Dyspnea in Takayasu arteritis — an ordinary cause with an extraordinary link

Abstract

Takayasu arteritis (TA) poses a diagnostic challenge as it may have a myriad of clinical presentations. Dyspnea, as an index presentation in TA, may be secondary to the involvement of the aorta, myocardium, and/or the pulmonary vessels, or can present as a manifestation of pulmonary infection with tuberculosis. Significant lymphadenopathy cannot be attributed to TA and serves to point towards a different diagnosis or concomitant infection. Tuberculosis has been associated with TA and has considerable pathogenic and therapeutic implications. We present a case of a young female with extensive intra-thoracic tubercular lymphadenopathy compressing the trachea and right main bronchus resulting in dyspnea. The patient was subsequently found to have active TA and improved after treatment with anti-tubercular therapy and steroids. We review the causes of dyspnea and mediastinal lymphadenopathy in a patient with TA.

Key words: Takayasu arteritis, extra-pulmonary tuberculosis, dyspnea

Introduction

Takayasu arteritis (TA) is a large vessel vasculitis that preferentially affects young females of Asian origin. It classically presents with intermittent claudication and asymmetry in pulse volume between the limbs due to its predilection for the aorta and its branches. Dyspnea is uncommon and can be attributed to the involvement of the aorta, myocardium, and/or pulmonary vessels. It may also be caused by pulmonary infection with tuberculosis and, as in the present case, by extrinsic airway compression due to mediastinal lymphadenopathy.

Case

A 16-year-old girl presented with acute onset dyspnea on exertion (mMRC class III) along with a dry cough and low-grade fever for one week. There was no postural or diurnal variation in the dyspnea, no sputum production, and the patient did not have contact with a patient with tuberculosis. She had a history of intermittent claudication of both legs on walking more than 500 meters. On examination, the respiratory rate was 28/min and breath sounds were reduced on the right side without audible wheezes or crepitations. On percussion, resonance was noted on the right side. Peripheral pulses were not palpable in the upper limbs, and only feeble pulsations were felt in bilateral femoral and popliteal arteries. Correspondingly, blood pressure was not recordable in either upper limb and was asymmetric between the two lower limbs (80/40 mm Hg in the left vs 110/70 mm Hg in the right). Bruits were audible over the right brachial artery, abdominal aorta, and right femoral artery. There was no pedal edema or neck vein distention, and cardiac auscultation was normal.

The patient's feeble pulses and low blood pressure initiated emergency fluid resuscitation protocols. Laboratory investigations revealed anaemia (haemoglobin 10.3 g/dL), leukopenia (2380 cells/mm$^3$), and elevated inflammatory markers with an erythrocyte sedimentation rate of
60 mm/h and C-reactive protein levels of 13 mg/dL (normal < 5 mg/dL). For suspected vasculitis, we tested for rheumatoid factor, anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, and antibodies to double-stranded DNA, along with serologies for HBV, HCV, syphilis, and HIV, which were all negative. Urinalysis was bland, without proteinuria, hematuria, or casts. Renal artery doppler screening ruled out significant renal artery stenosis. ECG and bedside echocardiographic examination ruled out left ventricular (LV) systolic dysfunction, pulmonary hypertension, and stenosis.

A chest X-ray revealed bulky lymph nodes (Figure 1). A subsequent contrast-enhanced computed tomography (CECT) scan showed necrotic conglomerated and lobulated lymph nodes up to 7.5 cm in diameter, located in the subcarinal and paratracheal locations, with compression of the trachea and right main bronchus (Figure 2). A tubercular aetiology of these lymph nodes was suggested by the presence of tiny well-formed granulomas with necrosis on endobronchial-ultrasound-guided transbronchial node aspiration (EBUS TBNA). GeneXpert™ from the TBNA was positive for rifampicin-sensitive tuberculosis.

