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Case Report

Pulmonary artery hypertension as an initial manifestation of Takayasu's arteritis: A case report

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ABSTRACT

Takayasu's arteritis is a rare chronic vasculitis of unknown etiology. Symptomatic pulmonary artery disease may be the first sign of Takayasu's arteritis. We describe a 51-year-old woman who presented with severe dyspnea. The initial evaluation and routine exams suggested the presence of pulmonary hypertension of unknown etiology. Absence of bilateral radial and brachial pulses in the physical examination led to an angiographic study, which confirmed the diagnosis of Takayasu's arteritis with severe pulmonary hypertension. During bosentan therapy, the patient's clinical symptoms and exercise capacity improved and her 6-min walking distance increased. We emphasize the importance of considering Takayasu's arteritis in the early diagnosis and therapy of pulmonary artery hypertension.

1. Introduction

Takayasu's arteritis (TA) is a chronic idiopathic vasculitis that mainly affects the aorta and/or its main branches and, to a lesser extent, the pulmonary arteries.[1] The incidence of Takayasu's arteritis is about 2/10,000 person-years, with a tenfold predominance in women, especially those under 40 years of age.[2] Clinical presentation may be insidious, and diagnosis is often delayed. Signs of pulmonary artery involvement as the initial predominant clinical manifestation are rare. Here, we present a case of Takayasu's arteritis that presented with symptoms and signs of pulmonary hypertension. This case report highlights the importance of differential diagnoses and the importance of modern-day imaging in diagnosis.

2. Case report

A 51-year-old female was referred to our hospital because of progressive dyspnea. A slight dyspnea on exertion appeared 4 years ago and deteriorated within the last 3–4 months, leading to shortness of breath at low physical activity levels. There were no associated symptoms such as orthopnea, paroxysmal nocturnal dyspnea, hemoptysis or cough. A year previously, a coronary angiography had been performed in another hospital, where this showed normal coronary arteries. At that time, her right and left brachial and radial pulses were absent. Aortography demonstrated stenosis of both the right and left subclavian arteries; warfarin therapy was started after this discovery. Upon physical examination, bilateral brachial and radial artery pulses were absent; as a result, blood pressure from the right and left upper extremities could not be measured. The patient's femoral pulses were present. The laboratory findings only showed a slightly elevated erythrocyte sedimentation rate (ESR: 48 mm/h) and an increased C-reactive protein level (CRP: 5.16 mg/dl); the patient's differential blood count was normal. The initial electrocardiography (ECG) showed right ventricular hypertrophy and right axis deviation. The chest radiograph and lung function tests were normal. Rheumatoid factor, antinuclear antibodies, anti-DNA antibody, anti-neutrophil cytoplasmic antibody, viral serology and anti-CCP were all negative. On admission, the patient was in the New York Heart Association (NYHA) functional class III, with a 6-min walk distance of 160 m.

The patient's echocardiography showed an ejection fraction of 72%, right ventricular enlargement with paradoxical septal motion, right atrial enlargement, severe tricuspid regurgitation and 95 mmHg maximal pulmonary artery pressure. Pulmonary hypertension due to thromboembolism was considered in the differential diagnosis, so a computed tomography of the chest was performed. The results showed that the right pulmonary artery was no longer visible from its origin (Fig. 1). The diameter of the main pulmonary artery was increased (35 mm). There was no finding of pulmonary embolism. A ventilation–perfusion scan revealed normal ventilation in both lungs but a near-total perfusion defect in the right lung. Low extremity vascular evaluation by Doppler ultrasonography showed no abnormality. Intra-arterial digital subtraction angiography revealed that the right subclavian artery after the origin of the right vertebral artery was completely occluded as the distal part

