

# Acute coronary syndrome in Behcet's disease caused by a coronary artery aneurysm and thrombosis

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## Abstract

Behcet's disease (BD) is a multisystemic vasculitis that can involve vessels of all sizes and is characterized by recurrent oral and genital ulcers with variable manifestations affecting the skin, eyes, and central nervous and musculoskeletal systems. Vascular involvement in BD is reported to be up to 40% in different series. The abdominal and thoracic aorta and pulmonary and femoral arteries are the most commonly involved arteries. However coronary arteries are rarely affected. Herein, we present a 29-year-old man who was consulted with progressive severe chest pain of 3 days in duration to our clinic. The patient was diagnosed with BD with mucocutaneous symptoms and a positive pathergy test 1 year ago and was in clinical remission for the last 6 months. At the first evaluation in the emergency department, the patient's vital signs were stable, whereas he had elevated troponin T levels with a normal electrocardiogram and hypokinetic areas in the apex of the heart in the echocardiography. Conventional and computed tomography coronary angiography revealed aneurysms and intramural thrombosis in the left anterior descending and right coronary arteries. Although ischemic symptoms and signs improved with anticoagulant and antiaggregant therapies, coronary aneurysms were observed to increase in size. Immunosuppressive (IS) treatment was started with pulse intravenous corticosteroids and cyclophosphamide. Because of the high re-stenosis risk, stents were not applied to the affected vessels during the acute thrombosis period. During routine investigations, an in situ pulmonary thrombosis was also detected bilaterally in the peripheral pulmonary arteries. In conclusion, coronary artery aneurysm is a rare and poor prognostic manifestation of BD. The treatment protocol for these aneurysms is not well clarified. IS therapies are definitely indicated, but the role of anticoagulants and invasive vascular interventions is controversial.

**Key words:** Coronary aneurysm, Behcet's disease, acute coronary syndrome, cardiac involvement

## Introduction

Behcet's disease (BD) is a multi-systemic chronic inflammatory disease characterized by mucocutaneous, articular, vascular, ocular, gastrointestinal, and neurologic manifestations. Vascular involvement in BD is reported to be between 8%-39% in different series and can involve both arteries and veins of any diameter (1-3). Arterial involvement in BD is far less common than venous involvement (20% versus 80%) (1-3). The frequently involved major arteries are the abdominal and thoracic aorta and pulmonary, iliac, and femoral arteries. However, coronary arteries are rarely affected and only reported as case presentations in the literature. We report a young male BD patient with acute coronary syndrome caused by coronary artery aneurysms and thrombosis.

## Case Presentation

A 29-year-old male presented to the emergency department with progressive severe retrosternal chest pain of 3 days in duration. The patient was diagnosed with BD with recurrent oral and genital ulcers, erythema nodosum, and pathergy positivity 1 year ago and was in clinical remission under colchicine treatment. On admission, besides tachycardia, the systemic physical examination was completely normal. No active mucocutaneous findings regarding BD were detected. Electrocardiography revealed sinus tachycardia without any signs of cardiac ischemia or infarction. However, cardiac biomarkers (troponin-I, creatinine kinase-MB) were elevated over 3 times the normal level. Acute phase reactants were elevated as well (erythrocyte sedimentation rate: 72 mm/h, C-reactive protein: 24 mg/L). Other serum biochemical evaluations, including lipid profile, were normal. Echocardiography showed apical hypokinesia. Coronary angiography revealed partially thrombosed aneurysms in the left anterior descending artery (LAD) and right coronary artery (RCA). In the cardiology ward, the patient was treated with antiaggregant and anticoagulant agents, including acetylsalicylic acid, clopidogrel, tirofiban, and enoxaparin. Chest pain improved and cardiac biomarkers normalized; however, the patient experienced gastrointestinal bleeding. Furthermore, aneurysm diameters were found to double in the control coronary angiography within 2 weeks. Thereafter, a rheumatology consultation was requested. The patient was evaluated for other BD manifestations. No signs of deep vein thrombosis were present in the lower extremity Doppler ultrasound, and the ophthal-