Magnetic resonance angiography (MRA) confirmed diffuse (60%) stenosis of the upper infrarenal abdominal aorta and occlusion of bilateral subclavian arteries with distal reformation suggestive of aortoarteritis (Figure 3). She fulfilled all six of the American College of Rheumatology (ACR) criteria and was thus diagnosed with TA. She was also diagnosed with extra-pulmonary tuberculosis. She was treated with a combination of corticosteroids (prednisone at 1 mg/kg for six weeks, followed by a slow taper over nine to twelve months) and anti-tubercular therapy (ATT, nine months). Repeat CT imaging at one year showed near resolution of lymph nodes (size 7.5 cm decreased to 1.5 cm), and an MRA confirmed reduction in disease activity with an increase in luminal patency. The patient is doing well at 1 year of follow-up without symptoms of claudication, cough, or dyspnea.

**Discussion**

Tuberculosis’ association with TA is not only a medical curiosity, but is also thought to play a role in the immunopathogenesis of TA. A systematic review evaluating this association found a high prevalence of active tuberculosis (16%) and latent tuberculosis (59%) in patients with TA, far higher than the general population [1]. They hypothesized that a loss of tolerance against self-
stress proteins is the main pathogenic event in TA, and the extensive sequence homology between mycobacterial and human stress proteins leads to epiphenomenal cross-reactions.

Treating these conditions simultaneously with corticosteroids and ATT is effective. Use of corticosteroids does not increase the risk of microbiological failure of ATT in pulmonary tuberculosis [2]. TNFα inhibitors have been used in steroid-refractory TA with an extremely low risk of reactivation of latent tuberculosis (0.9%) similar to other rheumatic disorders [3]. This suggests that the association between TA and tuberculosis is predominantly epiphenomenal, instead of a result of latent infection.

There are several mechanisms by which patients with TA can manifest dyspnea (Table 1). A previous case reported dyspnea as the index presentation which was attributed to the involvement of pulmonary arteries [4]. Pulmonary arterial involvement on pathological examination occurs in half of the cases but is rarely symptomatic. Since it presents with progressive dyspnea and angina, chronic thromboembolic pulmonary hypertension should be kept as a differential. Systolic cardiac failure resulting from dilated cardiomyopathy, with or without histological evidence of myocarditis, may be the first presentation of TA [5]. Other cardiovascular complications resulting in dyspnea include aortic regurgitation secondary to aortic root dilation [6] and acute myocardial infarction [7].

Lymphadenopathy cannot be attributed to TA alone. However, aortitis with concomitant lymphadenopathy narrows the list of differentials (Table 2). In patients with underlying TA, lymphadenopathy may be coincidental due to infections or malignancy, but the occurrence of tuberculosis is more likely. Lymph node involvement was present in 14% (16 out of 110) of adult cases of TA with active tuberculosis identified in the above-mentioned systematic review [1]. One must also consider that a distinct disease process resulted in the aortitis and lymphadenopathy exemplified by tubercular aortitis [8].
IgG-4 disease-related periaortitis [9], syphilitic aortitis [10], and possibly sarcoidosis [11]. The visualization of necrotizing granulomas and AFB, or a positive GeneXpert\textsuperscript{TM} from nodal tissue, as found in our case, establishes the diagnosis of tubercular lymphadenopathy.

Our patient presented with extrinsic airway compression by large mediastinal lymph nodes which was eventually attributed to tuberculosis. Further evaluation confirmed active TA necessitating appropriate treatment for both conditions with steroids and ATT. To the best of our knowledge, this unusual cause of dyspnea in TA is the first in literature.

### Conclusions

Takayasu arteritis possibly results from an epi-phenomenal cross-reaction with tubercular and human stress proteins, and these patients often have active or latent tuberculosis at presentation. TA patients with dyspnea should be evaluated for cardiac, pulmonary, and vascular involvement, as well as pulmonary tuberculosis or mediastinal lymphadenopathy.

### Conflict of interest

None declared.
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