to 5 mm with percutaneous transluminal angioplasty. The right renal artery was completely occluded. Urine output improved immediately and serum creatinine fell to 1.7 by hospital day 10. Bronchoscopy demonstrated bloody secretions without obvious source, and the patient was extubated. A two-dimensional echocardiogram revealed a severely decreased ejection fraction with normal left ventricle wall thickness. Cardiac catheterization confirmed no pulmonary hypertension or coronary artery disease. An endocardial biopsy and histological analysis did not demonstrate myocarditis. MRA of the pulmonary vessels did not show evidence of vasculitis. She was discharged on hospital day 20 with a serum creatinine of 0.9 mg/dL and was maintained on 60 mg of prednisone once daily and lisinopril, amlodipine, and furosemide.

She was seen in follow-up 10 months after discharge complaining of bilateral lower extremity paresthesias that worsened with exercise. Her serum urea nitrogen was 11 mg/dL and creatinine was 0.9 mg/dL. Her blood pressure was 160/94 on 12.5 mg of prednisone every other day, 10 mg of amlodipine once daily, 50 mg of losartan twice daily, 81 mg of aspirin once daily, and oral contraceptive pills. An angiogram showed occlusions of the bilateral distal iliac arteries, reconstituting distally. She underwent successful aortobifemoral bypass grafting.