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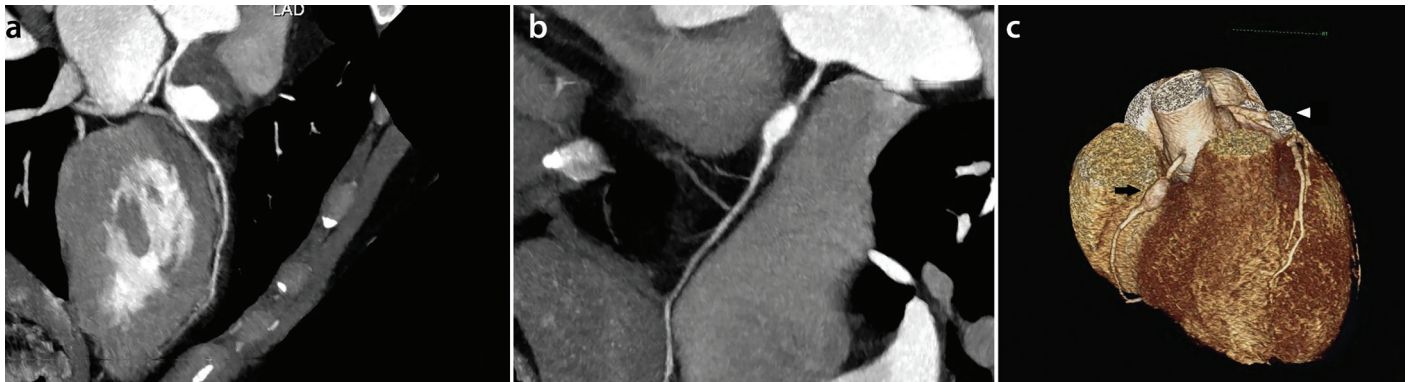
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**Figure 1. a-c.** Aneurysms at left coronary artery (a), right coronary artery (b), in three dimensional view (c), arrow and arrow head indicate RCA and LAD respectively



mologic examination did not detect any sign of acute or previous uveitis. Pulmonary computed tomography (CT) angiography revealed bilateral thrombosis in subsegmental branches of the pulmonary arteries, whereas pulmonary artery diameter was normal. Coronary CT angiography demonstrated a 24-mm aneurysm in the LAD and a 13-mm aneurysm in the RCA (Figure 1). The patient was diagnosed with acute coronary syndrome caused by coronary artery aneurysm and thrombosis due to BD. Methylprednisolone 1 mg/kg/day and intravenous (iv) cyclophosphamide 1 g/month were initiated as the immunosuppressive (IS) treatment. Surgical or endovascular interventions were not considered because of the increased risk of acute complications and re-stenosis in the acute thrombosis state without IS treatment. As the patient had a history of gastrointestinal (GI) bleeding, upper and lower GI endoscopy was performed. No signs of ulcer or entero-Behçet were detected. Acetylsalicylic acid was re-started without anticoagulant therapy. In the clinical course of the patient, chest pain did not reoccur. IS treatment with methylprednisolone (with gradual dose tapering) and 6 cycles of iv cyclophosphamide was planned. After the third cycle of cyclophosphamide, the coronary artery aneurysm diameter was planned to be checked with coronary CT angiography. Surgical intervention will be considered if aneurysms or ischemia persists.

