

Pulmonary Thromboembolism in Behcet's Disease: A Case Report

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Behcet's disease is a vasculitis which presents as recurrent oral and genital aphthous ulceration, uveitis and skin lesions. Unlike other types of vasculitis, venous system involvement is a common manifestation of Behcet's disease. Despite the high incidence of deep vein thrombosis in Behcet's disease, pulmonary artery thromboembolism (PTE) is a rare complication. In this article, we report on a 44-year old man who experienced recurring painful oral ulcers, bilateral panuveitis, superficial phlebitis and positive pathergy which had led to a diagnosis of Behcet's disease 12 years earlier. He developed sudden onset dyspnea, pleuritic chest pain and hemoptysis two days before admission. The patient had tachypnea and mild respiratory distress at the time of admission. CT angiography showed filling defects in the inter-lobar arteries of both lungs with sub-segmental consolidation. A lung perfusion scan showed multiple segmental and sub-segmental perfusion defects in both lungs which did not match the ventilation scan. A diagnosis of PTE was made and anticoagulation with enoxaparin and warfarin was begun. The tachypnea, chest pain and hemoptysis disappeared after three days and he was discharged after 10 days with warfarin. His disease was in complete remission at eight months after discharge.

Keywords: Behcet's disease, deep vein thrombosis, *in situ* thrombosis, pulmonary thromboembolism

Introduction

Behcet's disease is a type of vasculitis which presents with recurrent oral and genital aphthous ulceration, uveitis and skin lesions. Arteries and veins of all sizes are involved in Behcet's disease which is typified by venous and arterial occlusions and arterial aneurysms [1]. Unlike other types of vasculitis, venous system involvement is a common manifestation of Behcet's disease and occurs in 10% to 25% of patients [1]. Tascilar et al. [2] carried out retrospective analysis of 5970 patients with Behcet's disease and identified 882 (14.7%) patients as having vascular involvement. The incidence of vascular involvement has been shown to differ by ethnic group [3].

Vascular involvement is a rare manifestation of Behcet's disease in Azerbaijan and occurs in only 9% of patients [4]. Vascular involvement is more common in young males with a male-to-female ratio of approximately four to one [2]. The first vascular event occurs in the majority of patients (75%) within five years of disease onset [2]. The

most common type of venous system involvement is deep vein thrombosis (DVT) [2,3].

Despite the high incidence of DVT, pulmonary thromboembolism (PTE) is a very rare complication of Behcet's disease [1]. Its cause relates to the specific nature of thrombosis in Behcet's disease [1]. Venous thrombi are thought to develop primarily from the inflammation of the blood vessels [1]. Moreover, unlike classic thrombi, they adhere to the vessel walls, making embolization difficult [1]. Despite the low incidence of PTE in Behcet's disease, other types of pulmonary artery involvement, such as pulmonary artery aneurysm (PAA) and *in situ* pulmonary artery thrombosis (PAT) are relatively common. Due to the similarity of clinical and imaging findings of various forms of pulmonary artery involvement, it can be difficult to diagnose PTE in a patient with Behcet's disease. In this article, we report on a case of Behcet's disease with PTE. Written consent has been obtained from the patient for this report.

Case Report

A 44-year old male with known Behcet's disease was admitted to our hospital because of pleuritic chest pain and dyspnea in September 2015. Recurring painful oral ulcerations, bilateral panuveitis, superficial phlebitis and positive pathergy had led to a diagnosis of Behcet's disease 12 years earlier. He was followed in the Behcet's disease clinic of the Connective Tissue Diseases Research center (CTDRC) in Tabriz, Iran and was treated with prednisolone 30 mg/d, methotrexate 15 mg/week and a monthly pulse of cyclophosphamide because of refractory panuveitis. With this treatment, the uveitis was controlled and he had reported no oral aphthous ulceration or phlebitis in the succeeding two months.

The patient experienced lower left limb pain and swelling one week before admission. He developed sudden onset dyspnea, pleuritic chest pain and hemoptysis two days prior to admission. At this time, the patient had tachypnea and mild respiratory distress. His respiratory and heart rates were 26 and 112, respectively. The patient was afebrile with a blood pressure was 110/75 mmHg. Chest examination was normal. Lower left limb examination showed 2+ swelling and tenderness.

