SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2013; 30; 78-81

23-year-old female with dyspnea, hematuria, and seizure progressing to respiratory failure

M. Yaqoob[1], Y.A. EI-Sameed[2]

[1] Internal medicine Division. Department of Medicine, Sheikh Khalifa Medical City, Abu Dhabi - U.A.E.; [2] Consultant, Division of Respirology, Department of Medicine, Sheikh Khalifa Medical City, Abu Dhabi - U.A.E.

Abstract. Takayasu arteritis is a rare chronic inflammatory disease on unknown etiology. We report a 23-year old female who presented with fever, shortness of breath and abdominal pain. Shortly thereafter the patient developed hematuria, hemoptysis and seizure progressing to respiratory failure. She was found to have aortitis and alveolar hemorrhage. We discuss the clinical manifestations and the diagnostic work up of Takayasu arteritis. The patient's response to therapy and a discussion on treatment modalities of the disease are also included in the report *(Sarcoidosis Vasc Diffuse Lung Dis 2013; 30: 78-81)*

Key words: alveolar hemorrhage, pulmonary hypertension, aortitis, seizures, Takayasu arteritis

A 23-year old Afghani female presented with fever, chest pain, shortness of breath (SOB), and postprandial abdominal pain of one week duration. In the emergency room (ER), the patient sustained an episode of generalized seizure. Two months earlier, she presented to the emergency room (ER) with similar respiratory complaints where she was treated for pneumonia. The patient was otherwise healthy and never smoked. She is a housewife and mother to one child. She did not have any recent contact with sick individuals.

Received: 19 April 2012
Accepted after Revision: 15 June 2012
Correspondence: Yaser Abu EI-Sameed, M.D.
Sheikh Khalifa Medical City,
Al Karamah Street. P.O. Box: 51900
Abu Dhabi, UAE
Tel. 00971-2-819-2755
Fax 00971-2-819-2118
E-mail: yelsameed@skmc.ae

Authorship rights: Both Dr. Yaqoob and Dr. El-Sameed have conceived and planned the submitted work. Both doctors wrote the paper and made substantive suggestions for revision. They both approved the final version of the paper.

On examination, the patient was found to be confused and disoriented. Her temperature was 98.7°F with a heart rate of 111 beat/minute and respiratory rate of 24 breath/minutes. Her blood pressure was 152/90 mm Hg in the right arm with a significant difference when measured in the left arm (112/70 mm Hg). The brachial artery pulse was reduced on that side as well. Her oxyhemoglobin saturation level was 94% while using a fraction of inspired oxygen of 100%. She had coarse breath sounds bilaterally. Her neurological evaluation was non-focal and the remaining physical exam was normal.

The WBC was 19,600 cells/μL with neutrophilic predominance. The hemoglobin concentration was 9.8 g/dL, and the platelet count was increased to 539,000 cells/μL. Her comprehensive metabolic panel was normal. The prothrombin time and the partial thromboplastin time were 15.4 s and 44.1 s respectively with a D-dimer of 0.80 mg/L. Her chest x-ray showed bilateral interstitial opacities in the lower lobes.

Shortly after admission, she started complaining of hemoptysis, hematuria and flank pain. She

was witnessed to have another episode of generalized seizure. Her respiratory status deteriorated with worsening SOB and hypoxia. She eventually went into respiratory failure and had to be intubated.

Her chest CT scan showed diffuse thickened interlobular septa with ill-defined parenchymal nodules predominantly in the lower lobes with air space consolidation in the left lower lobe (Figure 1). There was diffuse thickening of the walls of the ascending aorta, aortic arch and its branches, descending thoracic and visible abdominal aorta. These areas of wall thickening were producing undulating margins and out pouching suggestive of aortitis (Figure 2). The left renal artery showed evidence of thrombosis with infarction of the upper pole of the kidney. Her transthoracic echocardiogram showed normal left ventricular size and function. However, she was found to have severe pulmonary artery hypertension with pulmonary artery systolic pressure (PASP) of 87 mm Hg (Figure 3).

