

Behçet Disease Presenting as Acute Myocardial Infarction

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Although acute myocardial infarction usually results from coronary atherosclerosis, several other etiologies should also be considered, especially in young adults without significant atherosclerotic risk factors. Myocardial infarction is rare among patients with Behçet's disease but should be considered in the appropriate context.

Behçet's disease is a systemic disease of unknown etiology. Genetic and immunological properties of Behçet's disease, such as Class I major histocompatibility complex association and the presence of autoantibodies suggest autoimmunity, but the clinical features indicate auto-inflammatory disease. Thus, Behçet's disease has both autoimmune and auto-inflammatory components [1].

Behçet's disease is characterized by recurrent, aphthous ulcers, genital ulcers, ocular findings, and mucocutaneous manifestations. It also affects the central nervous system and gastrointestinal tract and causes large joint arthropathies. Thrombosis of large vessels occurs in about 7–40% of patients [1].

The vascular lesions are most often venous, manifested by disorders such as superficial thrombophlebitis and deep vein thrombosis. Arterial involvement is relatively rare but carries a greater risk of death. Major arteries are affected in 2–17% of patients.

We report a case of a 21-year-old man in whom Behçet's disease was di-

agnosed after an episode of myocardial infarction with an atherothrombotic lesion of the proximal portion of the left anterior descending artery.

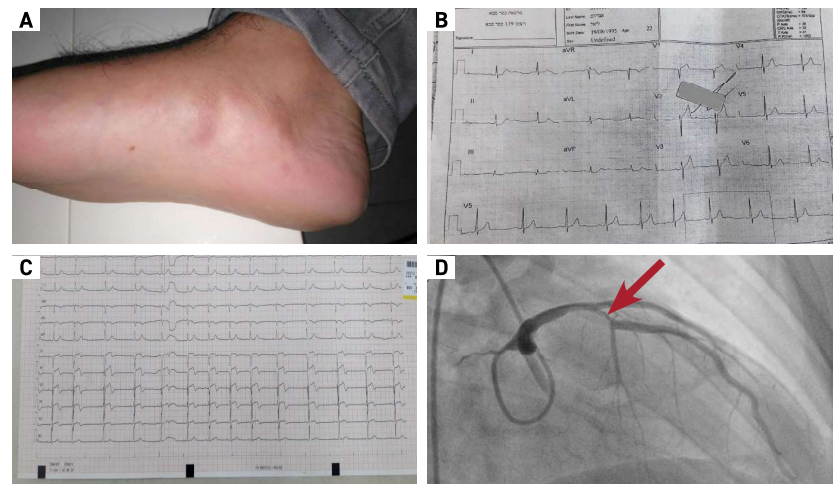
PATIENT DESCRIPTION

A 21-year-old man of Indian–Kurdish origin was admitted to the emergency department in August 2017 complaining of acute, constrictive chest pain that had started 2 days previously. The pain was radiating to both hands. He also had shortness of breath, diaphoresis, and nausea without vomiting. His medical history included two previous episodes of superficial venous thrombosis in both legs and one of erythema nodosum [Figure 1A]. The patient provided permission prior to inclusion in the study.

The patient had been examined by a physician 2 days prior to hospital admission due to chest pain. Electrocardiogram demonstrated ST elevation in the chest leads, with reciprocal depression in the inferior leads [Figure 1B]. He was misdiagnosed with pericarditis, referred to a cardiologist and naproxen was initiated. Two days later, the patient was reexamined by a cardiologist. The second electrocardiogram showed bi-phasic T waves in the chest leads. He was then referred to the emergency department.

On physical examination, blood pressure was 100/60 mmHg, and heart rate 87 beats per minute. Cardiac sounds were normal with no pathological pulmonary findings. Other organ systems were normal.

Figure 1. Patient presenting to the emergency department complaining of acute, constrictive chest pain [A] previous erythema nodosum, [B] electrocardiogram at the acute phase of myocardial infarction, elevated ST segment in anterior leads, [C] electrocardiogram of the patient on admission to the emergency department, [D] coronary arteriography showing significant stenosis at the proximal portion of left anterior descending coronary artery



Electrocardiogram revealed normal sinus rhythm with biphasic T waves in leads V1–V4 and Q waves on leads V1 and V2 [Figure 1C]. This presentation was consistent with the diagnosis of anterolateral wall infarction. Troponin levels were elevated up to 3000 ng/L (normal range 0–14).

A percutaneous coronary intervention (PCI) was performed, showing 75–90% stenosis on the proximal left anterior descending artery [Figure 1D]. An onyx drug eluting stent (DES; Medtronic Corp., Dublin, Ireland) was inserted in the proximal left anterior descending artery. After PCI, significant bleeding from the femoral artery was noted, which was stopped by compression.

An echocardiogram 24 hours after the PCI showed moderate, left ventricular systolic dysfunction, anteroseptal and anterior akinesia of the entire length including the apex, in addition to 2/3 distal septal akinesia and distal posterior and inferior akinesia, including the apex.

After the procedure, the patient was interviewed again and reported that there was no family history of coronary artery disease or any personal prior symptoms of other atherosclerotic disease. He had no history of drug abuse, smoking, or dyslipidemia. He was diagnosed with erythema nodosum in 2013 and had episodes of superficial venous thrombophlebitis in 2011 and 2015. Immunological tests in the past ruled out antiphospholipid antibodies, systemic lupus erythematosus, factor V Leiden, dependent anticardiolipin antibody and lupus anticoagulant. Antinuclear antibodies were negative.

The patient denied having genital ulcers, diarrhea, or visual disturbance, but he reported recurrent aphthous ulcerations every 7 to 8 months. Thus, after detailed anamnesis, in accordance with the International Criteria for Behçet's disease [2] and based on oral ulcerations, erythema nodosum, and a history of two episodes of superficial venous thrombophlebitis, Behçet's disease was diagnosed.