The laboratory data was as follows: leukocyte count: $4.5 \times 10^3/\mu\text{L}$ (62.1% neutrophils; 32% lymphocytes), hemoglobin: 12.7 mg/dL; erythrocyte sedimentation rate: 28

mm/h and C-reactive protein 6.7 mg/L (normal ≤ 10). Urea, creatinine, urine analysis, liver function tests and electrolytes were normal. Color Doppler ultrasonography showed subacute thrombosis in the popliteal vein of the lower left limb. The transthoracic cardiac echocardiography was normal. Chest computer tomography (CT) showed no lesions in the lung parenchyma and mediastina. CT angiography of the pulmonary arteries showed eccentric filling defects which formed acute angles with the vessel wall in the short and long axis in the inter-lobar arteries of both lungs with sub-segmental consolidation (Figure 1). The lung perfusion scan with 99 mTc showed multiple segmental and sub-segmental perfusion defects in both lungs which did not match the ventilation scan. A diagnosis of PTE was made and anticoagulation with enoxaparin and warfarin was started.

The tachypnea, chest pain and hemoptysis disappeared after three days and he was discharged after 10 days with warfarin 5 mg/d. Treatment with prednisolone 30 mg/d, methotrexate 15 mg/week and a monthly pulse of cyclophosphamide was continued. He was followed in the Behcet's disease clinic at CTDRC and, after control of the uveitis, the prednisolone dose was decreased to 7.5 mg/d. The second ventilation perfusion scan performed three months later showed complete resolution of the perfusion defects. His disease was in complete remission by eight months after discharge

Table 1. Reports of pulmonary thromboembolism in patients with Behcet's disease

Study	year	PTE cases
Behcet's disease complicated with thrombosis: A report of 93 Chinese cases	2014	15.1% (14/93 patients developed thrombosis) of the 766 patients with BD Among 153 patients with Behcet's disease according to the criteria of the International Study Group for Behcet's disease, seven (5 men and 2 women mean aged at 26.6 +/- 6 years) were diagnosed as having pulmonary embolism. This was inaugural in 3 cases; for 2 females, pulmonary embolism complicated pregnancy
Pulmonary embolism and Behcet's disease	2006	
Thrombolytic therapy in pulmonary embolism of Behcet's disease	1996	A patient with Behcet's disease who presented with deep vein thrombosis and pulmonary embolism

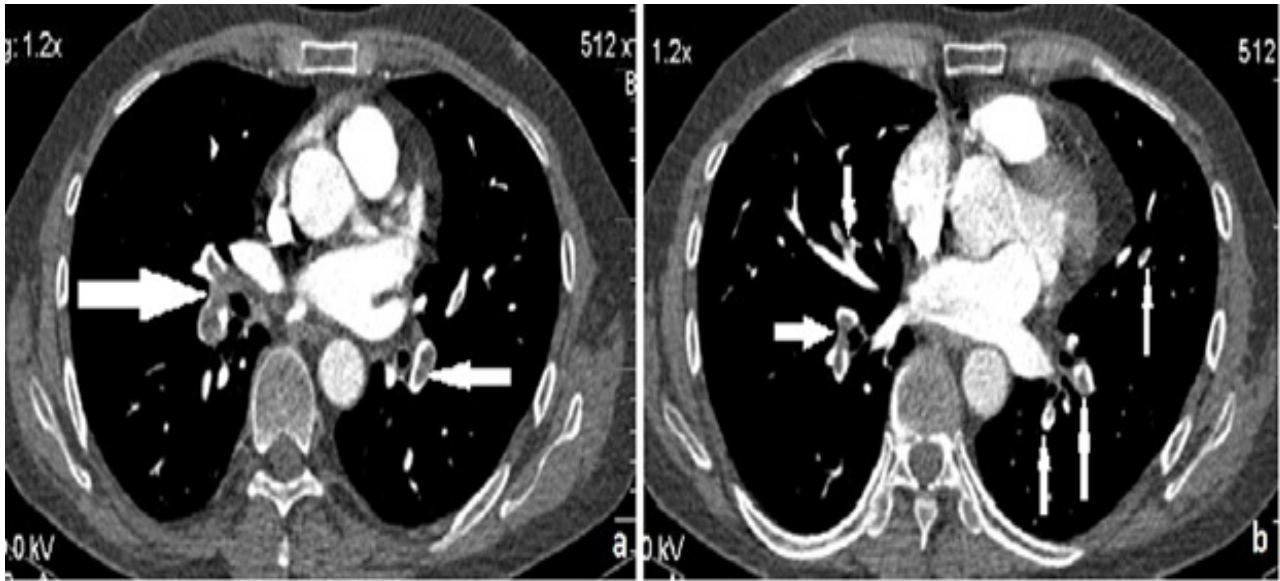


Figure 1. Thromboembolism in the: (a) right and; (b) left pulmonary artery branches (white arrows).

