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# Consider Behcet's disease in young patients with deep vein thrombosis

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# ABSTRACT

Behcet's disease is a multi-systemic and chronic inflammatory vasculitis of unknown etiology characterized by recurrent oral and genital ulcers, uveitis, arthritis, arterial aneurysms, venous thrombosis, skin lesions and GIS lesions. Although pulmonary artery aneurysms are rare, it is a critical condition due to high risk of rupture. Venous involvement of Behcet's disease primarily occurs in the lower extremities. In the presence of deep vein thrombosis(DVT) and pulmonary embolism, the mainstay of treatment in Behcet's disease is immunosuppressant therapy. Anticoagulants can be used only after initiation of immunosuppressant therapy and suppression of the disease. Anticoagulant therapy alone may lead to fatal hemoptysis. We report the case of a 24 year-old patient who presented to the emergency service with complaints of shortness of breath, general condition disorder and hemoptyhis while using warfarin for DVT and whose thoracic CT angiography showed pulmonary embolism and pulmonary artery aneurysm and diagnosed with Behcet's disease.

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#### 1. Background

Behcet's disease is a multisytemic and vasculitic disease of unknown etiology, which was described by Hulusi Behçet in 1937. Although it is reported from all over the world, Behcet's disease is more prevalent in Mediterranean countries like Turkey, Greece and Israel [1]. The main features of pulmonary involvement in Behcet's disease include arterial and venous thrombosis, pulmonary artery aneurysms, pulmonary infarction, recurrent pneumonia and pleurisy [2]. Life threatening pulmonary artery aneurysms may show regression with medical treatment [3]. Vascular involvement in Behcet's disease occurs in more than 40% of the cases, and it most common affects the lower extremities [4]. While these involvements are seen concomitantly, the treatment remains controversial.

A patient who was on warfarin for deep vein thrombosis (DVT) was presented for hemoptysis. His thoracic CT angiography showed pulmanory embolism accompanied by pulmonary artery aneurysm. He was clinically and radiologically diagnosed with Behcet's

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# 2. Case presentation

A 24 year-old male patient was presented to the emergency service with a complaint of hemoptysis. His body temperature was 36.9 °C; pulse rate was 76/min; respiratory rate was 14/min; arterial blood pressure was 110/60 mmHg; and he had normal breath sounds. The chest x-ray showed that peripheral consolidation in the right middle zone (Fig. 1). The investigations showed WBC 7600/ml, Hgb 12.8 gr/dl, and platelet count 224.000, and his biochemical findings were normal. D-dimer level was 2260, sedimentation was 48 mm/h and INR was 3.2. Rheumatoid factor was 46 IU/ml, and HLA B51 antigen was not present. Anti-nuclear antibodies, anti-double stranded DNA, cytoplasmic, and perinuclear types of anti-neutrophil cytoplasmic antibodies were negative. Pathergy skin test was not performed due to immediate initiation of steroid treatment. The patient received a diagnosis of DVT 2 months ago in an external center, and his treatment was initiated with warfarin. Thoracic CT angiography showed pulmonary embolism and pulmonary

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Case report





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Fig. 1. Chest X-ray showed infiltration in right middle zone, and right sinus was closed.

artery aneurysm (Fig. 2). Echocardiography revealed that the right-sided cardiac structures were larger than normal, and pulmonary artery pressure was 44 mmHg. His medical history of genital and oral ulcers, young age, presence of DVT and pulmonary artery aneursym clinically and radiologically suggested Behcet's disease. Without any prior diagnosis of Behcet's disease, the patient was admitted to the Chest Diseases Clinic. Treatment with coumadin was ended due to hemoptysis. He was initiated on treatment with prednisolone 1000 mg for three consecutive days. His CRP level decreased from 25 mg/L to 4 mg/L, and after development of hemopthysis, his therapy was switched to methylprednisolone 40 mg IV b.i.d. and azathioprine tablet 50 mg PO t.i.d. The lower extremity venous Doppler examination was repeated on the seventh day of his therapy due to complaint of pain, swelling and heat in his leg, and after demonstration of minimal recanalization of the left common femoral and popliteal vein with total thrombus, patient was started to be given enoxaparin Na 0.4 ml SC b.i.d. Hemopthysis did not recur after treatment with enoxaparine sodium. During control tests, Ddimer levels was reduced to 220, and pulmonary artery pressure was reduced to 28 mmHg on echocardiography. Uveitis was not detected during eye examination.

