Takayasu arteritis presented with acute heart failure: case report and review of literature

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Abstract

Acute heart failure due to myocarditis is not common in Takayasu arteritis, let alone in combination with thrombosis affecting both ventricles and pulmonary arteries. The concomitant infection of non-tuberculosis mycobacterium further complicates the clinical scenario and poses challenges for implementation of tailored treatments. This case report describes a teenage girl with a history of intermittent claudication and Erythema Nodosum who developed acute heart failure. Detailed clinical investigations and imaging techniques confirmed the diagnosis.

Keywords Takayasu arteritis; Acute heart failure; Myocarditis; Ventricular thrombosis; Pulmonary arterial thrombosis; Non-tuberculosis mycobacterium

Introduction

First described in 1908, Takayasu arteritis (TA) has now been recognized as a non-specific inflammatory disease of unknown aetiology, predominantly affecting the aorta and its main branches, pulmonary arteries, and coronary arteries of young females. Its identical pathology is inflammatory infiltrates involving all arterial layers, including acute exudative inflammation and chronic granulomatous inflammation situated mainly in the media and adventitia while hyperplasia and neovascularization are found in the intimal layer. Manifesting as non-specific systemic inflammatory symptoms, TA can also induce ischaemic symptoms related to vascular stenotic lesions. Sometimes, it progresses into relatively rare and potentially fatal scenarios including acute visual loss, myocardial infarction, heart failure, cerebral thrombosis, and malignant hypertension. Here, we present a case of a young female suffering from TA and non-tuberculosis mycobacterium infections. Apart from typical symptoms such as fever and claudication, she developed acute heart failure due to myocarditis and thrombosis involving both ventricles and pulmonary arteries.

Case report

Our patient was a 15-year-old female resident in Inner Mongolia. She started to develop intermittent claudication 1 year prior to admission. She was also noted to have low-grade fever of 37.5°C, bilateral rash over her lower limbs, and apparent hair loss. Local hospital made the diagnosis of Erythema Nodosum and prescribed unclear regimen of thymosin and traditional Chinese medicine to treat the disease. Although the fever and rash resolved slowly, the claudication kept worsening gradually. One month ago, she could only climb up two floors and complained of decreased appetite, intermittent emesis, coughing white frothy sputum, and pitting oedema of lower limbs and eyelids. One week ago, she suddenly developed shortness of breath and hemoptysis. Chest computed tomography (CT) showed multiple infiltrates, ground-glass opacities, budding signs, and bilateral pleural effusions. Cardiac ultrasound revealed diffuse biventricular hypokinesia, left ventricular thrombosis, and moderate pulmonary arterial hypertension (56 mmHg). Left ventricular ejection fraction (LVEF) was 28%. Tricuspid annular plane systolic excursion (TAPSE) was 7 mm. Acute
Heart failure was diagnosed, and diuresis was initiated. Her discomforts slightly improved, and she was admitted to the Cardiac Care Unit in our hospital for further investigation. Past medical history and family history revealed nothing significant.

On admission, her height was 163 cm and weight was 57.5 kg. Her body mass index (BMI) was 21.6 kg/m². Her blood pressure in the upper extremities were 160/110 mmHg (left) and 140/90 mmHg (right). The number could not be interpreted in the lower limbs. Her heart rate was 120 bpm of regular rhythm. Respiration rate was 25 per minute and oxygen saturation was 98% on room air. Physical examination revealed a 3/6 systolic murmur over the right cervical region, asymmetrical radial pulses, and disappearance of both dorsalis pedis artery pulses. Jugular vein distentions, bilateral rales in lung bases, liver enlargement, and pitting oedema of lower limbs were also noted. Blood tests revealed low albumin level of 23 g/L (33–52 g/L) and markedly increased BNP of 2009 ng/L (<300 ng/L). Twenty-four-hour urine albumin was 5.2 g with G/P 100% while antinuclear antibodies (ANA), anti-neutrophilic cytoplasmic antibody (ANCA), high sensitivity C reactive protein (hsCRP), erythrocyte sedimentation rate (ESR) were normal. The 12-lead electrocardiogram showed normal sinus rhythm, left atrial overloading, and left ventricle enlargement. Echocardiography revealed multiple abnormalities: (i) enlargement of the entire heart, with left atrium diameter of 41 mm and left ventricular end diastolic diameter of 53 mm; (ii) mural thrombus of both ventricles. Two were in the left while one was in the right; (iii) diffuse hypokinesis of left ventricle and severe impairment of both ventricle’s systolic and diastolic functions. The estimated LVEF was 12%; (iv) moderate pulmonary hypertension of 49 mmHg; (v) small amount of pericardial effusion (Figure 1). Vascular ultrasounds detected multiple arterial stenosis, including right cephalic artery, common femoral arteries, and superficial femoral arteries. Thickening of the femoral arterial walls was also noted.