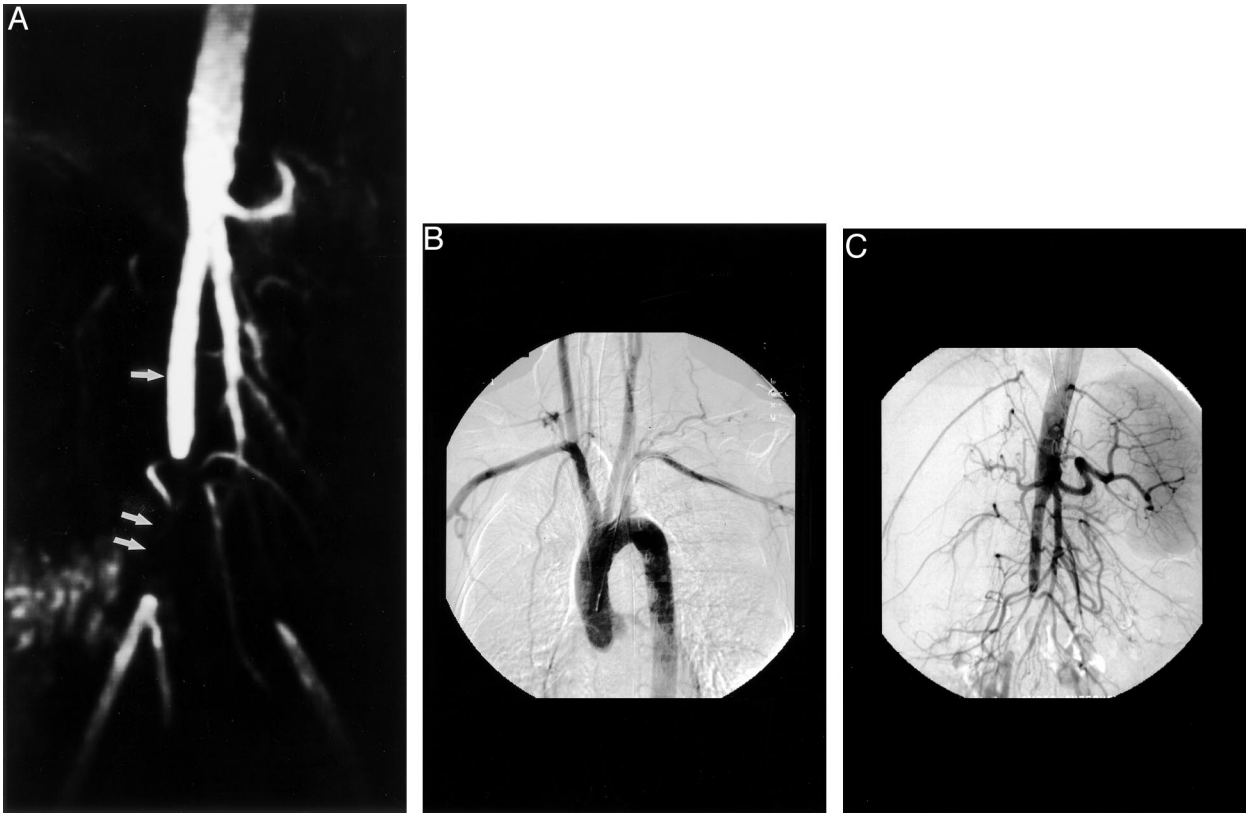

Figure 1. (A) MRA demonstrating narrowing of the distal abdominal aorta with bilateral renal and common iliac artery occlusion. (B) Angiogram of thoracic aorta. (C) Angiogram of abdominal aorta.

Discussion

Epidemiology. Takayasu arteritis is a rare, inflammatory, idiopathic disease of the aorta and its major branches that primarily affects young women. The disease is chronic, with the gradual development of stenoses that may lead to vascular occlusions. Subsequent organ and/or limb ischemia produces a variety of clinical presentations and manifestations reflecting inadequate perfusion. The nonspecific and subacute nature of the signs and symptoms combined with the low prevalence of the disease usually results in a delay in diagnosis. The estimated incidence derived from a retrospective Mayo Clinic study of 32 cases was 2.6 cases per million persons per year.[2] The number was based on a predominantly white population in Olmstead County, Minnesota. The median time to diagnosis was 18 months in 1 study[2] and 10 months in another.[3] The median age at diagnosis was 31 years (range, 15–48 years).[2] Women under 20 are frequently involved. Mortality rate is 3 to 6% at ~5 years from diagnosis. The 2 largest North American studies to date found the relative percentage of women with Takayasu arteritis to be 81% and 97% of the population, respectively.[2,3] In both studies, the Asian population was over-represented based on census data at the time of the studies, possibly indicating a genetic predisposition for disease development.

Pathogenesis. In 1830, Yamamoto provided the first description of a patient with diminished or absent pulses. In 1905, Takayasu was the first to describe coronary anastomosis of the central retinal vessels in a 21-year-old woman. Ophthalmologic findings were later associated with absent pulses, subsequently referred to as "pulseless disease," a name coined by Sano in 1951. Ohta first reported the vasculitic nature of the disease, showing involvement of the large vessels on pathological examination, in 1940.[4] As part of the Mayo Clinic study, further pathological studies delineated active and chronic phases of the disease, although overlap existed.[2] The granulomatous (active) phase shows involvement of the media and adventitia by lymphocytes, plasma cells, histiocytes, and varying numbers of multinucleated giant cells. The sclerosing (chronic) phase demonstrates transmural involvement with fibrous intimal hyperplasia, medial degeneration, and adventitial fibrosis. Both phases of this disease are associated with thrombosis and aneurysm formation. Cell-mediated cytotoxicity via perforin-expressing natural killer cells is thought to play a substantial role in the vascular injury process.[5] Recent experimental studies indicate monoclonal anti-endothelial cell antibodies may also contribute to the pathogenesis of the vascular lesions in Takayasu arteritis.[6] Finally, the close correlation between levels of interleukin 6 and chemokine regulated upon activation, normal T cell expressed and secreted (RANTES) and disease activity suggests a possible pathogenetic role of these cytokines.[7]