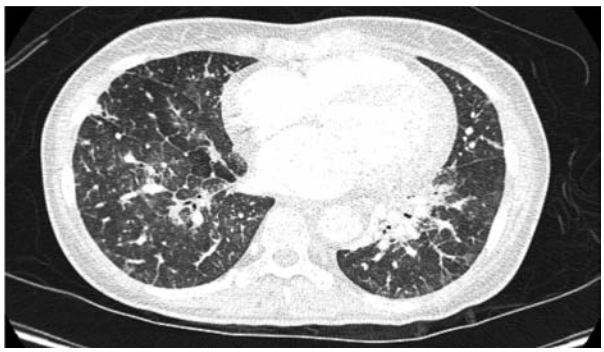

Fig. 1. Chest CT scan showing diffuse thickened interlobular septa with ill-defined parenchymal nodules

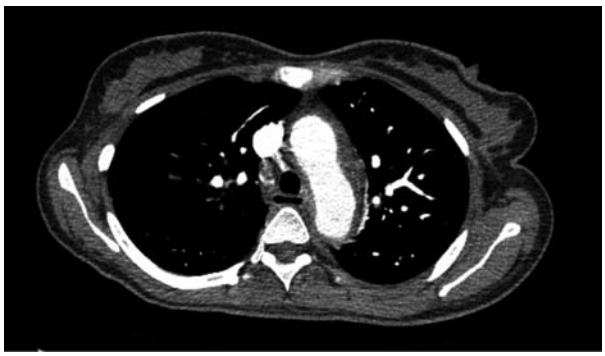

Fig. 2. Figure 2. Chest CT scan showing areas of aortic wall thickening suggestive of aortitis

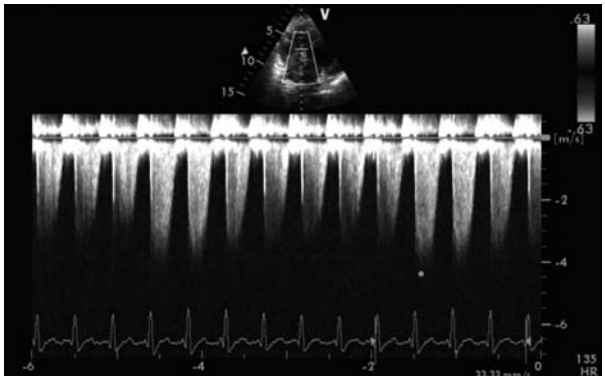

Fig. 3. Transthoracic echocardiogram showing high velocity of tricuspid valve regurgitation indicating severe pulmonary artery hypertension.

Bronchoscopy with bronchoalveolar lavage was performed and showed an increasingly bloody return, consistent with alveolar hemorrhage. Her blood, urine and bronchoscopy cultures were negative. Her autoimmune profile, including anti-nuclear antibody, rheumatoid factor, anti-neutrophil cytoplasmic antibody and anti-glomerular basement membrane antibody were all negative. The anti-cardiolipin antibodies were negative as well.

Diagnosis

Based on the patient's presentation of pulmonary hemorrhage, diffuse aortitis with renal artery thrombosis, pulmonary hypertension, and seizures, the diagnosis of Takayasu arteritis (TA) was proposed.

Discussion

Takayasu arteritis (TA) is a chronic vasculitis of undetermined etiology. The reported incidence in the United States is 0.26 cases/100,000/year, and probably higher in Japan and Asia. It has a higher tendency to affect women, particularly between 20 and 40 years of age (1-3).

TA patients present with a multitude of nonspecific symptoms including fever, back pain, headache, myalgia, and arthralgia (4). Other symptoms include dysphagia, diarrhea, and abdominal pain (5). The skin may be involved with pyoderma gangrenosum or

erythema nodosum (6-8). TA can also present with seizure, vertigo and visual impairment (9). These symptoms can occasionally be confused with epilepsy or stroke (1, 3, 10). Presentation as subclavian steel phenomenon is also described. (11) The possible reason behind the variable disease presentation is the presence of a pre-pulseless phase that overlaps with the characteristic pulseless stage (7, 12).

