

## Takayasu's arteritis with dilated cardiomyopathy associated with tuberculosis: A case report

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### ABSTRACT

Takayasu arteritis (TA) is a rare, chronic inflammatory large-vessel vasculitis of unknown etiology. A possible relationship between TA and tuberculosis (TB) has been suggested. Both the diseases show similar chronic inflammatory lesions (granulomas) on the arterial walls. Although TA may have various presentations, it presents rarely as dilated cardiomyopathy (DCM). We hereby report a case of TA with DCM, associated with TB.

**Key words:** Dilated cardiomyopathy, Hypertension, Takayasu arteritis, Tuberculosis

**T**akayasu's arteritis (TA) is a chronic granulomatous inflammatory disease of large vessels which affects mainly the aorta and its major branches along with the coronary, pulmonary, and renal arteries [1]. It is common in Asia and usually affects adolescents and young woman. However, recently, TA has been shown to affect both the sexes, any age, and all ethnic groups [2]. The etiology of TA is unclear.


Moreover, a possible relationship between TA and tuberculosis (TB) has been suggested. Both diseases show similar pathological changes in the form of granulomas on the arterial walls [3]. Clinically, TA presents with acute early phase with non-specific symptoms such as low-grade fever, fatigue, headache, night sweating, and weight loss. If untreated, arterial wall inflammation continues and late-phase symptoms appear due to ischemia of the organs such as fatigue, renovascular hypertension, and stroke. TA is the most common cause of renovascular hypertension in India [4]. It may cause dilated cardiomyopathy (DCM) in small proportion (5%) of affected patients and also present with congestive cardiac failure [5]. Congestive cardiac failure in TA is mainly due to hypertension and aortic regurgitation. We report a case of TA with DCM and hypertension associated with TB.

### CASE REPORT

A 12-year-old girl presented with the complaint of difficulty in breathing for 1 month which was aggravated in the past 5 days. This was associated with vomiting and abdominal pain for 2 days. She was having a history of orthopnea and limitation of

activity for 2 years (New York Heart Association Class II). Her grandfather had history of pulmonary TB. There was no family history of asthma or hypertension.

On examination, her built was found to be thin. Her weight was 21 kg and height 139 cm. She appeared sick, had respiratory rate 44/min and pulse rate 127/min. Peripheral pulses were felt well in upper limb but poor in both lower limbs. Blood pressure (BP) was high in all four limbs (160/85 mmHg in right upper limb, 152/80 mmHg left upper limb, 148/78 mmHg in right lower limb, and 144/82 mmHg in left lower limb). Child appeared pale, but there was no icterus, clubbing, edema, and lymphadenopathy. On systemic examination of chest, the air entry was equal with fine crepitations present bilaterally. On cardiovascular examination, jugular venous pressure was raised. Both heart sounds were normal. A systolic murmur Grade II/VI was heard in the left parasternal and apical area. Per abdominal examination, liver was 6 cm below the right costal margin, soft, and tender with smooth surface. Spleen was not palpable. Central nervous system examination was essentially normal. Fundus examination did not show evidence of hypertensive changes in retina. Blood investigation showed hemoglobin 8.4 g% with microcytic hypochromic anemia, Total leucocyte count is 11,600/cmm (neutrophils 62% and lymphocytes 30%), Platelets count is  $5.5 \times 10^5$ /cmm, erythrocyte sedimentation rate 27 mm at the 1<sup>st</sup> h, and serum thyroid-stimulating hormone was normal. Liver function test, kidney function test, and serum electrolytes were within normal limit. Urine routine examination was normal, blood and urine culture were sterile, C-reactive protein was positive, Mantoux test turned out to be positive (16 mm), and cartridge-based nucleic acid amplification test sputum was negative. Chest X-ray showed features suggestive

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of cardiogenic edema with cardiomegaly. Ultrasound abdomen showed hepatomegaly, bilateral minimal pleural effusion, and relatively small right kidney (right kidney 7.2 cm and left kidney 8.6 cm).

Electrocardiogram showed sinus tachycardia with the left axis deviation and left ventricular (LV) hypertrophy. Echocardiography showed left atrium and LV dilatation and ejection fraction was 29% with global hypokinesia and severe LV systolic dysfunction with moderate mitral and mild tricuspid regurgitation. Thin rim of pericardial effusion was present. The findings were suggestive of DCM (Fig. 1).

