



## Case Report

# Endocarditis, Intra-cardiac Thrombus, and Pulmonary Artery Aneurysm in a Patient with Behcet's Syndrome

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### Abstract

Behçet's Syndrome (BS) is a chronic vasculitis of unknown etiology. Arterial involvement occurring in the pulmonary artery is associated with poor prognosis. It may cause pulmonary thrombus (PTE) and aneurysm (PAA) which may also lead to a rare complication, intracardiac thrombus. PAA and PTE can be complications of BS and are associated with high morbidity and mortality. A 30-year-old male patient had a fever of 38.4°C, recurrent oral-genital ulcers, shortness of breath, cough, and sputum. In this case report, medical history, clinical and laboratory examinations, radiography, echocardiography, and computer tomography imaging examinations were performed. PAA, PTE, intracardiac and left popliteal vein thrombosis, and infective endocarditis were present. The patient was diagnosed with BS according to the International Study Group criteria. Surgery was performed for intracardiac thrombus. Vegetation within the thrombus was demonstrated histopathologically. The patient's clinical condition and laboratory tests improved with intervention and medical treatments. The patient with BS, PAA, PTE, intracardiac thrombus, and infective endocarditis was successfully treated with pulmonary embolization, antibiotics, and systemic immunosuppression, despite its rarity, poor prognosis, and high morbidity and mortality rates.

**Keywords:** Aneurysm, Behcet, cardiac, endocarditis, fever, pulmonary, thrombus

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Behçet's Syndrome (BS) is a chronic vasculitis of unknown etiology.<sup>[1]</sup> BS was described in 1937 by Dr. Hulusi Behçet.<sup>[2]</sup> Its major diagnostic criteria include relapsing oral and genital ulcers, ocular and skin lesions, and a positive pathergy test. The minor diagnostic criteria for BS include arthropathy, neurologic symptoms, and cardiovascular and gastrointestinal lesions. The condition is mainly characterized by vasculitis, nonspecific inflammation, necrosis, aneurysm, thrombosis, and vascular occlusion and

may affect vessels of any type, location, and size.<sup>[3]</sup> The major vascular presentation of BS is venous thrombophlebitis, which is more often a poor prognostic marker and requires aggressive treatment.<sup>[4]</sup> Arterial involvement, though rare, can cause serious complications in the lungs, and it is also a poor prognostic marker. A rare coronary artery disease, as well as intracardiac thrombus, is usually associated with pulmonary artery involvement.<sup>[5]</sup> Pulmonary artery aneurysm (PAA), pulmonary thromboembolism (PTE), and

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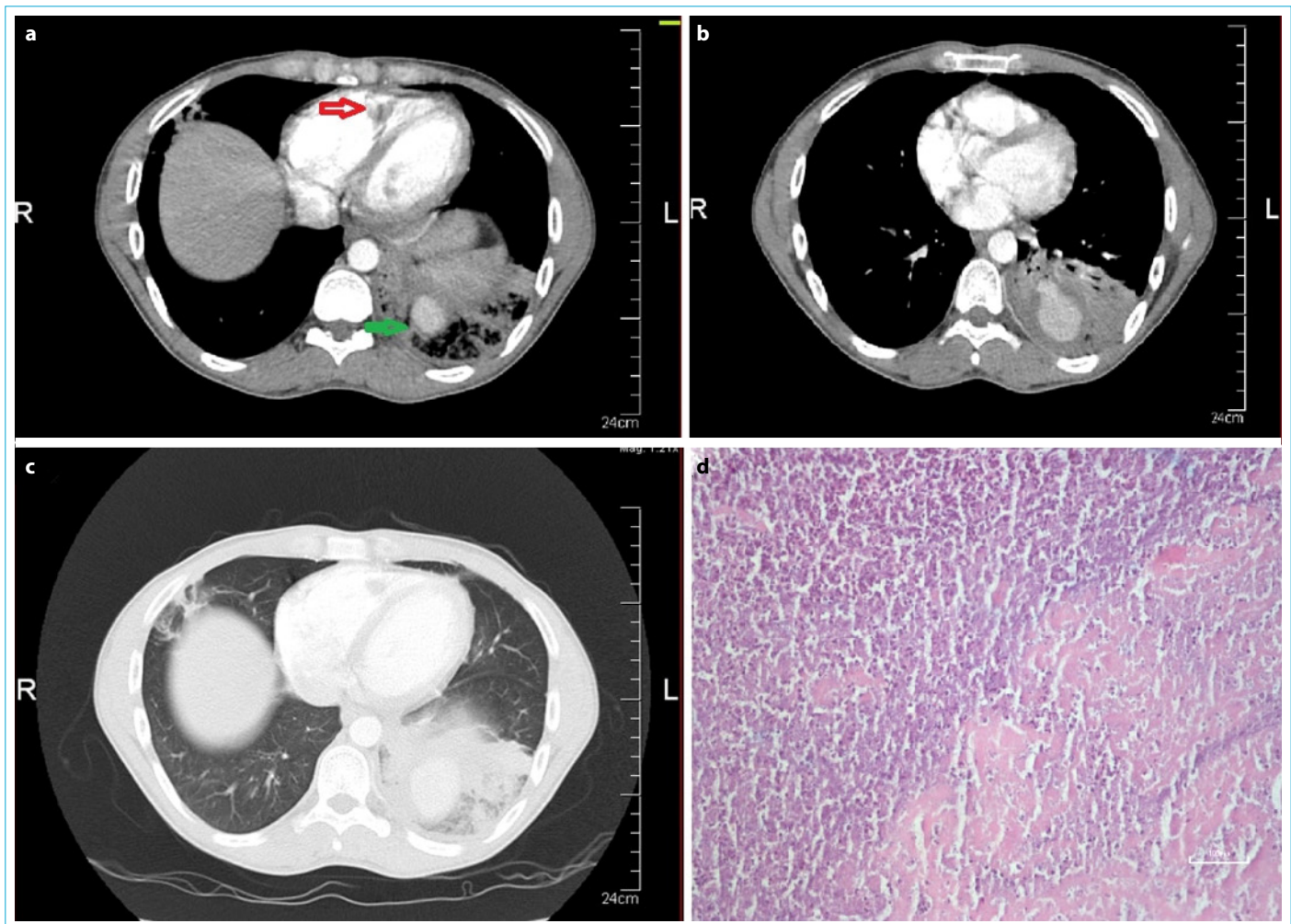
pulmonary infarction could be complications of BS. In this study, we present an exceptional BS patient with PAA, pulmonary thromboembolism (PTE), intracardiac thrombus, and infective endocarditis (IE).