The pulmonary artery is involved in 14% to 86% of TA cases (13-14). Pulmonary manifestations of TA includes dyspnea, chest pain, and unresolving pneumonia (15-17). It may also present with alveolar hemorrhage, and occasionally pleural effusion (15-17). The symptoms from pulmonary arteritis are usually overshadowed by the manifestations of systemic circulation involvement (18).

Although many diagnostic criteria have been proposed, the low prevalence of the disease presents a great challenge in establishing a definite diagnosis. (19) Clinical and radiological elements are relied upon for establishing the diagnosis given (20, 21). In 1990, the American College of Rheumatology (ACR) proposed a set of diagnostic criteria for TA (22) (Table 1). Presence of three out of six criteria is required for the diagnosis. Our patient fulfilled four of the criteria. She was 23 years old, had a difference in her blood pressure measurement between both arms, had decreased brachial pulses, and had angiographic findings suggestive of TA.

The angiographic findings of TA have been classified into five types (23) (Table 2). Type 1 has been reported to be the most common followed by type 5 then type 4. (24) According to this classification, our patient fell into Type 5 P+.

The differential diagnosis of TA includes other causes of large vessel vasculitis and inflammatory aortitis like giant cell arteritis, Behcet's disease, lupus, rheumatoid arthritis, Kawasaki disease, syphilis and tuberculosis (25). Other disorders in the differential include coarctation of the aorta, neurofibromatosis and Wegener Granulomatosis (25, 26). Another multisystem disease that has neurologic, pulmonary and renal manifestations is Erdheim-Chester disease (27). However, the lack of bone pain, exophthalmos, diabetes insipidus, cerebellar signs like ataxia, and pericardial effusion rules out this possibility.

Table 1. The American College of Rheumatology (ACR) diagnostic criteria for TA

- age <40 years
- claudication of an extremity
- decreased brachial artery pulse
- >10 mm Hg difference in systolic pressure between left and right arm
- bruit over the subclavian arteries or aorta
- angiographic evidence of narrowing or occlusion of the aorta or its proximal branches

Table 2. T TA classification by angiographic findings.

Type 1	Primarily involves the branches from aortic arch
Type 2a	Involves ascending aorta, aortic arch and its branches
Type 2b	Involves the ascending aorta, aortic arch, its branches and thoracic descending aorta.
Type 3	Involves descending thoracic aorta abdominal aorta and or renal arteries
Type 4	Affects mainly the abdominal aorta and renal arteries
Type 5	Combines features of both type 2b and 4. Moreover involvement of the coronary and pulmonary arteries is designated C+ and P+ respectively

TA is a large vessel vasculitis. Therefore, histological diagnosis is usually impractical given the risk of surgery (26, 28). This risk applies to our patient given that her arteritis involved the aorta and the renal arteries. Biopsy is usually limited to the time of surgical re-vascularization procedures (26). Otherwise, the diagnosis of TA should be made based on the diagnostic criteria and the characteristic angiographic findings mentioned before.

The treatment of TA consists primarily of glucocorticoids especially in the prepulseless stage (29, 30). In glucocorticoid-resistant cases, methotrexate, azathioprine cyclophosphamide, anti-tissue necrosis factor agents can be useful (31-33). Although the majority of patients achieve initial remission, many relapse during the course of treatment as the dose of corticosteroids is reduced (24, 34). Long term methotrexate has been considered to lower the relapse rate (35). In the pulseless stage, where chronic fibrotic vascular changes are established, surgical procedures such as revascularization can be considered (30). In several studies, the reported five-year survival is between 80 and 90 % (36-37). The presence of pulmonary hypertension negatively impacts the prognosis (38).