Table 2. Clinical Features of Takayasu Arteritis

Clinical Features	% at Presentation or during Course
1. Vascular	
a. Diminished or absent pulse	60–98
b. Carotid bruit	50–70
c. Claudication	9–70
d. High blood pressure	33–59
e. Subclavian	22–55
f. Carotodynia	32
g. Abdominal	10–24
h. Femoral bruit	5
2. Central nervous system	
a. Lightheadedness, dizzy	33–41
b. Visual abberation	9–24
c. Visual loss	8
d. Stroke	8
e. Transient ischemic attack	8
3. Musculoskeletal	
a. Chest wall	30
b. Joint pain	30
c. Myalgia	12
4. Constitutional	
a. Malaise	33
b. Fever	27
c. Weight loss	14–38
d. Night sweats	2
5. Cardiac	
a. Aortic regurgitation	19
b. Angina	7
c. Palpitations	8
d. Congestive heart failure	7
e. Pericarditis	2
f. Myocardial infarction	1–12

For more information, see ref. 3.

Diagnosis. Diagnosis of Takayasu arteritis is based on clinical features. Although the pathology of Takayasu arteritis has been defined, tissue is not required for diagnosis. A number of systemic symptoms are present in persons with Takayasu arteritis. These symptoms are summarized in Table 2.[3] Three separate, specific clinical diagnostic criteria have been proposed.[8–10] A frequently cited set of criteria was established in 1990 by the American College of Rheumatology (Table 3). The presence of at least 3 of 6 criteria has a sensitivity of 90.5% and a specificity

Table 3. 1990 American College of Rheumatology Criteria for Diagnosing Takayasu Arteritis

Age at disease onset less than 40
Claudication of the extremities
Decreased brachial artery pulse
Blood pressure difference between arms of >10 mm Hg
Bruit over subclavian arteries or aorta
Arteriogram abnormality

For more information, see ref. 9.

Table 4. Angiographic Classification of Takayasu Arteritis (anatomic areas of involvement)

I.	Branches of aortic arch
IIa.	Ascending aorta, aortic arch and its branches
IIb.	Ascending aorta, aortic arch and its branches, plus thoracic descending aorta
III.	Thoracic descending aorta, abdominal aorta, and/or renal arteries
IV.	Abdominal aorta and/or renal arteries
V.	Whole aorta and its branches
Additional descriptors:	
C (+)	equals carotid artery involvement
P (+)	equals pulmonary artery involvement

For more information, see ref. 1.

of 97.8%.[9] Inherent differences with the separate criteria seem to stem from the anatomic variability of the lesions from subjects of different races. Age at diagnosis is also a point of disagreement among authors. Although many authors believe age under 40 years at diagnosis is an obligatory criterion, Sharma et al[10] removed age as one of their criteria. The removal was prompted by case reports reporting onset after age 40 years in up to 15% of patients.[10] Evidence to support removing age as a diagnostic criterion comes from a recent review in the largest prospective study in North America to date, performed over a 20-year period by the National Institutes of Health (NIH).[3] In the series at NIH, 8 of 60 patients with Takayasu arteritis (13%) were diagnosed after age 40.[3]

Angiographic abnormalities in Takayasu arteritis are usually seem as occlusions, stenoses, lumen irregularities, and ectasias or aneurysms of large vessels. Classification of the angiographic findings in Takayasu arteritis underwent revision at the 1994 International Conference on Takayasu arteritis (Table 4).[1] The revision was proposed after it was noted that South Asians and South Americans more often had involvement of the descending and/or abdominal aorta than East Asians (Japanese). Thus, the revision has clinical significance for disease expression and progression by placing importance on the anatomic pattern predilection of certain ethnic groups.

