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AORTIC THROMBOSIS OCCURRING IN A PATIENT WITH BEHÇET DISEASE AND MULTIPLE THROMBOPHILIAS: A CASE REPORT

Alexandru Stieber[1], Camelia Badea[2,3]
[1] Internal Medicine Department, "Dr. Carol Davila" Central University Emergency Military Hospital, Bucharest, Romania
[2] Department of Internal Medicine, Colentina Clinical Hospital, Bucharest, Romania
[3] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
Corresponding Author: Alexandru Stieber, alexandru.stieber@gmail.com
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Abstract

Behçet disease represents an inflammatory condition capable of affecting blood vessels in both venous and arterial circulations, a clinical pattern like the one encountered in antiphospholipid syndrome, although disease mechanisms differ. This case report presents the occurrence of an acute episode of paraparesis due to aortic thrombosis in a patient with a known history of Behçet disease, treated by way of a thromboembolectomy.

There were no systemic inflammatory syndrome or other suggestive symptoms for a relapse of the patient's underlying condition. A hypercoagulable workup revealed the presence of several prothrombotic factors, including antithrombin III and protein S deficiencies, alongside the confirmation of a positive lupus anticoagulant. This case highlights the clinical challenge that the aortic thrombosis posed, which was finally attributed to the particular association of prothrombotic factors, in a patient with an apparently inactive Behçet disease and an antiphospholipid syndrome that had probably played the most significant role in the acute presentation.

Keywords*: Behcet disease, Paraparesis, Thrombectomy, Antiphospholipid Syndrome, Thrombophilia*

Rezumat

Boala Behçet reprezintă o afecțiune inflamatorie care poate afecta vasele sanguine atât din circulația venoasă, cât și din cea arterială, un tablou clinic similar cu cel întâlnit în sindromul antifosfolipidic, deși mecanismele bolii diferă. Cazul clinic de față a debutat prin instalarea unui episod acut de parapareză cauzată de o tromboză aortică la un pacient cu antecedente cunoscute de boală Behçet, tratat prin tromboembolectomie.

INTERNAL MEDICINE

Clinical Cases

Sindromul biologic inflamator a fost absent, precum și alte simptome sugestive pentru o recidivă a afecțiunii inflamatorii subiacente a pacientului. Un bilanț de hipercoagulabilitate a relevat prezența mai multor factori protrombotici, inclusiv deficite de antitrombină III și proteină S, alături de confirmarea unui anticoagulant lupic pozitiv. Acest caz evidențiază provocarea clinică pe care a reprezentat-o episodul trombotic, care a fost în final atribuit asocierii particulare a factorilor protrombotici, la un pacient cu boală Behçet aparent în remisiune și sindrom antifosfolipidic, acesta din urmă fiind probabil actorul principal în această complicație acută.

***Cuvinte cheie**: Boala Behçet, Parapareză, Trombectomie, Sindrom antifosfolipidic, Trombofilie*

Introduction

Behçet disease is a systemic inflammatory disorder, characterized by a process of vascular inflammation affecting vessels of any size from both arterial and venous sides of the circulatory system. In the absence of other systemic disorders, the diagnosis of Behçet disease relies on clinical criteria, requiring the presence of recurrent oral aphthosis and at least two of the following: recurrent genital aphthae, ocular complications, skin lesions or a positive result on pathergy testing.[1]

The involvement of both arterial and venous tracts can be seen in 25% of patients, with superficial and deep thrombophlebitis of the lower extremities being the most common manifestations.[2] Pulmonary artery involvement associated with aneurysm formation represents the leading cause of death in Behçet disease patients, being unique to this inflammatory condition.[3] Aortitis, as well as vasculitis involving carotid, femoral or popliteal territories can be seen.[2]

Hypercoagulability disorders, also known as thrombophilia, is a group of hereditary and acquired conditions defined by their ability to induce thrombi formation in the veins or arteries.[4]

Arterial thrombosis, observed in cases of stroke or myocardial infarction, has different pathophysiological and therapeutic implications when compared with instances of venous thrombosis, such as a pulmonary embolism or deep vein thrombosis.[5] Among the most prevalent hypercoagulable states there are the factor V Leiden mutation, the prothrombin G20210A mutation, elevated

factor VIII, hyperhomocysteinemia and the antiphospholipid syndrome (APS), the latter being the most common cause of acquired thrombophilia.[4] APS is characterised by recurrent thrombosis and/or pregnancy complications in the presence of certain persistently positive autoantibodies (lupus anticoagulant, anti-β2-glycoprotein I and anticardiolipin antibodies).[6]

Case report

The case concerns a 37-year-old male patient with a known history of Behçet disease, under methylprednisolone, colchicine and azathioprine. The disease had been diagnosed in 2006 and had a course characterised mainly by flares of fever, arthralgias, mucous and cutaneous lesions. In 2009, the patient suffered from an acute episode of oral aphthosis, polyarthralgia and pseudo follicular lesions, with a new onset of headache, postural tremor of his upper extremities and vertigo.

A cerebral MRI revealed small lesions in the putamen and the external capsule, 6-7 mm in diameter, seen as hyperintensities on T2-weighted and hypointensities on Fluid-Attenuated Inversion Recovery (FLAIR) images, respectively. Their probable origin seemed to be vascular and a diagnosis of neuro-Behçet was put forward.

At the same time, laboratory investigations showed absent cryoglobulins, but a weakly positive anti-beta2 glycoprotein I antibody. An ophthalmologic exam showed no abnormalities. Considering all these findings and the patient's newly uncovered cerebral vasculitis, clinicians recommended monthly pulse therapies of cyclophosphamide and methylprednisolone (6 sessions were done in total), which gradually improved his symptoms, and long-term prophylaxis with 75 mg of aspirin daily.

