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Case Report

Intracardiac Thrombus Resulting in Multiple Cardiovascular Complications as a Manifestation of Behçet Disease: A Case Report

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Behçet disease (BD) is a chronic systemic inflammatory condition with recurrent manifestations, including oral and genital ulcers, skin lesions, and ocular involvement. The disease is considered a syndrome with diverse phenotypes—vascular, gastrointestinal, and neurologic—often linked to higher morbidity and mortality. Cardiovascular manifestations are not common, with complications like thrombosis, aneurysms, myocarditis, and intracardiac thrombi. Diagnosis is challenging because of the variability in presentation, especially when typical symptoms are absent. Early recognition and treatment, including immunosuppression, are vital. Multidisciplinary care improves outcomes, particularly in managing serious vascular complications such as spontaneous or procedural pseudoaneurysms.

Novel Teaching Points

- Cardiovascular involvement in Behçet disease is not a common manifestation, but when present, it is associated with high morbidity and mortality.
- Cardiovascular complications in Behçet disease can be the first manifestation of the condition: aneurysms, thrombosis, and intracardiac thrombus may occur before typical symptoms like oral or genital ulcers appear, making early diagnosis challenging.
- Given the associated complications, it is crucial to suspect Behçet disease when these manifestations occur and to establish a multidisciplinary team to administer early immunosuppressive treatment and carefully plan surgical interventions.
- Being an autoimmune disease, Behçet can have various triggers that provoke its onset, such as SARS-CoV-2 in our case.

Case Presentation

A 23-year-old man currently undergoing treatment with adalimumab for suspected ankylosing spondylitis, negative for HLA-B27, experienced a recent hospitalization 3 weeks prior because of SARS-CoV-2–related acute myopericarditis and a large pericardial effusion, without hemodynamic compromise.

On follow-up echocardiography, 1 month later, a thrombus measuring 1.4 × 0.8 cm was found at the cardiac apex, attached to a small peduncle inserted in the lower third of the interventricular septum (Supplemental Fig. S1). Global and segmental contractility were preserved, and there were no valvular abnormalities. The electrocardiogram was normal, and all laboratory tests, except for a slightly elevated C-reactive protein level, were within normal limits. Further tests for antinuclear antibodies, rheumatoid factor, and antiphospholipid antibodies were negative (Supplemental Tables S1 and S2). The patient was heterozygous for factor V Leiden mutation, negative for von Willebrand disease, and had normal levels of proteins C and S. Extensive testing for infectious diseases was negative at this point.

Initially, anticoagulant therapy was initiated, and after consultation with the Heart Team, daily echocardiography was conducted. Because of the high risk of embolization and

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persistent thrombus size despite reduced peduncle size, surgical removal was recommended. A transapical thrombectomy was performed, and samples from this surgery, including both the thrombus and its supporting base, as well as endomyocardial biopsies, were sent to the pathology laboratory for histologic analysis (Supplemental Fig. S2).

During this time, the patient developed different complications including extensive bilateral iliac artery thrombosis, femoral pseudoaneurysm, gastrointestinal bleeding requiring temporary cessation of anticoagulation, and after that an ischemic stroke with hemorrhagic transformation. Given the numerous vascular complications, a fluorodeoxyglucose positron emission tomography (FDG-PET) scan was performed to investigate the potential inflammatory nature of the disease. This revealed hypermetabolic foci consistent with inflammatory lesions in the left ventricle and over the left femoral pseudoaneurysm (Supplemental Fig. S3).

A multidisciplinary team comprising internal medicine, rheumatology, infectious diseases, neurology, cardiac surgery, and cardiology departments reviewed the case.

The etiology was challenging, with a presumed autoimmune vasculitis suspected. In addition to anticoagulation, immunosuppressive therapy with high-dose corticosteroids and mycophenolate mofetil was initiated.

Follow-up echocardiograms showed preserved ejection fraction without new thrombus.

At a 4-month follow-up, echocardiography revealed an apical pseudoaneurysm measuring up to 3.5 cm with systolic expansion and turbulent flow (Supplemental Fig. S4). A narrow neck generated a gradient of 25-30 mm Hg, likely related to the previous surgical site, necessitating a second surgical intervention for closure.

Given the diverse complications presented, a differential diagnosis of various vasculitis was considered, with negative antibody associations as previously described (Supplemental Tables S1 and S2). The occurrence of both venous and arterial thromboses, along with the complication of a pseudoaneurysm at the surgical access site, suggested Behçet disease as the most probable differential diagnosis.

Once again, the case was brought to the attention of the multidisciplinary team, and the medical history was expanded, revealing a history of recurrent ulcers reported by the patient. Skin examination revealed pseudofolliculitis lesions on the trunk, with positive pathergy test and normal ophthalmologic findings. Additionally, the patient had been under rheumatologic evaluation for oligoarthritis in previous years.

Despite incomplete diagnostic criteria, it was decided to initiate a first cycle of cyclophosphamide before surgical intervention, given the known higher postoperative vascular complications in surgical access areas in Behçet syndrome, and intensive immunosuppressive treatment was recommended beforehand.