Impact of Geography. The predominant type of Takayasu arteritis varies with geographic region. For example, type IV Takayasu arteritis is actually less common in North America. Interestingly, Moriwaki et al[11] and Deutsch[4] suggested the possible influence of geographic variation in influencing the anatomic regional involvement of pathological lesions. In the former study, Japanese patients had a significantly greater relative frequency of type I and type IIA lesions, whereas in the latter study, Indian patients had a greater relative frequency of type IV lesion.[11] However, the most common classification for both groups was type V (involvement of the whole aorta and its branches), found in more than 50% of patients in both Japanese and Indian groups studied. Analysis of the NIH data shows a similar profile of the Japanese group studied (Figure 2).[3,11]

There is also geographic variation when comparing clinical sequelae of the disease. By combining Moriwaki's data with the National Institutes of Health data, one can make interesting comparisons among the groups (Figure 3).[3,11] As one would expect, there seems to be a strong correlation between the angiographic findings and the complications of the disease. For example, the greater incidence of abdominal aorta involvement in the Indian population leads to complications such as renovascular hypertension. Conversely, the increased frequency of aortic regurgitation in the Japanese population stems from a higher frequency of ascending aorta dilation.[12]

Disease Activity. Another clinical lesson learned by the NIH study was the difficulty in assessing disease activity. Many times, biopsy and angiographic findings do not correlate with clinical course.[3] The arbitrary criteria used to determine active disease, prompting medical therapy, requires new onset or worsening of 2 or more of the following: systemic features without other identifiable cause (eg, fever, musculoskeletal symptoms), elevated erythrocyte sedimentation rate, features of vascular

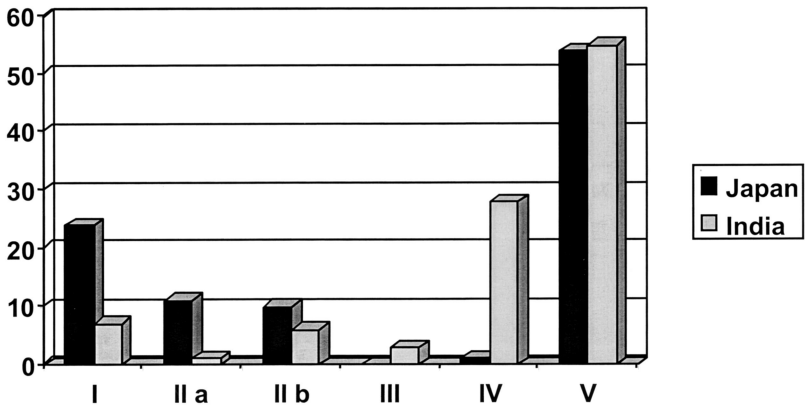

Figure 2. Frequency of angiographic classification by country of origin in Takayasu arteritis.[3,11]

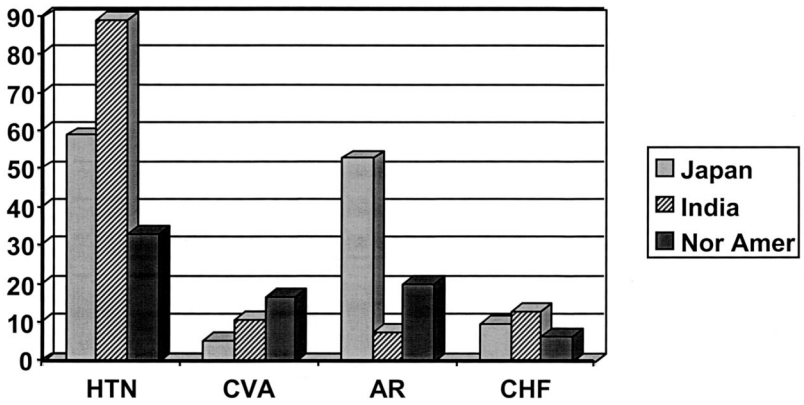

Figure 3. Comparing frequency of complications among three separate series of Takayasu patients.[3,11] HTN, hypertension; CVA, cerebrovascular accident; AR, aortic regurgitation; CHF, congestive heart failure.