In April 2019, the patient presented to his local Emergency Department because of an acute episode of lower limb anaesthesia, paraparesis and pain.

Clinical examination was significant for absent femoral pulses bilaterally. CT angiography revealed an occlusion of the abdominal aorta, 2,57 cm from the emergence of the common iliac arteries. The final diagnosis was that of bilateral acute lower limb ischemia, stage 2B, which prompted transfer to a vascular surgery center in Bucharest, where a thromboembolectomy was performed. The following months have been dedicated to an intensive recovery program carried out at the patient's residence, accompanied by an anticoagulant treatment with Dabigatran and an increased dosage of methylprednisolone.

In November of the same year, the patient presented to our clinic for a comprehensive evaluation following the cardiovascular incident, in the context of his underlying rheumatological disease.

On further questioning, he described pain of great intensity in both of his lower limbs, with a distal topography. Clinical examination was significant for reduced sensation on the lateral border of his left leg with preserved muscle strength.

An electromyography (EMG) was highly suggestive for a predominantly axonal, left lumbosacral plexopathy. A Doppler ultrasound carried out in October 2019 had shown patent main arteries in both lower extremities. Given the fact that his Behçet disease didn't show any objective signs of relapse, the suspicion of a possible accompanying thrombophilia was raised for this patient. Further investigations revealed the presence of both antithrombin III and protein S deficiencies, a heterozygous status for the MTHFR gene and a positive lupus anticoagulant (the latter had first come back positive in June 2019).

Taking into consideration all these prothrombotic traits and his recent massive arterial thrombus, the decision was made, in agreement with the vascular surgeon, to switch the patient's Dabigatran to Acenocoumarol.

Per his latest visit to our clinic in August 2022, the Behçet disease is still maintained in remission with the regimen of 8 mg methylprednisolone daily, 50 mg colchicine daily and 1 mg azathioprine daily, without any other disease flares. The reduced sensation of the left leg persisted with slight localized atrophy, but with preserved muscle strength.

Discussions

At first glance, the occurrence of acute paraparesis in a patient with Behçet disease prompted the consideration of related autoimmune complications in the form of a possible transverse myelitis. Neurological manifestations are present in only 5% of Behçet disease patients, with a higher predominance for the male population.[7] However, clinical examination and eventual imaging studies revealed a thrombus involving the distal segment of the descending aorta, cutting vital circulation to the patient's lower extremities.

A thrombotic event occurring in the arterial circulation would prompt the consideration of a new relapse of the patient's underlying inflammatory disorder. Although it affects only a minority of patients, arterial involvement represents a unique feature of Behçet disease, characterized mainly by aneurysms potentially affecting both visceral and pulmonary arteries.[8] In spite of the severe and striking arterial involvement, taking into account the patient's previous patterns of relapse, marked by significant oral aphthosis, cutaneous lesions, fever and articular involvement, and the absence of any other new, compatible symptoms, the probability that the acute episode had been caused by the patient's Behçet disease diminished.

Furthermore, reported instances of significant arterial involvement were accompanied by aneurysm formation[9] and/or objective signs of systemic inflammation[10] or active disease[11], which did not apply to our patient at the time of his presentation.

With the patient's rheumatological disease kept in remission, by all accounts, the possibility of an underlying thrombophilia was being discussed.

Further laboratory investigations not only demonstrated the presence of multiple prothrombotic factors (antithrombin III and protein S deficiencies, heterozygous status for the MTHFR gene), but also a positive lupus anticoagulant. While antithrombin III (ATIII) and protein S deficiencies usually cause thrombosis in the venous circulation,[4] the hallmark manifestations of APS are recurrent

thrombotic events occurring in both the venous and the arterial sides of the circulation. Arterial involvement in APS remains less common and it tends to involve the cerebral vasculature.[12] However, there have been reported cases of APS causing thrombosis in the thoracic aorta[13] and even at the aortoiliac level;[14] the latter is an instance very similar to our patient's situation, but there were no other accompanying rheumatological conditions or specific thrombophilia. A meta-analysis by Islam et al[15] revealed a significantly high prevalence of antiphospholipid antibodies in patients with Behçet disease when compared with controls, but their significance in the disease process remains debatable.

Finally, considering the new paraclinical data, the patient's aortic thrombosis was attributed to a rather particular combination of thrombophilic factors, his antiphospholipid syndrome probably having played the most significant role in the acute presentation, while also considering his Behçet disease as inactive.

Similarly, a reported case by Bayraktar et al[12] presented the isolated occurrence of a thrombus in the posterior wall of the infrarenal aorta in a patient with Behçet disease in apparent remission and significantly lowered protein C levels at the time of the presentation; previously, the same patient had suffered from mesenteric artery thrombosis, but in the setting of a severe relapse of his autoimmune disease.

Conclusions

The present report highlights the case of a patient presenting with acute onset paraparesis caused by aortic thrombosis, in the context of a known history of Behçet disease and the presence of antiphospholipid syndrome and several other prothrombotic factors.

Although arterial involvement is a less common, but characteristic feature of Behçet disease, manifested mostly by aneurysm formation, our patient's clinical picture lowered the probability that his inflammatory condition had caused the thrombosis. The confirmation of a present lupus anticoagulant inclined towards the consideration of APS as the possible main driver for the thrombosis, since this clinical entity is known for affecting the arterial side of the circulation.

In view of the patient's inflammatory condition being in apparent remission, alongside the confirmed antiphospholipid syndrome and the thrombophilia traits that typically cause venous involvement, our patient's aortic thrombosis remains a rare occurrence, with a curious association of potentially prothrombotic factors that highlights the multitude of interactions taking place within the coagulation cascade.

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