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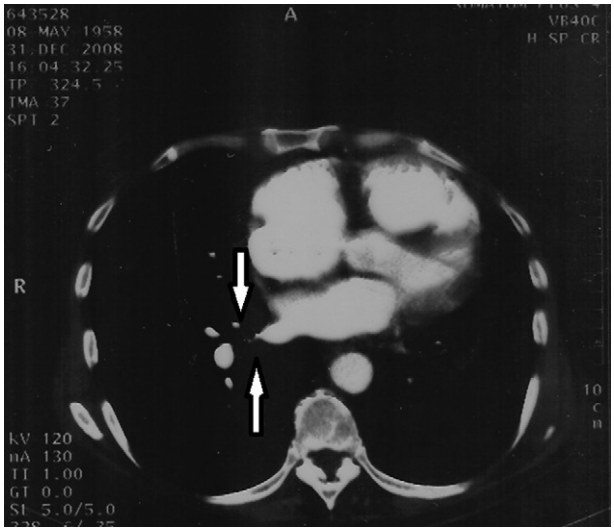

Fig. 1. Thorax CT showing complete occlusion of the right pulmonary artery (arrows).

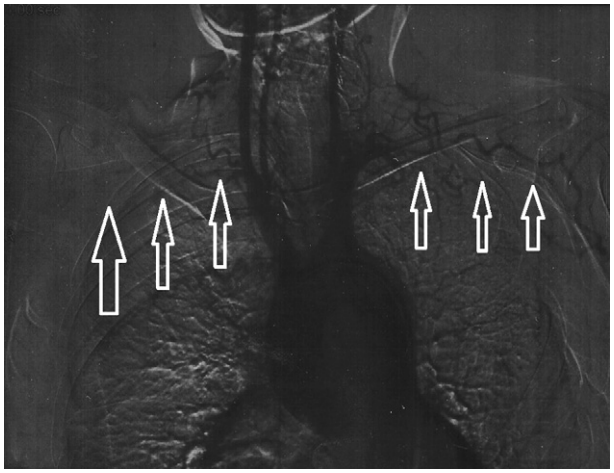

Fig. 2. Digital subtraction angiography revealing total occlusion of the right and left subclavian arteries (arrows).

of the left subclavian artery (Fig. 2). A magnetic resonance angiography scan of the abdomen showed normal abdominal aorta, renal arteries and celiac trunk. Consequently, a coronary angiogram was performed, which showed normal coronary arteries. A mean pulmonary artery pressure of 50 mmHg and a pulmonary artery wedge pressure of 10 mmHg were found after performing a right heart catheterization.

We diagnosed the patient as having Takayasu's arteritis based on the following findings, which fulfilled the American College of Rheumatology 1990 criteria[3]: decreased brachial artery pulse, pulse pressure difference of more than 10 mmHg between the two upper extremities and angiography findings.

Other differential diagnoses that were considered and excluded were Wegener's granulomatosis, giant cell arteritis, Behçet's disease, sarcoidosis, neoplastic disorders and systemic infectious diseases. The illness of patient was in the chronic phase; therefore, no immunosuppressive therapy was started. Due to the high risk of arterial thromboembolism, warfarin therapy was continued. Additionally, the patient was treated with bosentan 125 mg/day. After 6 months of bosentan treatment, the patient's clinical symptoms had improved significantly: her 6-min walk distance increased to 255 m and she improved rapidly to NYHA class II; in addition, transthoracic echocardiography showed that there was a decrease in pulmonary artery pressure.