ischemia or inflammation, and typical angiographic features. Elective surgical procedures are recommended during times of disease remission. Even during these periods of "remission," 44% of surgical biopsy specimens still showed evidence of active vasculitis. Eighty-eight percent of those with clinically active disease demonstrated new angiographic lesions. Surprisingly, among those in "remission," 61% demonstrated new angiographic lesions. In addition, 72% of those with clinically active disease had an elevated erythrocyte sedimentation rate compared with 56% of those in supposed remission. Therefore, in about half of the patients studied, clinical parameters and erythrocyte sedimentation rate were not reliable markers for disease activity.[13] A preliminary report from the International Network for the Study of the Systemic Vasculitides published in 1998 stated that no serological test presently available can replace vascular histopathology in establishing disease activity, despite the obvious impracticalities inherent in obtaining tissue initially and in follow-up.[14]

A popular notion of Takayasu arteritis proceeding through stages of an early systemic illness to vascular inflammation to a final, inactive phase does not hold true. In the NIH study, only 33% had, or could recall having, constitutional symptoms at presentation, whereas 18% of patients never progressed to a final, inactive phase. Also, 20% of the study patients had a monophasic illness not requiring therapy.[3]

Selected Clinical Manifestations. Cardiac manifestations in Takayasu arteritis are not uncommon. Classic presenting symptoms include angina, palpitations, and dyspnea. Congestive heart failure occurs in an estimated 6 to 13% of patients secondary to systemic hypertension, coronary artery disease, aortic insufficiency, pulmonary hypertension, and myocarditis.[16] In some patients with congestive heart failure, there is evidence for myocardial inflammation. Talwar et al.[17] performed myocardial biopsies on 16 patients and found evidence of myocarditis in 50%; clinically active disease was present in all 8 patients. Of the remaining 8 patients, 3 were classified as having active disease whereas 5 had inactive disease. Of note was that 7 of 16 patients were diagnosed with congestive heart failure, 5 of whom had biopsy-proven myocarditis. Three patients with myocarditis were biopsied serially and demonstrated lesion improvement with medical therapy correlating with clinical improvement.[17] Thus, although congestive heart failure may be the end result of systemic hemodynamic changes, active myocardial inflammation may play a role in some patients.

Pulmonary involvement in Takayasu arteritis usually presents as dyspnea, pleurisy, and/or hemoptysis. Usually, pulmonary artery involvement is responsible for the symptom complex once a cardiac cause is excluded. Pulmonary artery involvement is seen in about 50 to 80% of patients with Takayasu arteritis by angiography. It may be the first manifestation of disease,[18] and it has also been reported in isolation without systemic Takayasu arteritis.[19] Clinically, it is suspected less often. For example, only 4 of 60 patients underwent pulmonary angiograms, secondary to the presence of pulmonary hypertension. All 4 patients had at least 1 stenosis present on angiography. Pulmonary hypertension was observed in 27% of patients with Takayasu arteritis in 1 series.[20] Pulmonary hypertension has been associated not only with pulmonary artery and cardiac disease but also with pulmonary capillary hemangiomatosis. Pulmonary capillary hemangiomatosis causes diffuse capillary proliferation in the lung, leading to pulmonary veno-occlusive disease.[21]

Other presentations and pathology associated with Takayasu arteritis have been reported.[22,23] Pulmonary artery stenoses have been reported to cause recurrent pulmonary hemorrhage resulting in respiratory failure 4 years after the diagnosis of Takayasu arteritis.[22] However, pulmonary hemorrhage was not the initial presentation of the disease, and there was no mention of renal involvement. An association with nonspecific bilateral pleural and parenchymal pulmonary involvement has been re-

ported.[23] Takayasu arteritis was also reported in a 30 pack-year smoker with interstitial lung disease without hemoptysis and a mild mesangial glomerulonephritis. The restrictive lung disease was established by pulmonary function testing 4 months before diagnosis of the glomerulonephritis and Takayasu arteritis.[24]