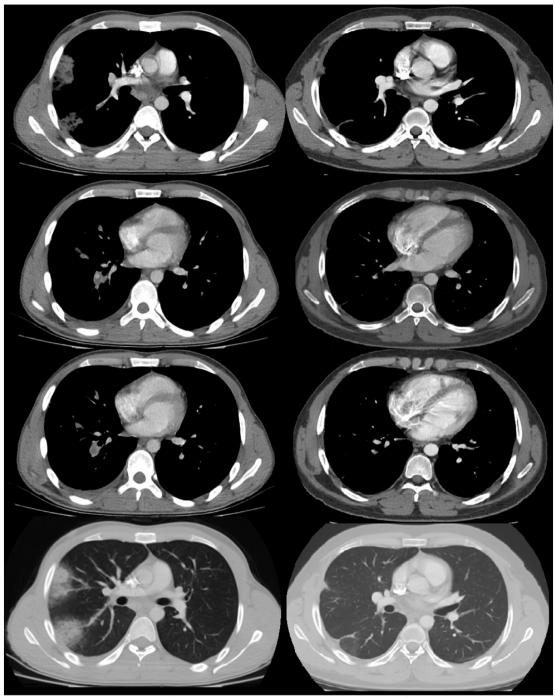
# 3. Discussion

The case of this patient showed us that young and male patients diagnosed with DVT should be examined for Behcet's disease before initiation of an anticoagulant therapy. It is to be considered that to initiate anticoagulant therapy before the exclusion of Behcet's Disease may lead to fatal hemoptysis in the presence of pulmonary artery aneursym. In Behcet's Disease, pulmonary embolism is not associated with DVT. Pulmonary embolism is associated with endothelial damage. The maintasy treatment is immunosuppresive therapy in the presence of pulmonary embolism.

Behcet's disease is a systemic vasculitis with vessel involvement of any type and size. Vessel involvement is the leading cause of mortality in Behcet's disease. The involvement can be both in the arterial and venous systems, however venous system involvement is more common. The prevalence of vessel involvement in Behcet's disease varies by country and region. The series of cases with more vessel involvement were reported from Morocco [5] (62.34%), while series of cases with less vessel involvement were from Japan [6] (7.7%) and Turkey [7] (8%). A common point of these studies was that vessel involvement of Behcet's disease was more common in males and they had a slower course in comparison to females. Moreover, pathergy positivity, superficial thrombophlebitis, erythema nodosum, neurological involvement and GIS involvement were significantly more common in patients with vesssel involvement, and those with eye involvement had less vessel involvement. The most common site is venous thrombosis which mainly occurs in the lower extremities. They occur in 25–30% of the patients. DVTs is common in the first years after onset of the disease. DVT has the potential to be more severe and bilaterally in Behcet's disease [8,9].

Although large vessel involvement varies by series, it has a prevalence of 5-10%. In Behcet's disease arterial system is involved around 5%, and it occurs in later years compared to the venous system involvement, but arterial manifestations are among the leading major causes of morbidity and mortality. Pulmonary artery aneurisym is the most common form of pulmonary involvement in patients with Behcet's disease. A literature review of many cases showed a pulmonary artery involvement of 3.9%. Pulmonary artery aneurysms may be complicated with rupture, resulting in pulmonary hemorrhage and hemoptysis leading to death [10]. The objective of treatment in Behcet's disease is the suppression of inflammation particularly in early years, and prevention of complications. An effective treatment is critical before irreversible organ damage. Use of systemic high dose steroids are common in active large vessel involvement. Cyclophosphamide therapy with an oral dose of 2-2.5 mg/kg/day or as weekly or monthly intravenous pulses of 500–100 mg is implemented in patients with large vessel involvement [11,12]. If thrombophlebitis develops during the course of Behcet's disease, role of heparin or oral anticoagulants is controversial. In a study comparing immunosupressive therapy and anticoagulant therapy in Behcet's disease with venous thrombosis, the patients were divided into three groups according to the treatment they received; immunosupressive therapy plus anticoagulation, immunosuppression alone, and anticoagulation alone. Although venous thrombosis recurrence was less common in the group receiving immunosupressive therapy plus anticoagulation, there was no statistically significant difference between the group receiving immunosupressive therapy alone [13]. Another approach is to screen each Behcet' disease patient with thrombosis for genetic markers (factor V Leiden, prothrombin gene, protein C, protein S, antithrombin and anticardiolipin antibody). Some authors believe that immunosupressive therapy is to be combined with anticoagulant therapy in Behcet's disease patients with presence of a marker facilitating thrombosis [14]. If warfarin is used as an anticoagulant, possible drug-drug interactions should be taken into consideration. In patients with Behcet' disease, azathioprine used for immunosupressive therapy may inhibit the anticoagulant effect of warfarin, which may result in development of resistance to warfarin [15]. Therefore, warfarin dose may need to be increased. As seen in our patient, if thrombophlebitis is accompanied by pulmonary artery aneurysm, hemoptysis may develop as a result of erosion of the pulmonary artery aneurysm into the lumen of a bronchus. Again, as seen in our patient, concomitant anticoagulant therapy that is initiated in Behcet's disease with undiagnosed pulmonary embolism may lead to fatal outcomes since it will contribute to aneurysmal hemorrhage. Studies have shown that despite





A: Images during the diagnosis

**B**: Images after the treatment.

Fig. 2. Thorax CT imaging, before and after treatment. A: Images during the diagnosis B: Images after the treatment.

medical treatment, hemoptysis occurs in 40% of patients with pulmonary artery aneurysms [16].

In conclusion, involvement of vessels in Behcet's disease is a subgroup of conditions which is more common in males with a high mortality. Endothelial dysfunction is the most important factor with an evidence of a role in the etiopathology of vessel involvement. Immunosupressive therapy (treatment with cyclophosphamide and corticosteroids) should be preferred for treatment of large vessel involvement. Anticoagulant therapy may be beneficial in Behcet's disease patients particularly with thrombosis if DVT persists after initiation of immunosuppressive therapy or provided that presence of aneurysm is excluded.

# **Conflict of interest**

The authors declare that they have no competing interests.

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