Discussion

Pulmonary involvement is not common in Behcet's disease, but is one of the main causes of mortality and morbidity in this disease [5]. Pulmonary vascular involvement such as PAA, *in situ* PAT, pulmonary hemorrhage, pulmonary infarction, PTE, arteriovenous shunt in the lung and aneurysmal fistula are the most common pulmonary disorders in Behcet's disease [3, 5, 6]. Pleural effusion, pneumonia, alveolitis, cavitary lesions, pulmonary obstructive airway disease and fibrosis are other forms of pulmonary involvement [3]. The pulmonary arteries are the second most-common sites of arterial involvement in Behcet's disease [3]. The most common form of pulmonary artery involvement in Behcet's disease is PAA and *in situ* PAT is less common [5].

Differentiation of the types of pulmonary artery involvement is very important because the mainstay of the treatment of PAA and PAT is aggressive immunosuppressive therapy [5]. Some case reports have shown a useful effect of anti-TNF agents in the management of resistant cases of pulmonary vasculitis [7, 8]. The use of anticoagulants by these patients is questionable, because the thrombi are generally organized [5] and anticoagulation of such patients may cause worsening of hemoptysis and increase mortality [5]. In cases of PTE, however, anticoagulation may be necessary [9].

It is not clear what percentage of vascular lung lesions in Behcet's disease are related to pulmonary emboli [2]. Thirty-three cases of PTE in Behcet's disease have been reported (Table 1) [5], but clinical data has not been reported in most of them. Cough, fever, hemoptysis, pleuritic chest pain and dyspnea are the main clinical manifestations of

PTE, *in situ* thrombosis and pulmonary artery aneurysms. Although angiography is the gold standard diagnostic method in vascular disease, it is invasive and has limitations for pulmonary vasculitis caused by Behcet's disease [9]. Newer imaging methods like CT angiography and MR angiography are less invasive and also permit physicians to evaluate lung parenchyma [9]. CT angiography can diagnose pulmonary artery aneurysms, but the angiographic findings of *in situ* thrombosis are very similar to PTE [10]. However, the shape of the filling defects in the CT angiography largely contribute to the differentiation of PTE from PAT. In the PTE, CT angiography shows multiple eccentric filling defects that form acute angles with the vessel wall [10]. Ventilation-perfusion scanning is very helpful to the diagnosis of PTE in the absence of cardiopulmonary disease. A scan suggesting a high probability of acute pulmonary embolism should be considered diagnostic [11]. However, interpretation of lung scintigraphy is questionable in Behcet's disease because, unlike classic PTE, pulmonary artery occlusion in Behcet's disease most often represents *in situ* thrombosis. A single mismatched defect on the ventilation/perfusion scintigraphy should not be diagnosed as PTE in a patient with Behcet's disease [5]. In addition, many case reports show PAA and perfusion defects on the lung scintigraphy [5].

Our patient developed dyspnea, pleuritic chest pain and hemoptysis in the lower limb five days after DVT. CT angiography of the pulmonary arteries showed eccentric filling defects which formed acute angles with the vessel wall in the inter-lobe arteries of both lungs with sub-segmental consolidation. The perfusion scan with multiple segmental and sub-segmental perfusion defects in the both lungs did not match the ventilation scan. These findings suggested

a high probability of PTE. The resolution of the perfusion defects in the second ventilation perfusion scan confirmed the diagnosis of PTE.

In conclusion, patients with BD may develop PTE. The diagnosis may be difficult due to the rarity of PTE in BD and nonspecific clinical manifestations; thus, a high degree of suspicion and appropriate imaging studies are essential for diagnosis. PTE can be differentiated from PAT through

observation of eccentric filling defects in the pulmonary arteries which form acute angles with the vessel wall in CT angiography and multiple segmental and sub-segmental perfusion defects which do not match the ventilation scan.

Conflict of interest

The authors declare no conflicts of interest.

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