Renovascular hypertension is the most common renal manifestation of Takayasu arteritis. In a study from India examining renovascular hypertension in patients under 50 years of age, 59% of those with renovascular hypertension were found by angiography to have Takayasu arteritis (2.2% of all young hypertensives).[25] As noted previously, the presence of hypertension in a patient with Takayasu arteritis is strongly associated with types IV and V and should spawn a consideration of a renovascular cause for the elevated blood pressure. Deyu et al[26] reported a series of 26 patients with Takayasu arteritis undergoing percutaneous transluminal angioplasty, 16 with bilateral disease. Blood pressure normalized in 17 of 26 (65%), improved in 5 of 26, and remained the same in 4 of 26 patients. Twenty-five percent of those with normalized blood pressures worsened during a median follow-up time of 5.4 years. Of the 16 with bilateral disease, the clinicians were able to relieve both stenoses in 7.[26]

As a corollary, Takayasu arteritis should be considered in the differential diagnosis in patients with suspected renal artery stenosis. Angiographic appearance differentiates Takayasu arteritis from other causes such as fibromuscular dysplasia and atherosclerosis. Angiotensin-converting enzyme inhibitor-induced acute renal failure has been described in a patient with Takayasu arteritis.[27] She was treated with bilateral aortorenal arterial bypass grafts and slowly normalized renal function over a 1-year period.[27] De novo acute renal failure is rarely or never reported in the literature as the initial presentation of Takayasu arteritis. To our knowledge, the presentation of Takayasu arteritis as a pulmonary-renal syndrome has not been described.

The relationship between Takayasu arteritis and glomerular disease is not known. The various case reports usually describe microscopic hematuria and non-nephrotic range proteinuria upon presentation.[28] The findings are nonspecific and can be seen in patients without glomerular disease. The most common finding on kidney biopsy is nonspecific ischemic change.[29] The most commonly associated glomerular disease is mesangial proliferative glomerulonephritis with mesangial deposits of IgM, IgG, IgA, and C3 by immunofluorescence.[29] Other associated glomerular diseases by case reports include membranoproliferative glomerulonephritis, IgA nephropathy, crescentic glomerulonephritis, and amyloidosis.[30–35]

Treatment. Secondary to the low mortality/high morbidity ratio of the disease, treatment focuses on decreasing disease activity. The objective is improved perfusion to vital organs and limbs and improved quality of life. The prospective nature of the NIH study made it possible to examine different medication regimens to treat arbitrarily defined "active disease."[3] Of the 60 study patients, 48 (80%) required medical therapy. Fifty-two percent (25 of 48) of patients achieved a remission with first-time glucocorticoids alone, although 60% (15 of 25) relapsed after medication taper. Thirty-two percent (8 of 25) of patients achieved remission with first-time cytotoxic agents plus glucocorticoids; 23% (11 of 48) never responded to medical therapy. A recent report of 3 cases by Daina et al[15] suggests mycophenolate mofetil dosed orally at 2 g daily in 2 divided doses may provide clinical benefit. Indications for surgical/interventional indications include hypertension with critical stenoses of the renal vessels, extremity ischemia limiting activities of daily living, cerebrovascular ischemia [symptomatic or greater than 70% stenosis of the vessel(s)], moderate aortic regurgitation, and cardiac ischemia with proven coronary artery stenosis.