## Case Report

A 30-year-old male was admitted to the infectious diseases outpatient clinic with complaints of cough with sputum and fever therefore, he was treated with an antibiotic. Although his cough and fever subsided, he was admitted to the pulmonology clinic due to severe chest pain, shortness of breath. Chest computer tomography (CT) revealed filling defects in the right peripheral pulmonary artery consistent with pulmonary embolism. The thrombus was also detected in the left popliteal vein. The patient was diagnosed with PTE and given heparin followed by warfarin therapy.

However, warfarin was discontinued due to hemoptysis. Since his body temperature was 39°C, iv ceftriaxone 2x1 gr, and clarithromycin 2x500 mg were started.

In the control chest CT, soft tissue density (STD) thrombi were observed in the right ventricle. STDs compatible with channeled thrombi were observed in segmental branches of the pulmonary artery (Fig. 1). In the left lower lobe, there was a 35x35 mm lobulated lesion showing significant enhancement, and lesion consolidation with air bronchograms was detected in parts of the interlobar pulmonary artery (Fig. 1). At the apical level of the right lower lobe of the lung, 12 mm of an aneurysmal pulmonary artery segment filled with a thrombus was observed. Pulmonary arteriography revealed extravasation consistent with a pseudoaneurysm, localized at the basal segment of the left lung, with filling from the posterior medial branch of the



**Figure 1.** (a, b) Contrast dynamic chest tomography (mediastinal window). Red arrow; Right ventricular thrombus image. Green arrow; Left Lung, Soft tissue densities compatible with canalized thrombus in places within the pulmonary arteries. (c) Dynamic Chest Tomography (Parenchyma Window); A 35x35 mm lesion with a lobulated contour that continues with the interlobar pulmonary artery at the level of the left lower lobe and a consolidation area with air bronchograms around the lesion. (d) Vegetation composed of fibrin, inflammatory cells, and bacterial clusters. (HE X10)

left pulmonary artery. Two major vascular branches feeding the aneurysm were embolized using coils.

After that, the patient was transferred to the rheumatology clinic with a preliminary diagnosis of BS. The patient had a history of relapsing oral and genital ulcers. On physical examination, the patient's temperature was 38.4°C, there was no uveitis, and the pathergy test was negative. There were papulopustular rashes on the arms and back, as well as an oral ulcer and a scrotal ulcer scar. Laboratory investigation showed that serological tests, sputum test for acid-fast bacilli (AFB) smear and culture, and five blood cultures were all negative. The laboratory tests are given in the Table 1. The patient was diagnosed with BS according to the International Study Group criteria.