## Discussion

Vascular involvement is a common complication of BD, affecting up to 40% patients and accounting for the major cause of the mortality. Venous involvement predominates over arterial involvement, as arterial involvement makes up only 15%-20% of vascular complications (1-3). Overall, arterial complications have been around 5% in most reports (3). Although any size of an artery may be affected in BD, resulting in either aneurysms or occlusions, coronary artery involvement is a very rare manifestation of BD. In an autopsy and clinical series,

its prevalence was reported to be 0.5% and 1%, respectively (4, 5). Most of the literature about coronary artery aneurysms of BD is composed of a few case reports. These data revealed that a coronary artery aneurysm often presents itself after the diagnosis of BD, as in our case, though occasionally, it may be the first manifestation (6, 7). In addition to spontaneous development, coronary artery aneurysms were reported to develop after coronary angiography or other manipulations, similar to the pathergy phenomenon (7). Like the more severe manifestations of BD, coronary artery involvement mostly occurs in men. Coronary artery aneurysm is a very rare condition in an otherwise healthy young male. Its concomitance with Kawasaki disease, Takayasu arteritis, and atherosclerosis has been described. Although our patient's diagnosis of BD was undoubted, atherosclerosis as a causative reason should be kept in mind, especially in elderly patients with cardiovascular risk factors, as we recently reported in an elderly female patient with a femoral artery aneurysm (8). Interestingly, BD, in contrast to other inflammatory rheumatic diseases, such as rheumatoid arthritis and systemic lupus erythematosus, is not associated with accelerated atherosclerosis (9). Therefore, in young BD patients without strong traditional cardiovascular risk factors but presenting with cardiac symptoms, vascular or cardiac involvement should be considered initially. As our patient had no traditional cardiovascular risk factors, the coronary aneurysm was attributed to BD. Histopathologic examination of vessels is not always possible but differs from atherosclerotic aneurysms. In BD, aneurysms are caused by inflammatory obliterative endarteritis of vaso-vasorum and fibrotic changes in the media layer of the artery (10).

Pulmonary artery thrombosis is a more frequent cause of chest pain in BD. In our case, pulmonary thrombosis might have aggravated the existing cardiac ischemia pain; however, its contribution to cardiac biomarker elevation is

debatable, as the pulmonary thrombosis was in the subsegmental branches and no right ventricular strain findings were detected in the echocardiography. Besides these, less frequent cardiac manifestations should also be considered in BD patients with chest pain. Cardiac manifestations in BD include pericarditis, myocarditis, valvular incompetence, endocarditis, intracardiac thrombus, endomyocardial fibrosis, coronary arteritis, coronary artery, and sinus of Valsalva aneurysms. In a French series of 806 BD patients, cardiac involvement was observed in 52 patients (6%), and the most frequent cardiac finding was pericardial effusion ( $n=20$ , 38.5%), whereas coronary arteritis or aneurysm-related myocardial infarction ( $n=9$ , 17.3%) was observed to be more rare (5). In the same series, patients with cardiac involvement had significantly lower 5-year survival rates compared to those without cardiac involvement (83.6% vs 95.8%). Treatment regimens with oral anticoagulants, IS, and colchicine were found to be factors associated with complete remission of cardiac involvement (5). Immunosuppression obviously plays a significant role in the treatment of vascular involvement in BD; however, there is no evidence-based treatment protocol for BD-related coronary aneurysm. The duration of IS and follow-up modality of coronary aneurysms are also uncertain. Successful results have been reported in various case reports with a combination of corticosteroids with methotrexate, mycophenolate mofetil, azathioprine, or infliximab. Furthermore, the role of anticoagulation, endovascular, or surgical interventions is still controversial. Without IS treatment, the risk of recurrence and complications in these procedures was reported to be high. In our case, though the initial sole antiaggregant and anticoagulant treatments (without IS) contributed to the recanalization of the coronary thrombosis and improvement of cardiac ischemia, they could not prevent the increase in the size of the aneurysm. Under sufficient IS treatment, surgery or endovascular coil embolization may

increase the success of therapy in patients with persistent ischemia and a high risk of rupture.

In conclusion, although coronary artery aneurysm, as a cardiac involvement, is a very rare manifestation of BD, it should be kept in mind in young BD patients presenting with chest pain. As the presence of cardiac involvement worsens the prognosis of BD, prompt diagnosis and initiation of IS treatment are of paramount importance.

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