Conclusions

Takayasu arteritis is a rare, idiopathic disorder with a variety of presentations and manifestations. Cardiac, pulmonary, and renal manifestations are not uncommon. Other organ systems affected include the central nervous system, musculoskeletal system, and gastrointestinal tract. Other causes of large vessel abnormalities must be ruled out when considering Takayasu arteritis as a diagnostic possibility. However, it must be considered in the differential diagnosis for young adults, especially women with hypertension, and/or claudication symptoms, and/or nonspecific complaints associated with bruits or significant cuff blood pressure differences when comparing both arms. As we have seen in our case, Takayasu arteritis can mimic a pulmonary-renal syndrome with hemoptysis, acute respiratory failure, and acute renal failure. The hemoptysis and acute respiratory failure were probably manifestations of renal vascular hypertension leading to pulmonary edema/hemorrhage. The acute renal failure resulted from acute renal artery thrombosis causing acute tubular necrosis from ischemic hyperfusion state. Such acute renal failure may not exhibit changes in the histology at the time of biopsy. Finally the elevated p–anti-neutrophil cytoplasmic autoantibodies, which usually represent a vasculitis or inflammatory disease, may have been elevated from prior use of propylthiouracil.[36] Early diagnosis and treatment can limit the morbidity associated with the disease.