Subsequently, the intervention was performed with closure of the apical defect (Supplemental Fig. S5), requiring extracorporeal circulation once again. The surgical outcome was favorable.

Two months later, the next complication occurred, where a computed tomographic (CT) angiography revealed a large oval lesion in the anterior mediastinum measuring 107 × 77 × 104 mm, consistent with a pseudoaneurysm (Supplemental Fig. S6), completely patent, with a narrow neck of 55 mm dependent on the anterior surface of the ascending aorta. This necessitated a third surgical intervention, this time with a high surgical risk. During the median sternotomy, rupture of the pseudoaneurysm occurred, which was repaired using multiple sutures and pericardial patches.

After this procedure, the surgeons reported that the patient's tissue broke down with sutures, so they suggested the possible association with some collagen disorder. The diagnostic battery was expanded by requesting a genetic test, including Ehlers-Danlos syndrome. The only findings in the genetic analysis were 2 mutations in the *COL6A2* gene related to Bethlem myopathy, which appeared to be an incidental finding without clinical significance or correlation.

At this point, the results of the samples sent to pathology department for histologic examination from the surgery were received. The samples corresponding to the epicardium showed extensive areas of liquefactive necrosis surrounded by reparative granulation tissue. The adjacent epicardial tissue showed a moderate polymorphic inflammatory infiltrate, with histopathologic alterations in this tissue that could correspond to subacute pericarditis. Regarding the thrombus sample, it was confirmed to be an organized thrombus. Additionally, the base of the endocardium where the thrombus was anchored was sent for examination, revealing ulcerated endocardium with dense granulation tissue and remnants of an adherent organized thrombus. At the base of this granulation tissue, there was a dense lymphoplasmacytic infiltrate accompanied by numerous histiocytes. Immunohistochemical studies show these histiocytes expressed CD68 and factor XIII, whereas they were negative for S-100 and CD1a. A mutational study for BRAF was negative, with no mutation detected. The myocardial tissue exhibited mild edema and a sparse lymphocytic inflammatory infiltrate, with occasional necrotic myocytes. No granulomas were identified.

The patient remained asymptomatic until 3 months later, when he attended hospital, with the emergency department reporting the appearance of a "lump" at the suprasternal level. Laboratory analyses showed no abnormalities. A chest CT angiography revealed a retrosternal hematoma apparently originating from the anterior wall of the aorta, following repair of the aortic pseudoaneurysm, and a mass in the right ventricle whose origin could not be determined. To further complement the diagnosis, a coronary CT and cardiac catheterization were performed, revealing a pseudoaneurysm of the right coronary artery (Supplemental Fig. S7).

On this occasion, the medical team opted for a percutaneous intervention with the placement of a nonfenestrated stent to exclude the coronary circulation from this pseudoaneurysm.

At this point in the process, the patient had completed 6 cycles of cyclophosphamide and continued treatment with acenocoumarol. Despite optimal treatment, because of ongoing complications, initiation of a newly approved potent immunosuppressant for this condition, a tumor necrosis factor alpha inhibitor (infliximab), was decided.

Currently, the patient remains asymptomatic and without new complications 3 years after starting treatment. Monthly echocardiographic and symptom monitoring continues.

Discussion

Behçet disease (BD) is a difficult-to-treat recurrent chronic systemic inflammatory disease, characterized by oral thrush, genital ulcers, skin and eye lesions, and repeated episodes of acute inflammatory disease.[1] Currently, it is considered a syndrome encompassing a spectrum of different phenotypes rather than a single entity. These phenotypes include vascular, gastrointestinal, and neurologic phenotypes, and those phenotypes are less associated with typical disease manifestations but more correlated with morbidity and mortality.[2]

The etiology of BD remains undetermined, although factors such as bacterial, viral, genetic, environmental, toxic, and immune factors have been proposed. Although there have been various theories regarding the etiology, the most widely accepted view of the pathogenesis of BD today is an increased response of both innate and acquired immune systems against environmental antigens and autoantigens, coupled with a genetic predisposition.

The most debated genetic marker is HLA-B51, which has been identified as having the strongest association with BD. However, only 10% of the cases in our geographic area are HLA-B51 positive.[2] Although the proportion of patients with this condition and cardiac involvement who possess this gene is unclear, previous studies have reported its presence in only 7% to 46% of them.[3]

BD has a characteristic geographic distribution, indicating an environmental factor that triggers an autoimmune response in patients with a genetic predisposition, and more common in males. In our case, we had a male patient with a history of a "possible" autoimmune arthritis and a possible trigger of these autoimmune disease, the SARS-CoV-2 infection.

The pathophysiological basis of systemic manifestations, including cardiovascular involvement in BD, is vasculitis. The histologic characteristics reported in the literature are notable infiltration of neutrophils and vascular wall destruction leading to aneurysm formation.[4] Endovascular and perivascular inflammation can result in stenosis, thrombosis, and aneurysms. Although it is true that these findings, commonly associated with this disease, are quite nonspecific, they were observed in the samples we sent to the pathology laboratory from our patient.

