CASE REPORT AND LITERATURE REVIEW

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BEHÇET'S DISEASE WITH BILATERAL JUGULAR VEIN THROMBOSIS WHO RESPONDED TO MYCOPHENOLATE MOFETIL THERAPY

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Abstract

Behçet's disease (BD) is a systemic vasculitis that may progress with recurrent oral and genital aphthous ulceration and uveitis as well as locomotor, vascular, gastrointestinal, pulmonary, and neurological involvement. Although the rate of vascular involvement in BD varies from country to country, it varies between 1-38% in series. Venous involvement is more common than arterial involvement, and the most common form of involvement is lower extremity deep vein thrombosis; thrombosis may also cause occlusion in the superior and inferior vena cava. In this article, a case of BD presenting with bilateral jugular vein thrombosis is discussed.

Keywords: Behçet's disease, thrombosis, mycophenolate mofetil, jugular vein

INTRODUCTION

Behçet's disease (BD) is a chronic, multisystemic autoimmune disease with exacerbation and remission, which was first reported in 1937 by Prof. Dr. By Hulusi Behçet and defined as "triple symptom complex" consisting of recurrent oral, genital aphthous ulceration and hypopionic uveitis (1,2). In other studies, it has been shown that this triple symptom complex is accompanied by articular, pulmonary, gastrointestinal, urogenital, cardiac, vascular, and neurological symptoms (3). Although BD can be seen at any age, the average age of onset is within the third decade and is more severe and mortal, especially in young males (4). The vascular involvement rate in BD has been reported as 1-38% in some studies (5). Venous involvement is more common than arterial involvement, while the most common form of involvement is lower extremity deep vent thrombosis; thrombosis may cause occlusion in the superior-inferior vena cava and dural sinuses (6). Here, we present the case of a patient who was admitted to our emergency department with headache and neck swelling and was diagnosed with bilateral jugular vein thrombosis and BD.

CASE REPORT

A 23-year-old male patient was admitted to the emergency department with a sudden headache and bilateral swelling of the neck. The patient, who was found to have bilateral jugular vein thrombosis on cervical Doppler ultrasonography, was admitted to our rheumatology service for further examination after being consulted for cardiovascular surgery and after initiating low-molecular-weight heparin (LMWH) treatment.

The 23-year-old single male patient had no previous comorbidities. It was learned that the patient had oral aphthae 2-3 times a month, ulcers that healed by leaving scars in the genital area, and widespread acneiform lesions in the body. On admission, the patient's body temperature was 38.1 °C, blood pressure arterial 123/82 mmHg, and pulse 88. On skin examination, there were acneiform pustular lesions on the face and back

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and swelling in the bilateral anterior neck triangle. There were three active oral aphids on opharyngeal examination. Two healed genital ulcer scars were detected on the scrotum. There were no pathological findings in the respiratory system, cardiac system examination, gastrointestinal system, or musculoskeletal system examination. Detailed laboratory parameters are given in Table 1, and the C-reactive protein value at the patient's admission was found to be high at 234. There was no evidence of infection in the examination of the patient, and no growth was observed in the urine and blood cultures of the patient. The serology of human immunodeficiency virus and hepatitis was negative. Lupus anticoagulants, antiphospholipid-anticardiolipin antibodies, antithrombin III, protein C, and protein S levels were normal. While the anti-nuclear antibody test was positive at 1/100-320 titer (spotted), the extractable nuclear antigen panel was negative. The pathergy test was found to be negative. Bilateral jugular venous thrombosis was detected by cervical Doppler ultrasonography, and no other pathology was observed by other venous and arterial system imaging. No signs of active or sequelae uveitis were observed on eye examination. The patient was accepted as having BD according to the clinical and biochemical findings and the international diagnostic criteria for BD. LMWH treatment was discontinued, and acetylsalicylic acid (100 mg/day) and methylprednisolone (1 mg/kg) treatment were initiated. Cyclophosphamide treatment was recommended to the patient for treating vasculitis as a steroid-sparing agent, but the patient refused the treatment because of possible side effects. Thereupon, azathioprine treatment was initiated for the patient. After azathioprine treatment, there was a 3-fold increase in liver function test's. Azathioprine treatment was discontinued because of hepatotoxicity, and mycophenolate mofetil treatment was started. Under methylprednisolone and mycophenolate mofetil treatment, both clinical and biochemical responses were obtained. Recanalization of the jugular veins was observed by cervical Doppler ultrasonography, and the patient was discharged from the polyclinic.