In the second control chest CT, a mild thrombus was detected in the right ventricle. On the transthoracic echocardiography (TTE), a 22x12 mm mass attached to the apex was observed in the right ventricle. The patient's fever persisted, and his drugs were changed to iv vancomycin 2x1 gr and gentamicin 3x80 mg. Transesophageal echocardiography (TEE) revealed a 35x15 mm mass attached to the apex of the

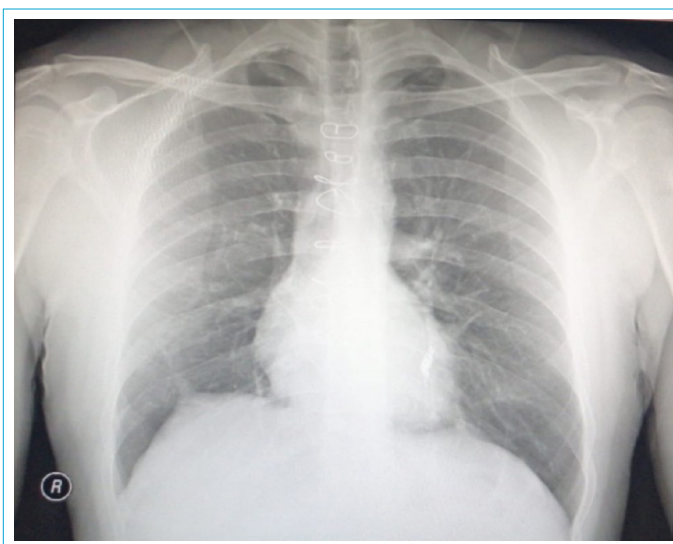
right ventricle and a mass lesion with cystic appearances in STDs (Video 1). Heparin was given and one week later control TEE was initiated. The size of the mass attached to the right ventricle apex was not changed. In the Council of Cardiology and Cardiovascular Surgery, because of the mass of the size, the recommendation was to proceed with surgery. The mass lesion was resected by cardiovascular surgery. The pathology of the mass showed myocardial and endocardial tissue characterized by hypertrophy and mild steatosis, with dense fibrin, inflammatory cells, and bacterial clusters in the focal area. The findings were consistent with vegetation (Fig. 1D). On the third day of antibiotic therapy, the fever and constitutional symptoms improved.

The patient's IE therapy was discontinued after 6 weeks. Consequently, drug therapy with oral colchicine (1mg/day), prednisolone (1mg/kg/day), and cyclophosphamide (600 mg/m<sup>2</sup> iv monthly) was initiated. Chest CT with iv contrast was performed after 8 cycles of cyclophosphamide treatment for the patient. The mediastinal structures were normal and there was no filling defect in the pulmonary artery or its branches. Subpleural sequelae fibrotic recessions in the bilateral lung parenchyma and 1 cm soft tissue density in the lower lobe of the right lung were observed. This lesion was evaluated as vasculitic sequela parenchymal changes. The control chest x-ray (radiograph) is shown in Figure 2. Acute phase responses returned to normal (CRP: 0.49 mg/dl (0-0.8). Complete blood count, and other laboratory tests were within normal limits. The patient's treatment was completed with 12 cycles of cyclophosphamide. Prednisone was tapered and discontinued. The maintenance treatment was azathioprine 100 mg/day and colchicine 1 mg/day. The patient's clinical and laboratory parameters improved.

**Table 1.** Laboratory tests

Parameters	Results tests	Normal range
WBC	11.900/mm <sup>3</sup>	4.3-10.3/mm <sup>3</sup>
Hgb	8.3gr/dl	13.6-17.2 gr/dl
Platelet	143.000/mm <sup>3</sup>	156-373/mm <sup>3</sup>
Procalcitonin	4.57 ng/mL	0-0.5ng/mL
Total protein	5.6 gr/dL	6.6-8.7gr/dL
Albumin	2.7 gr/dL	3.4-4.8gr/dL
AST	22 IU/L	<31 IU/L
ALT	18 IU/L	<31 IU/L
BUN	30 mg/dL	5-20mg/dL
Creatinin	1.1 mg/dL	0.8-1.2mg/dL
ESR	74 mm/Hour	5-15
CRP	87 mg/L	0-8 mg/L
aPTT	14.5 sec	10.5-13.2 sec
INR	1.26	0.85-1.2
C3	0.49 g/L	0.89-1.87 g/L
C4	0.114 g/L	0.165-0.380g/L
ANA	Negative	Negative
Anti-ds DNA	Negative	Negative
ANCA	Negative	Negative
ACA	Negative	Negative

Antinuclear antibodies, anti-dsDNA; Anti-double Stranded DNA Antibodies, ANCA; Antineutrophil cytoplasmic antibodies, ACA;Anticardiolipin antibodies AST;Aspartate Aminotransferase, ALT:Alanine Aminotransferase, aPTT; Activated partial thromboplastin time, BUN; blood urea nitrogen, C3\*C4: complement, CRP; C-reactive protein, ESR: Erythrocyte sedimentation rate INR; International Normalization Rate, WBC; white blood cell count.