During hospitalization and after PCI, he was medically stable, without

chest pain. Pulses were palpable. Blood tests were stable. He also underwent an ophthalmological examination, with no evidence of ocular pathology. On chest computed tomography (CT) angiogram, there was no evidence of dissection of the ascending aorta or pulmonary embolism.

Based on the arterial involvement, the patient was considered to have severe Behçet's disease. Therefore, he was treated with oral corticosteroids and azathioprine, in addition to conventional treatment for myocardial infarction.

Four months after discharge, the patient had a normal total body CT angiogram, with no evidence of aneurysms.

COMMENT

Vascular involvement, which occurs in 40% of patients with Behçet's disease, worsens the prognosis. It is often found in young men during the first years following disease onset. Venous manifestations are the most frequent vascular involvement, affecting 14% to 40% of patients with the disease, of which superficial and deep, lower limb thromboses are the most frequent. Arterial involvement occurs in 2–17% of patients. Aneurysms and occlusions/stenosis are less frequent than are venous lesions. However, they are considered severe complications and are associated with increased morbidity and mortality [3].

Cardiac involvement (seen in 6% of patients) includes pericarditis (in 38.5%), intraventricular thrombosis (right ventricle and atrium), regurgitant valvular heart disease, coronary artery aneurysms, myocarditis, endocarditis (in 26.9%), and myocardial infarction (in 17.3%). Myocardial infarction is the most severe cardiac complication and 70% involve the left anterior descending artery [3].

A case series reporting cardiac lesions associated with Behçet's disease from 1990 to 2010 [4], showed that 86.5% of patients with cardiac involvement were men, as compared to 64.9% of Behçet's disease without cardiac lesions ($P < 0.01$), with a mean age at diagnosis of 29.3 years. In addition,

those with cardiac lesions had more arterial (42.3% vs. 11.1%, $P < 0.01$) and venous lesions (59.6% vs. 35.8%, $P < 0.01$), respectively, compared to those without cardiac manifestations.

The patient described here had similar parameters, including infarction of the left coronary system at a young age. He also had previous episodes of aphthous ulcerations and venous involvement, which have been reported in 100% and 60% of cases, respectively, with cardiac involvement [4].

Behçet's disease includes occlusive or more commonly, aneurismal lesions. Occlusive and stenotic lesions can involve the pulmonary, femoral, popliteal, subclavian, and carotid arteries. Coronary arteries are rarely involved, although stenosis, thrombosis, and pseudoaneurysms have been reported. Thrombosis can be due to vasculitis and hypercoagulability. Vasculitis in Behçet's disease usually involves all layers of a vessel. It is characterized by the presence of lymphocytic infiltrates during the acute phase. Fibrosis and scarring develop at later stages [5].

The hypercoagulability seen during Behçet's disease is thought to be due to inhibition of fibrinolysis and to increased platelet aggregation. This increased aggregation is thought to be related to endothelial dysfunction, which leads to increased production of von Willebrand factor and decreased levels of prostacyclin. Increased production of fibrinogen and factor VIII might be additional etiological factors explaining hypercoagulability [5].

The prognosis of patients with cardiac manifestations is poor, but anticoagulation, immunosuppressant agents, and colchicine seem to improve the outcomes of these patients. Our patient was treated with corticosteroids and azathioprine and then with azathioprine and methotrexate. Under this regimen, liver enzymes became elevated. Treatment was changed to anti-tumor necrosis factor: fully humanized antibody therapy. At the time of this report, he had remained stable for 28 months since the myocardial infarction with follow-up every 6 months.

CONCLUSIONS

Physicians should be aware that Behçet's disease symptoms do not necessarily appear concurrently. Therefore, they should explore the patient's history thoroughly to determine a diagnosis. We emphasize that it is important to ask "why?" three times when young patients present with vascular manifestations such as thrombophlebitis and signs of myocardial infarction.

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Capsule

Metastasis: a matter of translation?

Solid tumors shed a small number of cancer cells into the bloodstream, some of which are believed to contribute to metastasis. The molecular features that confer these circulating tumor cells (CTCs) with metastatic potential are poorly understood. **Ebright** and colleagues studied CTCs from breast cancer patients and found that cells with increased expression levels of certain ribosomal proteins

and regulators of translation had greater metastatic capacity in a mouse model. Consistent with this finding, patients with higher levels of this subset of CTCs tended to have a poorer prognosis.

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 Eitan Israeli

Capsule

Knocking down neurodegeneration

Antisense oligonucleotides (ASOs) target RNAs to prevent the production of an encoded protein. This therapy can therefore be used to suppress the expression of pathogenic proteins. In a perspective, **Leavitt** and **Tabrizi** discussed the progress in developing and testing ASOs in patients with Huntington's disease. They also discuss the development of ASOs for potential application to

other neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease. These drugs are promising therapeutics for the treatment of neurological diseases as well as non-neurological conditions such as cancer.

Science 2020; 367: 1428
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Capsule

Tracking growth dynamics

Very few screening tests have increased the survival of individuals diagnosed with cancer. In a perspective, **Pashayan** and **Pharoah** discussed the importance of understanding tumor growth dynamics, especially when metastases are seeded from the primary tumor. Metastasis is the major cause of mortality from cancer, so the ability to detect tumors before metastases arise is an important challenge. In particular, many tests based on imaging can

only detect tumors of a certain size and others cannot discriminate which will progress, potentially causing harm. It is important to develop screening tests that can account for growth dynamics to identify individuals with tumors that are most likely to spread and cause mortality.

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