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References

1. **Hata A, Noda M, Moriwaki R, et al.** Angiographic findings of Takayasu arteritis: new classification. Int J Cardiol 1996;54(Suppl):S155–63.
2. **Hall S, Barr W, Lie JT, et al.** Takayasu arteritis. A study of 32 North American patients Medicine 1985;64:89–99.
3. **Kerr GS, Hallahan CW, Giordano J, et al.** Takayasu arteritis. Ann Intern Med 1994;120:919–29.
4. **Numano F, Kakatu T.** Takayasu arteritis—five doctors in the history of Takayasu arteritis. Int J Cardiol 1996; 54(Suppl):S1–S10.
5. **Seko Y, Minota S, Kawasaki A, et al.** Perforin-secreting killer cell infiltration and expression of a 65-kD heat-shock protein in aortic tissue of patients with Takayasu's arteritis. J Clin Invest 1994;93:750–8.
6. **Blank M, Krause I, Goldkorn T, et al.** Monoclonal anti-endothelial cell antibodies from a patient with Takayasu arteritis activate endothelial cells from large vessels. Arthritis Rheum 1999;42:1421–32.
7. **Noris M, Daina E, Gamba S, et al.** Interleukin-6 and RANTES in Takayasu arteritis. A guide for therapeutic decisions? Circulation 1999;100:55–60.
8. **Ishikawa K.** Patterns of symptoms and prognosis in occlusive thromboaortopathy (Takayasu's disease). J Am Coll Cardiol 1986;8:1041–6.
9. **Arend WP, Michael BA, Bloch DA.** The American College of Rheumatology 1990 criteria for the classification of Takayasu's arteritis. Arthritis Rheum 1990;33:1129–34.
10. **Sharma BK, Jain S, Suri S, et al.** Diagnostic criteria for Takayasu arteritis. Int J Cardiol 1996;54(Suppl):S141–7.
11. **Moriwaki R, Noda M, Yajima M, et al.** Clinical manifestations of Takayasu arteritis in India and Japan—new classification of angiographic findings. Angiology 1997;48:369–79.
12. **Numano F.** Differences in clinical presentation and outcome in different countries for Takayasu's arteritis. Curr Opin Rheumatol 1997;9:12–5.
13. **Hoffman G.** Takayasu arteritis: lessons from the American National Institutes of Health experience. Int J Cardiol 1996;54 Suppl:S99–102.
14. **Hoffman G, Ahmed A.** Surrogate markers of disease activity in patients with Takayasu arteritis. A preliminary report from the International Network for the Study of the Systemic Vasculitides(INSSYS) Int J Cardiol 1998;66(Suppl. 1): S191–4.
15. **Daina E, Schieppati A, Remuzzi G.** Mycophenolate mofetil for the treatment of Takayasu arteritis: report of three cases. Ann Intern Med 1999;130:422–6.
16. **Sharma BK, Jain S, Sagar S.** Systemic manifestations of Takayasu arteritis: the expanding spectrum. Int J Cardiol 1996;54 Suppl:S149–54.
17. **Talwar KK, Chopra P, Narula J, et al.** Myocardial involvement and its response to immunosuppressive therapy in nonspecific aortoarteritis(Takayasu's disease)—a study by endomyocardial biopsy. Int J Cardiol 1988;23:323–34.
18. **Nakabayashi K, Kurata N, Nangi N, et al.** Pulmonary artery involvement as first manifestation in three cases of Takayasu arteritis. Int J Cardiol 1996;54 Suppl:S177–83.
19. **Lie JT.** Isolated pulmonary Takayasu arteritis: Clinicopathologic characteristics. Mod Pathol 1996;9:469–74.
20. **Kawai C, Ishikawa K, Kato M, et al.** 'Pulmonary pulseless disease': Pulmonary involvement in so-called Takayasu's disease. Chest 1978;73:651–7.
21. **Kakkar N, Vasishta RK, Banerjee AK, et al.** Pulmonary capillary haemangiomatosis as a cause of pulmonary hypertension in Takayasu's aortoarteritis. Respiration 1997;64: 381–3.
22. **Koyabu S, Isaka N, Yada T, et al.** Severe respiratory failure caused by recurrent pulmonary hemorrhage in Takayasu's arteritis. Chest 1993;104:1905–6.
23. **Kumar S, Sherman CB.** Unusual pulmonary manifestations of Takayasu's arteritis [letter]. J Rheumatol 1997;24(8): 1661–2.
24. **Greene NB, Baughman RP, Kim CK.** Takayasu's arteritis associated with interstitial lung disease and glomerulonephritis. Chest 1986;89:605–6.
25. **Sharma BK, Sagar S, Chugh KS, et al.** Spectrum of renovascular hypertension in the young in North India: a hospital based study on occurrence and clinical features. Angiology 1985;36:370–8.
26. **Deyu Z, Lisheng L, Ruping D, et al.** Percutaneous transluminal renal angioplasty in aortoarteritis. Int J Cardiol 1998;66(Suppl 1):S205–11.
27. **Dardik A, Ballermann BJ, Williams GM.** Successful delayed bilateral renal revacularization during active phase of Takayasu's arteritis. J Vasc Surg 1998;27:552–4.
28. **Takagi M, Ikeda T, Kimura K, et al.** Renal histological studies in patients with Takayasu's arteritis. Nephron 1984; 36:68–73.
29. **Korzets Z, Barenboim E, Bernheim J, et al.** Mesangioproliferative glomerulonephritis, antiphospholipid antibodies, and Takayasu's arteritis—is there a link? Nephrol Dial Transplant 1998;13:991–3.
30. **Koumi S, Endo T, Okumura H, et al.** A case of Takayasu's arteritis associated with membranoproliferative glomerulonephritis and nephrotic syndrome. Nephron 1990;54:344–6.
31. **Cavatorta F, Campisi S, Trabassi E, et al.** IgA nephropathy associated with Takayasu's arteritis: report of a case and review of the literature. Am J Nephrol 1995;15:165–7.
32. **Hellman DB, Hardy K, Lindenfield S, et al.** Takayasu's arteritis associated with crescentic glomerulonephritis. Arthritis Rheum 1987;30:451–4.
33. **Logar D, Rozman B, Vizjak A, et al.** Arteritis of both carotid arteries in a patient with focal, crescentic glomerulonephritis and anti-neutrophil cytoplasmic autoantibodies. Br J Rheumatol 1994;33:167–9.
34. **Jain S, Taraphdar A, Joshi K, et al.** Renal amyloidosis complicating Takayasu's arteritis: a rare association. Nephrol Dial Transplant 1992;7:1133–5.
35. **Sousa AE, Lucas M, Tavora I, et al.** Takayasu's disease presenting as a nephrotic syndrome due to amyloidosis. Postgrad Med J 1993;69:488–9.
36. **Gunton JR.** Prevalence of positive anti-neutrophil cytoplasmic antibody (ANCA) in patients receiving anti-thyroid medication. Eur J Endocrinol 2000;142:587.