The prevalence of cardiovascular involvement varies between 7% and 29% according to different series. In one of the largest case series published, it was observed that among patients with cardiovascular involvement, only 6% had cardiac complications.[5]

Cardiac involvement in this pathology can manifest in various forms, including endocarditis, myocarditis, endomyocardial fibrosis, coronary arteritis, myocardial infarction, valvular disease, and more rarely as an intracardiac thrombus.

Intracardiac thrombus is an uncommon complication of BD. A genetic predisposition to this form of presentation is suspected, as it occurs predominantly in patients from the Mediterranean basin and the Middle East. It could be one of the most serious cardiac complications, often causing pulmonary or cerebral embolisms as initial manifestations of the disease. Fewer than 100 cases of intracardiac thrombus have been reported in the literature.[6]

There are still several aspects of the disease that are not well understood, posing a diagnostic challenge. The diagnostic criteria for this disease are those proposed by the Japanese Committee in 1987, based on major and minor criteria such as genital ulcers, skin lesions, and ocular manifestations. Recently, it has been suggested that this diagnosis should also be considered in cases of vasculo-Behçet or cardiac Behçet despite the absence of these classic criteria.

Clinical findings strongly suggestive of vascular BD include saccular aneurysms without atherosclerosis in patients aged <50 years, superior vena cava syndrome or deep vein thrombosis in bilateral legs without apparent causes, and multiple superficial thrombophlebitis.[7] It is very difficult to diagnose BD in patients whose initial manifestation is vascular lesion, as vascular BD involves few ocular lesions. In such a case, it is very important to find out not only the oral and genital ulceration but also the history of arthritis.

In our case, the patient presented both arterial and venous thromboses in different territories, as well as aneurysms at surgical access sites and spontaneous aneurysms too. The possibility of SARS-CoV-2 infection serving as a trigger for this syndrome is also considered. Reviewing the patient's history, he was under rheumatology follow-up for a history of arthritis pending classification, and oral ulcers suggested a potential diagnosis of this pathology.

The treatment of vasculo-Behçet with cardiovascular involvement is primarily empirical and aimed at vasculitis. Managing arterial involvement such as aneurysms and thromboses poses a challenge because of the high bleeding risk in these patients. This disease is a chronic inflammatory disorder characterized by relapses and remissions. It has been observed that males or early-onset cases tend to have a more severe course.

Therefore, the prognosis of this disease is poor, although recovery can be achieved with close monitoring, immunosuppressive therapy, and anticoagulation.[7] However, in the small number of cases in the published literature, medical management has been associated with a better outcome. Irrespective of the mode of management, the presence of intracardiac thrombus confers a poor prognosis, with many fatalities in these young patients. One of the major differences in our case is that despite multiple complications, the patient remains stable 3 years after the diagnosis, following the administration of cyclophosphamide cycles prior to interventions and chronic anti−tumor necrosis factor alpha (anti-TNF-α) therapy.

To summarize, BD is a recurrent chronic systemic inflammatory disease with varied phenotypic manifestations, including serious cardiovascular complications. The etiology of BD is complex, involving genetic and immunologic factors. Diagnosis is challenging because of its variable presentation, and treatment is empirical, focusing on vasculitis and managing complications such as thrombus. Early detection and treatment are essential for improving prognosis. Forming multidisciplinary teams, including rheumatologists, cardiologists, and dermatologists, is crucial for effective management, enabling comprehensive evaluation and improving patient quality of life. We must consider BD beyond the classical criteria to ensure timely and accurate diagnosis and treatment.

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Ethics Statement

This case report was conducted in compliance with all applicable ethical standards and guidelines. Written informed consent for publication was obtained from the patient. All authors confirm adherence to ethical principles and the patient's confidentiality was maintained.

Patient Consent

The authors confirm that informed written consent was obtained for the submission and publication of this case report, including the accompanying text and images as per COPE guidelines.

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Disclosures

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References

1. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis 2018;77:808-18.
2. Demirelli S, Degirmenci H, Inci S, Arisoy A. Cardiac manifestations in Behcet's disease. Intractable Rare Dis Res 2015;4:70-5.
3. Mogulkoc N, Burgess MI, Bishop PW. Intracardiac thrombus in Behçet's disease. Chest 2000;118:479-87.
4. Emmi G, Bettiol A, Silvestri E, et al. Vascular Behçet's syndrome: an update. Intern Emerg Med 2019;14:645-52.
5. Eren H, Öcal L, Kalçik M, et al. Intracardiac thrombus in Behçet's disease. J Cardiovasc Echogr 2016;26:22-4.
6. Sarica-Kucukoglu R, Akdag-Kose A, KayabalI M, et al. Vascular involvement in Behçet's disease: a retrospective analysis of 2319 cases. Int J Dermatol 2006;45:919-21.
7. Ishibashi H. What is vascular Behçet's disease? Ann Vasc Dis 2018;11:52-6.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjco.2024.12.012.