The gradient across descending thoracic aorta (DTA) was suggestive of obstruction in DTA (Fig. 2).

Computed tomographic (CT) angiography of aorta and its branches (Fig. 3) showed thickening of wall of DTA and suprarenal aorta with multiple areas of stenosis, occlusion of the right main renal artery at its origin with hypoenhancing right kidney, stenosis of the left renal, celiac, and superior mesenteric arteries suggestive of non-specific aortoarteritis (type III), and cardiomegaly with pulmonary hypertension.

On initial evaluation of the child, the provisional diagnosis of hypertension with congestive heart failure was made and she was put on anticongestive measure in the form of furosemide and antihypertensive drugs. Differences in upper and lower limb pulses, lower BP in lower limb than upper limb, hypertension, and features of congestive cardiac failure led to the diagnosis of TA, with differential diagnosis of coarctation of aorta and other autoimmune disorders such as systemic lupus erythematosus and Behcet's disease.

On detailed investigations, a diagnosis of TA was made according to Ishikawa (1988) and American College of Rheumatology (1990) criteria for diagnosis of aortoarteritis [6]. This child also had DCM, hypertension, and TB. The patient was started on anti-tuberculous drugs according to her body weight along with anti-hypertensive drugs (nifedipine, atenolol, and furosemide), and prednisolone was started in view of active disease process. The patient's condition gradually improved with subsidence of features of heart failure and BP decreased below 95<sup>th</sup> percentile. She was discharged

after 12 days of hospital stay and was on follow-up in the outpatient department.

The child was readmitted after 2 months of discharge with features of hypertensive emergency in the form of two episodes of generalized seizures with BP in the right upper limb 190/100 mmHg and left upper limb 176/100 mmHg. The patient was shifted to the pediatric intensive care unit where she was conscious and alert. The child was started on intravenous labetalol and gradually shifted on oral labetalol and prazosin and her previous antihypertensive drugs (nifedipine, atenolol, and furosemide) were continued. She improved gradually with current treatment but still BP was between 90 and 95<sup>th</sup> percentiles. We referred her to cardiology center for stenting of renal vessels in view of uncontrolled hypertension despite multiple antihypertensive drugs, with advice to continue antituberculous treatment.

## DISCUSSION

TA is currently categorized as a systemic granulomatous large-vessel vasculitis in the Chapel Hill Consensus Conference

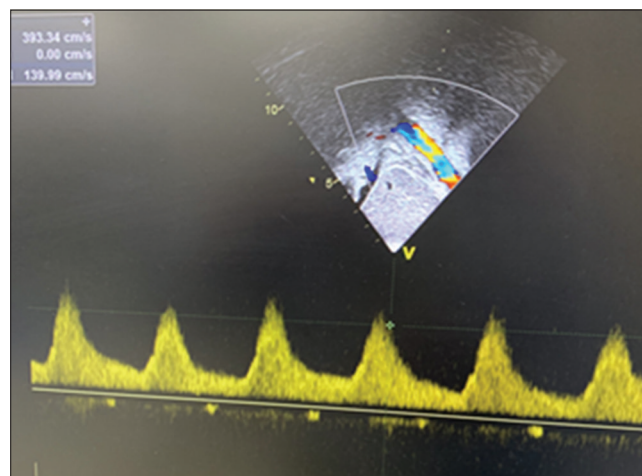


Figure 2: The gradient across descending thoracic aorta suggesting obstruction

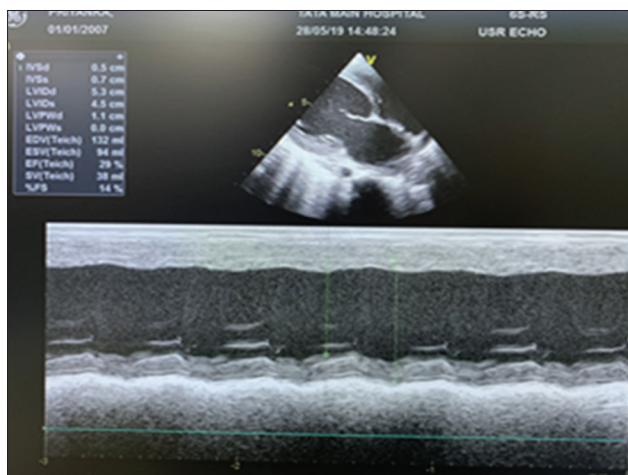


Figure 1: Echocardiography PLAX view, Showing DCM (EF 29%)