Our patient was started on glucocorticoids in addition to azathioprine. She gradually improved and was weaned off the ventilator. During follow up,

her Chest CT scan showed improvement in both the lung involvement and the diffuse aortitis.

Conclusions

Takayasu arteritis initial presentation is usually nonspecific. Therefore, a high index of suspicion should be exercised in order to establish early diagnosis and avoid potential complications. Basic principles, like measurement of the blood pressure in both arms, are extremely important. TA vascular complications include pulmonary vasculitis, pulmonary hypertension, and internal organs infarction. Early diagnosis and treatment is essential, and can be life-saving.

References

1. Sikaroodi H, Motamedi M, Kahnooji H, et al. Stroke as the first manifestation of Takayasu arteritis. Acta Neurol Belg 2007; 107 (1): 18-21.
2. Petitpierre S, Bart PA, Leimgruber A, et al. Large vessel vasculitis: giant cell arteritis and Takayasu arteritis. [Article in French] Rev Med Suisse 2007; 3 (108): 1056-60, 1062-3.
3. Quéméneur T, Hachulla E, Lambert M, et al. Takayasu arteritis. [Article in French] Presse Med 2006; 35 (5 Pt 2): 847-56.
4. Karageorgaki ZT, Bertsias GK, Mavragani CP, et al. Takayasu arteritis: epidemiological, clinical, and immunogenetic features in Greece. Clin Exp Rheumatol 2009; 27 (1 Suppl 52): S33-9.
5. Wu H, Virdi A. Refractory abdominal pain--atypical presentation of Takayasu's arteritis. Pain Med 2009; 10 (5): 941-3.
6. Aoussar A, Ismaïli N, Berbich L, et al. Pyoderma gangrenosum revealing Takayasu's arteritis. [Article in French]. Ann Dermatol Venereol 2007; 134 (3 Pt 1): 264-7.
7. Pascual-López M, Hernández-Núñez A, Aragüés-Montañés M et al. Takayasu's disease with cutaneous involvement. Dermatology 2004; 208 (1): 10-5.
8. Reichman N, Kaufman N, Mader R, et al. Purpura--an unusual presentation of Takayasu arteritis. [Article in Hebrew] Harefuah. 1998; 135 (5-6): 197-8, 254.
9. Kuwahara C, Imamura Y, Okamura N, et al. Severe proliferative retinopathy progressing to blindness in a Japanese woman with takayasu disease. Am J Ophthalmol 2003; 135 (5): 722-3.
10. Ringleb PA, Strittmatter EI, Loewer M, et al. Cerebrovascular manifestations of Takayasu arteritis in Europe. Rheumatology (Oxford) 2005; 44 (8): 1012-5.
11. Peera MA, LoCurto M, Elfond M. A case of Takayasu arteritis causing subclavian steal and presenting as syncope. J Emerg Med. 2011; 40 (2): 158-61.
12. Erten N, Saka B, Karan MA, et al. Takayasu arteritis presenting with Fever of unknown origin: two case reports. J Clin Rheumatol 2004; 10 (1): 16-20.
13. Vanoli M, Castellani M, Bacchiani G, et al. Non-invasive assessment of pulmonary artery involvement in Takayasu's arteritis. Clin Exp Rheumatol 1999; 17 (2): 215-8.
14. Yamada I, Shibuya H, Matsubara O, et al. Pulmonary artery disease in Takayasu's arteritis: angiographic findings. AJR Am J Roentgenol 1992; 159 (2): 263-9.
15. Achari V, Prakash S. Takayasu's disease presenting with pain chest, prolonged pyrexia and pleural effusion. J Assoc Physicians India 2005; 53: 722-4.
16. Sakamoto N, Mukae H, Ishii H, et al. Case of nonspecific interstitial pneumonia associated with aortitis syndrome. [Article in Japanese] Nihon Kokyuki Gakkai Zasshi 2008; 46 (2): 116-9.