3. Discussion

In this study, we report a case of Takayasu's arteritis with pulmonary artery involvement. Takayasu's arteritis, a chronic inflammatory arterial disease of unknown cause, occurs predominantly in young women.[4] After reviewing the literature and specifically searching for pulmonary artery involvement, it was found in an average of 56% of the cases studied.[5] A few reported cases of patients with Takayasu's arteritis complained of symptoms of pulmonary hypertension.[6–8] Our patient demonstrated atypical manifestations of Takayasu's arteritis, which are typically associated with pulmonary artery involvement and pulmonary artery hypertension. The increasing breathlessness noted during the 4 months prior to admission is probably related to progressive pulmonary hypertension. It is difficult to distinguish these cases from primary lung disease and chronic pulmonary embolism. The patient had no signs of acute pulmonary embolism or history of vein thrombosis. In the absence of systemic involvement, the differential diagnosis between Takayasu's arteritis and chronic thromboembolic disease may be facilitated by an accelerated ESR, but as was the case for our patient, a normal ESR cannot rule out a diagnosis of Takayasu's arteritis. Other diagnoses, including primary pulmonary hypertension, fibrosing mediastinitis and congenital stenosis of the pulmonary artery and tuberculosis, were suspected based on the initial clinical presentation. In the case of large vessel involvement, temporal arteritis and anti-phospholipid syndrome should be considered in the differential diagnosis. However, temporal arteritis was unlikely since the patient did not suffer from headache and her temporal artery pulsation was normal. A diagnosis of anti-phospholipid syndrome seemed unlikely since antinuclear antibody and anti-cardiolipin antibody assays were negative and the patient did not have a history of abortus. In our case, CT and MRI were decisive in diagnosing Takayasu's arteritis. In the literature, the interval between the onset of symptoms and diagnosis of Takayasu's arteritis ranges from 1 to 16 years.[6,7] Our patient was 51-year-old woman. Total occlusion of left pulmonary artery and symptoms and signs related to its involvement were very late manifestations in the present case. The most characteristic findings of pulmonary artery involvement in Takayasu's arteritis are stenosis or occlusion, mainly of the segmental and subsegmental arteries and less commonly of the lobar or main pulmonary arteries.[1] Unilateral total occlusion of the right or left pulmonary artery is very rare and can occur in advanced and late-phase disease.[9] In the present case, chest CT findings were consistent with pulmonary artery involvement, and our patient had total occlusion of the left pulmonary artery.

Our patient had severe pulmonary hypertension accompanied by severe symptoms. Since pulmonary artery stenosis develops chronically, most patients only show signs of mild-to-moderate pulmonary hypertension. Lupi et al. retrospectively analyzed 22 patients with Takayasu's disease and found that 50% of the cases had pulmonary involvement.[10] No patients had pulmonary symptoms, but 63% had clinical, radiological and electrocardiographic findings suggesting pulmonary hypertension or right heart strain. We also ruled out chronic pulmonary emboli by chest CT and ventilation–perfusion scan. The patient was started on oral warfarin and intravenous heparin concurrently. After the PT reached therapeutic levels with an INR between 2 and 3, heparin treatment was discontinued.

ET-1 is a potent endogenous vasoconstrictor and a mitogen for fibroblasts, smooth muscle and endothelial cells.[11] The endothelin (ET) system, especially ET-1 and the ETA and ETB receptors, has

been implicated in the pathogenesis of pulmonary arterial hypertension (PAH), as plasma ET-1 levels are elevated in patients with PAH and Takayasu's disease.[12] Bosentan shows an almost equal affinity for both receptors, with an ETA: ETB affinity ratio of 40:1. Bosentan is thus commonly referred to as a dual endothelin receptor blocker.[13] Following its approval by the US Food and Drug administration (FDA) in 2001, bosentan is now available in many parts of the world. For patients who have no positive acute vasodilator testing and are considered to be less risky based on clinical assessment, oral therapy with an endothelin receptor blocker would be the first line of therapy recommended. Bosentan has been approved for the treatment of WHO-FC II and III patients.[14] The mechanism is thought to involve inhibition of vasoconstriction, cell hyperplasia and hypertrophy and an increase in the extracellular matrix. Our patient was considered to have PAH associated with Takayasu's disease. Bosentan treatment was started at a dose of 62.5 mg twice daily, which was increased to 125 mg twice daily after 4 weeks. Six months after starting 62.5 mg twice-daily bosentan, the patient's clinical symptoms had improved significantly, and echocardiography revealed a reduction in mean PAP.

In conclusion, this case report demonstrated that symptoms arising from pulmonary hypertension in Takayasu's arteritis may exist. The diagnosis of Takayasu's arteritis is often mistaken for a different pathological diagnosis, depending of the signs and symptoms at a particular time. Takayasu's arteritis should be considered in the presence of pulmonary hypertension of unknown etiology. Our interesting case suggests that the endothelin receptor blocker bosentan may provide an effective solution to attenuate the PAH in Takayasu's disease.

Conflict of interest

The author has no conflict of interest.

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