Figure 3: Computed tomographic angiography of aorta and its branches showing thickening of descending thoracic aorta wall and multiple areas of stenosis

2012 [7]. The disease characteristically affects young to middle-aged Asians and generally involves large vessels, mainly aorta and its primary branches. TA leads to progressive fibrosis and narrowing of lumen and occasionally destroys the arterial media inducing aneurysm formation.

Since the original report of Takayasu's disease in 1908, the estimated worldwide incidence is 2.6 cases/million annually, with women more commonly affected than men with wide geographical variation. In Japan, it is 8:1, in Mexico 5:1, in India 4:1, and in Israel 1.2:1. Panja *et al.* reported an incidence of 6.4:1 in India [6]. In the pediatric population, the female preponderance is less obvious [8].

Despite the association with TB, and the similarity between granulomatous lesions in TA and TB, the exact role of mycobacterium TB in the pathogenesis of TA is still unknown. Most recent reports suggest that cross-reactivity between mycobacteria and a human heat shock protein (HSP) might have a key role [9]. This augmented immune response, in particular to its 65 kDa HSP, suggests the possible role of this organism in the immunopathogenesis of the disease. This aspect is especially relevant in Asian and African countries where TB is endemic. There have been a few reported cases of active TB with TA in the pediatric population [10].

A link between TB and TA has been suggested for a long time based on several observations. There were nine anecdotal case reports of TA identified associated active TB mainly in the lymph nodes and lungs and occasionally in the internal organs in an Indian study [11].

The presentation differs in different demographic locations. The aortic arch is more involved in Japan while the involvement of the abdominal aorta is more in Indian and Korean patients. Clinical presentation of TA is non-specific. The clinical course is divided into an early active inflammatory phase and late chronic phase. The active phase lasts week to months and may have a relapsing and remitting course. It is characterized by constitutional symptoms such as fever, malaise and weight loss, night sweat, headache, dizziness, arthralgia, and skin rashes. The late chronic phase is due to arterial stenosis and/or occlusion and ischemia of organs and depends on site of arterial involvement which usually includes diminished or absent pulses (84–96%) and vascular bruit (80–94%) [12,13]. Hypertension (33–83%) generally due to renal artery stenosis which is seen in 28–75% of patients, congestive cardiac failure (28%) (due to hypertension and DCM), and pulmonary artery involvement in 14–100% of patients are observed [12]. Our case presented with hypertension and features of congestive cardiac failure. Khan *et al.* also reported a case of TA with features of congestive cardiac failure [14].

Hypertension in TA is most commonly due to renal artery stenosis as reported from a study in China of a case series of 411 cases by Chen *et al.* [15]. In our case, the child presented with hypertension and on evaluation, the child was having bilateral renal artery stenosis on imaging study.

Diagnostic imaging is fundamental to the diagnosis of TA and plays an essential role in disease monitoring. Arteriography using catheter-directed intravascular injection of contrast dye, magnetic resonance angiography (MRA), or CT angiography (CTA) provides information on vascular luminal dimensions. MRA and CTA are safe and non-invasive techniques for assessing vessel patency in TA and play an essential role in disease monitoring [16].

Therapeutic modalities include steroids, immunosuppressive agents, and antihypertensive drug therapy. Different studies have reported 20–100% success rate of steroids [17]. Cyclophosphamide and methotrexate are often needed to control intense inflammatory response. Mycophenolate mofetil and tacrolimus are also used, especially for corticosteroid-resistant disease. Hypertension should be aggressively managed. In addition, balloon dilatation or stenting is often necessary [18]. Drug therapy can slow down progression of cardiomyopathy and in some cases even improve the heart condition.

## CONCLUSION

The present case report highlights the casual association of TB with TA. TB should be ruled out in a case of TA, particularly in India, where TB is an endemic disease. Although medical treatment is the mainstay of treatment modality, surgical management should be kept in mind when indicated.

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