17. Maziarka D, Meleniewska-Maciszewska A, Ku J. Pulmonary changes as a result of pulmonary artery involvement during Takayasu disease-case report. [Article in Polish] Pneumonol Alergol Pol 1994; 62 (5-6): 299-303.
18. Haque U, Hellmann D, Traill T, et al. Takayasu's arteritis involving proximal pulmonary arteries and mimicking thromboembolic disease. J Rheumatol 1999; 26 (2): 450-3.
19. Richards BL, March L, Gabriel SE. Epidemiology of large-vessel vasculidities. Best Pract Res Clin Rheumatol. 2010; 24 (6): 871-83.
20. Atalay MK, Bluemke DA. Magnetic resonance imaging of large vessel vasculitis. Curr Opin Rheumatol 2001; 13 (1): 41-7.
21. Zlatkin S, Aamar S, Specter G, et al. Takayasu's arteritis identified by computerized tomography: revealing the submerged portion of the iceberg? Isr Med Assoc J 1999; 1 (4): 245-9.
22. Arend WP, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 1990; 33 (8): 1129-34.
23. 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 (5): 369-79.
24. Cong XL, Dai SM, Feng X, et al. Takayasu's arteritis: clinical features and outcomes of 125 patients in China. Clin Rheumatol 2010; 29 (9): 973-81.
25. Michel BA, Arend WP, Hunder GG. Clinical differentiation between giant cell (temporal) arteritis and Takayasu's arteritis. J Rheumatol 1996; 23: 106-11.
26. Kerr GS, Hallahan CW, Giordano J, et al. Takayasu arteritis. Ann Intern Med 1994; 120: 919-29.
27. Egan AJ, Boardman LA, Tazelaar HD, et al. Erdheim-Chester disease: clinical, radiologic, and histopathologic findings in five patients with interstitial lung disease. Am J Surg Pathol 1999; 23 (1): 17-26.
28. Johnston SL, Lock RJ, Gompels MM. Takayasu arteritis: a review.J Clin Pathol 2002; 55(7): 481-6.
29. Eklund KK, Pettersson T. Large-vessel vasculitides. [Article in Finnish] Duodecim 2011; 127 (15): 1539-47.
30. Sharma BK, Siveski-Iliskovic N, Singal PK. Takayasu arteritis may be underdiagnosed in North America. Can J Cardiol 1995; 11 (4): 311-6.
31. Mekinian A, Néel A, Sibilia J, et al. Efficacy and tolerance of infliximab in refractory Takayasu arteritis: French multicentre study. Rheumatology (Oxford) 2012; 51 (5): 882-6.
32. Bicakcigil M, Aksu K, Kamali S, et al. Takayasu's arteritis in Turkey - clinical and angiographic features of 248 patients. Clin Exp Rheumatol. 2009; 27 (1 Suppl 52): S59-64.
33. Henes JC, Mueller M, Pfannenberg C, et al. Cyclophosphamide for large vessel vasculitis: assessment of response by PET/CT. Clin Exp Rheumatol 2011; 29 (1 Suppl 64): S43-8.
34. Maksimowicz-McKinnon K, Clark TM, et al. Limitations of therapy and a guarded prognosis in an American cohort of Takayasu arteritis patients. Arthritis Rheum 2007; 56(3): 1000-9.
35. de Franciscis S, Serra R, Luongo A, et al. The management of Takayasu's arteritis: personal experience. Ann Vasc Surg 2007; 21 (6): 754-60.
36. Hall S, Barr W, Lie JT, et al. Takayasu arteritis. A study of 32 North American patients. Medicine (Baltimore) 1985; 64 (2): 89-99.
37. Ishikawa K. Natural history and classification of occlusive thromboaortopathy (Takayasu's disease). Circulation 1978; 57(1): 27-35.
38. Matsubara O, Yoshimura N, Tamura A, et al. Pathological features of the pulmonary artery in Takayasu arteritis. Heart Vessels Suppl 1992; 7: 18-25.