Rheumatology, pulmonology, and infectious diseases were consulted, and the following diagnoses were made: (i) acute decompensated heart failure; (ii) Takayasu arteritis. Our patient met four out of five diagnostic criteria of TA (age < 40 years old, symptoms of limb ischaemia, physical findings of decreased pulses, and unsymmetrical blood pressure, evidence of arterial stenosis provided by imaging); (iii) multiple ventricular thrombosis; (iv) pulmonary tuberculosis. This preliminary diagnosis was based on multiple infiltrates of her lungs and high incidence of tuberculosis in TA patients. Continuous intravenous nitroglycerin infusion, vigorous furosemide boluses, and oral beta blockers were administered to counter heart failure while low molecular weight heparin was injected subcutaneously for anticoagulation. Intravenous methylprednisolone 40 mg daily and cyclophosphamide 400 mg weekly were tailored to treat

**Figure 1.** In the apical four chamber view, echocardiography showed mural thrombus in both ventricles.
TA while an anti-tuberculosis regimen of oral isoniazid, rifampicin, ethambutol, and pyrazinamide was initiated at the same time. One week later, her symptoms began to resolve. Serum BNP and urine albumin excretion level gradually decreased while her ESR level raised up to 96 mm/h (<20 mm/h). After two weeks, repeated echocardiography showed her heart’s dimensions returned to normal with LVEF 41%. Cardiac magnetic resonance imaging (MRI) detected small patches of delayed enhancement in myocardium of the ventricular septum and left ventricular inferior wall (Figure 2). Both coronary arterial angiograms and Technetium sestamibi (99mTc-MIBI) static myocardial perfusion imaging were negative. Thoracic CT found her left lobe had greatly improved while multiple infiltrates and patches remained in the right lobe. Pulmonary embolism was suspected, and CT pulmonary angiogram found multiple emboli in the right pulmonary artery (Figure 3). We gradually transitioned from low molecular weight heparin to warfarin and switched from intravenous methylprednisolone to oral prednisone before discharge. At her 2 month follow-up, we discontinued the warfarin as both echocardiography and computed tomography pulmonary angiography (CTPA) showed the complete dissolve of the thrombus. Her pulmonary lesions disappeared at her 4 month follow-up, and she remained on her steroid and anti-tuberculosis regime.

**Discussion**

Takayasu arteritis is currently categorized as systemic granulomatous large-vessel vasculitis in the Chapel Hill Consensus Conference 2012. The disease characteristically affects young to middle-aged Asians and generally involves large vessels, including the aorta and its primary branches. A detailed sub-classification exists based on its vascular distributions obtained by angiographies. While the American College of Rheumatology 1990 diagnostic criteria have demonstrated a sensitivity of 90.5% and a specificity of 97.8%, in clinical practice, the diagnosis is often delayed due to its various manifestations. A number of modern imaging modalities include high-resolution Doppler ultrasound, cardiovascular magnetic resonance, 18F-fluorodeoxyglucose positron emission tomography can aid in the early identification of the disease. Early initiation of medical treatments, especially the combination of corticosteroids and immunosuppressive agents, is generally advised to minimize vascular injuries.

As a 15-year-old Asian female, our patient fitted in with TA’s characteristic epidemiology. She presented with typical signs and symptoms of arterial blockages. The skin lesions mimicking Erythema Nodosum have been reported in other TA cases. As mentioned earlier, her most striking symptoms were total heart failure. Mwipatayi and Jeffery
retrospectively analysed 272 TA patients and identified 90 individuals with cardiac failure, which accounted for 46% of all-cause mortality (29 out of 57).

Main causes of heart failure in TA patients were increased afterload due to renovascular hypertension and aortic regurgitation. Myocardial ischaemia induced by myocarditis, accelerated atherosclerosis, or severe pulmonary hypertension were also noted. For our patient, both echocardiography and cardiac MRI conformed to the findings of significant decrease in systolic function and diffuse biventricular hypokinesis. Her MRI showed patches of delayed enhancement in myocardium, which were highly suggestive of myocardial lesions. After excluding etiologies including prolonged hypertension, coronary heart disease, virus infections, valvular heart disease, and drug abuse, our suspicion fell to myocarditis. Occurring not uncommonly in TA patients, myocarditis tends to occur early in disease course and appears to correlate with the disease’s activity.