Table 1. Laboratory findings

Parameters	Results
Complete blood count	
White blood cell, $\times 10^3$/mL	16.1
Neutrophil, %	94.1
Lymphocyte, %	2.2
Monocyte, %	3.2
Eosinophil, %	0.3
Hemoglobin, g/dL	11
Hematocrit, %	33.4
MCV, fL	82.7
MCHC, g/dL	33
Platelets, $\times 10^3$/mL	323
Blood biochemistry	
Glucose, mg/dL	143
Creatinine, mg/dL	0.77
Aspartate aminotransferase, U/L	13
Alanine aminotransferase, U/L	9
Alkaline phosphatase, U/L	99
Total protein, U/L	6.93
Albumin, g/L	3.6
LDH, U/L	135
Erythrocyte sedimentation rate, mm/hour	72
C-reactive protein, mg/L	234.6
Procalcitonin, ng/mL	0.34
Rheumatoid factor, IU/L	Negative
Anti-nuclear antibody	1/100-320 (spotted) positive
ENA panel	Negative
Thrombosis panel	No mutations
Spot urine protein	0.14
Coagulation	
INR	0.89
APTT, s	38
PT, s	11
Molecular nasopharyngeal swab (COVID-19 PCR)	Negative

ENA: Extractable nuclear antigen, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction, INR: International normalized ratio, APTT: Activated partial thromboplastin time, PT: Prothrombin time, LDH: Lactate dehydrogenase

DISCUSSION

BD is a systemic vasculitis that can affect arteries and veins of all sizes. Perivascular infiltration of neutrophils and monocytes and endothelial dysfunction caused by immune-mediated vasculitis increase the risk of thrombosis (7). Venous involvement in BD can be seen as superficial and deep vein thrombosis. Recurrent thrombophlebitis is most commonly observed in lower extremity veins. Thrombosis may also be seen in the superior-inferior and dural sinuses of the vena cava, which have a worse prognosis (2,8). Our case is a case of BD that progressed with bilateral jugular venous thrombosis and responded to mycophenolate mofetil treatment.

Early initiation of steroid and immunosuppressive therapy is essential for prognosis in vascular involvement of BD. Glucocorticoids and immunosuppressives, such as cyclophosphamide, azathioprine, or cyclosporine, are recommended as the first choice for treating Behçet's disease venous thrombosis. It has been reported that monoclonal anti-tumor necrosis factor treatments can also be used in resistant cases (9). In different BD case reports, it has been reported that clinical response was obtained from mycophenolate mofetil treatment for treating cerebralsinus thrombosis (10,11). We also preferred methylprednisolone and azathioprine as the first choice for treating our patient, and clinical and biochemical responses were obtained in the patient, who was continued with mycophenolate mofetil treatment because of the development of hepatotoxicity under azathioprine treatment.

Anticoagulation is controversial for treating BD associated with venous thrombosis. Due to the possibility of aneurysm seen in BD, anticoagulant therapy is generally not recommended in BD, as thrombosis is firmly attached to the vascular wall and the possibility of embolism is low. However, in cases of life-threatening venous involvement such as Budd-Chiari and treatment-resistant cases, anticoagulant therapy can be administered after pulmonary artery aneurysms are excluded (12). In this study, anticoagulant treatment was administered during the first week during which the examinations continued. Anticoagulant treatment was discontinued after the diagnosis of BD was made and glucocorticoid and immunosuppressive therapy was initiated.

CONCLUSION

BD should also be considered in the differential diagnosis, especially when a young male patient comes across with venous thrombosis. The patient should be evaluated from this perspective.

Ethics

Informed Consent: Information of informed consent from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.D.Y., G.Ş., Design: T.D.Y., G.Ş., Literature Search: T.D.Y., G.Ş., Writing: T.D.Y., G.Ş.

Conflict of Interest: The authors have no conflicts of interest to declare.

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