**Figure 2.** Control X-ray chest radiograph.

## Discussion

BS vascular involvement is seen in more than 25% of the cases.<sup>[6]</sup> Venous involvements are more common than arterial ones. Deep vein thrombosis in the lower extremities constitutes 60-80% of vascular lesions. Since the etiopathogenesis of BS is uncertain, genetic predisposition and environmental factors may play a role in its pathophysiology, as observed in most auto-inflammatory and autoimmune diseases. The mechanism of thrombus formation in BS is uncertain. It has been argued that endothelial cell injury or dysfunction with or without hypofibrinolysis contributes to the pathogenesis of BS, while neutrophilic inflammation plays a role in BS vascular events.<sup>[5]</sup> The fibrinogen, thrombin, factor Xa, and factor VIIa contribute to the inflammatory cascade in thrombosis pathogenesis.

The arterial pathology of BS constitutes both aneurysmal and occlusive lesions. The prevalence of arterial involvement was found to be 1%. PAA is generally formed in the main pulmonary artery, and its prevalence has been reported to be between 0.16% and 1.1%.<sup>[7]</sup> It mainly affects young adults (mean age of diagnosis is 30 years), is more severe in males, and is the most common pulmonary involvement of BS with pulmonary vasculitis.<sup>[8]</sup> The risk of rupture of a major aneurysm is very high, and the risk of mortality is about 60%. PTE is a rare pulmonary manifestation of BS. The mechanism of thrombus formation is related to pulmonary vasculitis and is an in situ thrombus caused by recurrent inflammation in the vessel wall. Unlike classical thrombus, it strongly adheres to the vessels and complicates embolization. Thrombi may be mistaken for embolism. PTE is one of the major causes of morbidity and death in patients with BS.<sup>[9]</sup> Aneurysm rupture in lung tissues may lead to pulmonary bleeding and heal with fibrosis. Hemoptysis is the most common finding of PAA. Chest pain, shortness of breath, and fever are also seen in PAA.

Mostly in the case of reports, fever, nonspecific complaints, and high acute phase reactant response are observed with thrombosis. The patient's five blood cultures were all negative. Blood culture negativity was attributed to long-term systemic antibiotic therapy at the beginning of treatment.

Cardiac involvement is seen in less than 5% of patients and has a poor prognosis in BS. Endomyocardial fibrosis or myocarditis is very rare, however, rare cardiac conditions, including intracardiac thrombus or coronary artery aneurysm, are associated with lung involvement. The coexistence of PAA and intracardiac thrombus is even rarer. Em-mungil et al.<sup>[10]</sup> reported 22 cases of intracardiac thrombus and only one case with intracardiac thrombus and massive pulmonary arteritis died. Cardiac findings of BS include

pancarditis, acute myocardial infarction, valvular disease, and transmission system disorders. Whether endocarditis or endomyocardial fibrosis leads to thrombus formation is still unknown. We suspect an intracardiac thrombus formed on an endocarditis layer. The histopathological findings of fibrin and bacteria clusters support our thesis. In a study by Kechida et al.<sup>[11]</sup> PTE, PAA, and intracardiac thrombus were 14.1%, 9.4%, and 3.1%, respectively.

Immunosuppressive therapies are required to prevent and inhibit vascular attacks. Steroids in combination with azathioprine or cyclophosphamide are found to be efficient in the treatment of PAA. In some cases, anticoagulant or thrombolytic agents are used in intracardiac thrombi therapy. It has been shown in a retrospective study that anticoagulants added to immunosuppressive therapy do not change the relapse rate in vascular BS.<sup>[12]</sup> European League Against Rheumatism (EULAR) recommends the use of only immunosuppressive therapy in BS with vascular involvement. It does not recommend antiplatelet, anticoagulant, or antifibrinolytic therapy.<sup>[13]</sup> In patients with major vascular involvement in BS refractory to conventional treatments, anti-TNF alpha drugs are recommended, and the response rate is reported to be 89%.<sup>[14]</sup>

In this very rare case presentation of BS with PAA and PTE, a mass consistent with a thrombus was detected in the right ventricle. Conditions that are associated with fever, such as IE, should be considered in the follow-up of BS patients in clinical practice. Thus, a patient with BS and PAA, PTE, intracardiac thrombus, and IE was successfully treated with pulmonary embolization, antibiotics, surgical resection of right ventricle mass, and systemic immunosuppression despite the rarity, poor prognosis, high morbidity, and high mortality associated with this form of the disease.

## Disclosures

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[Video 1. Intra-cardiac thrombus attached to the apex of the right ventricle in the TEE.](#)

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