In 1988 and 1991, Talwar et al. separately performed serial endomyocardial biopsies in TA patients and myocarditis were identified in 8 out of 18 and 24 out of 54 patients. Takeda performed an LV endomyocardial biopsy on a 15-year-old male with TA, and the specimen showed infiltration of CD16+ natural killer cells and T-cell receptor + T lymphocytes plus severe myocyte necrosis. Immuno-histochemical study of the cardiac myocytes was also positive for human leukocyte antigen (HLA) Classes I and II, and ICAM-1, indicating involvement of an active inflammatory process. The pathophysiology was believed to be direct immune cytotoxicity towards the myocardium. However, Breinholt et al. reported a 15-year-old girl with TA who developed left ventricular dysfunction, and endomyocardial biopsy revealed increases in immune complex deposition in the walls of small myocardial vessels, suggesting vasculitis affecting small vessels might also be involved. For the treatment and outcomes, early implementation of immunosuppressive therapy seemed to be responsive. Talwar et al. chose combined therapy of prednisolone and cyclophosphamide over 12 weeks, and improvements were evident not only in clinical and haemodynamic states but also myocardial morphology. Takeda used steroid therapy for 2 months, and the patient’s symptoms were markedly alleviated, and his cardiac function and morphology greatly improved. For our patient, we initiated the treatment regimen of corticosteroids and cyclophosphamide, and her symptoms resolved after 2 weeks, together with the heart’s structural and functional improvement. The result also supported our suspicion of myocarditis as the underlying disease even without performing endomyocardial biopsy.

Thrombosis involving both ventricles and pulmonary arteries was sequentially identified in our patient. Kim et al. discovered a large mural thrombus in the left ventricle from a 14-year-old girl with TA. Heidi performed a cohort study on 21 paediatric TA patients, revealing one case of thrombosis in the superior mesenteric artery. While vessel wall inflammation was believed to play a major role in thrombus formation, Akazawa et al. also contested that TA could induce a state of hypercoagulability. Having measured 30 patients’ plasma levels of platelet factor 4, beta-thromboglobulin, thrombin-antithrombin III complex, fibrinopeptide A, and D-dimer, he found that all these parameters were significantly elevated in TA patients, which lead to hypercoagulable state and thrombus formation. As for the treatment, anti-platelet therapy is generally advised to prevent further ischaemic events. Anticoagulation therapy should be initiated once thrombus were identified without contraindications. Patients should be considered for endovascular procedure or surgery if they have severe and symptomatic aortic branch arterial disease. For our patient, the thrombus in her right ventricle dissolved completely by anticoagulation therapy before discharge.

Previous epidemiological studies have uniformly shown that TA tends to concur with tuberculosis. The pathophysiology perhaps lies in the cross-reactivity against vascular peptides that mimic the antigens of Mycobacterium tuberculosis. For our patient, we made the empirical diagnosis of pulmonary tuberculosis based on her pulmonary lesion pattern and started the anti-tuberculosis regimen immediately along with the immunosuppressive therapy. Later, the PCR of her sputum turned out to be positive for non-tuberculous mycobacteria (NTM) while her tuberculosis...
skin test and QuantiFERON-TB Gold test were negative. We failed to obtain another sputum sample to determine the exact strain because her coughing already resolved. Though scant epidemiological studies have been conducted to explore the relationship existed between TA and NTM infections, Hernandez et al. found that 78% TA patients had significantly elevated agalactosyl IgG antibody to the purified 65 kDa heat shock protein of *Myobacterium leprae*. Additionally, the serum antibody levels seemed to be positively correlated with disease activity.13 Because the treatment regimens were basically the same between NTM and TM, PCR could be conducted if the pulmonary infection worsened during follow-up.

Noticeably, our patient’s ESR level remained within normal range prior to and on admission to our hospital despite her worsening symptoms. The level began to rise after immunosuppressive therapy was initiated. This phenomenon seemed to contradict with the prevailing view that elevated ESR level not only correlated with the disease activity but also seemed to contradict with the prevailing view that elevated ESR level remained within normal range prior to and on admission to our hospital despite her worsening symptoms. The level began to rise after immunosuppressive therapy was initiated. This phenomenon seemed to contradict with the prevailing view that elevated ESR level not only correlated with the disease activity but also acted as a potential diagnostic utility in existing criteria such as EULAR/PRINTO/PRES or modified Ishikawa’s diagnostic criteria.2,3,6 However, Lee et al. found elevated ESR (>21 mm/h) only in 54.9% (112/ 202) of the TA patients, respectively.16

### Conclusions

Various presentations of TA have been recorded, including cardiac involvement, mural ventricular thrombosis, and pulmonary arterial embolus. However, the deadly combination of these conditions is extremely rare and has not been reported as far as we are aware, let alone the concomitant infections of NTM. The clinical scenario poses great challenge for in-time diagnosis and prompts decisive implementation of a well-tailored treatment regimen because contraindications exist.

### Conflict of interest

None declared.

### Author contributions

Xuanqi An is the first author who contributed to caring for the patient as a resident in the medical team in coronary care unit (CCU) and finished the paper by himself. Yechen Han is the second author. He was the attending in charge of the patient. Bingqing Zhang, Lin Qiao, and Yuxing Zhao are other residents taking part in caring for the patient. Xiaoxiao Guo is the attendant who spent time performing echocardiography in CUU. Professor Ligang Fang, Professor Wenling Zhu, Professor Quan Fang, and Professor Zhujun Shen all supervised patient care. Professor Shuyang Zhang, the vice president of Peking Union Medical College Hospital, also provided detailed treatment regimen for the patient, and she is our corresponding author.

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