

CASE REPORT

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Behçet's Disease-Related Budd-Chiari Syndrome Responding to Combination of Cyclophosphamide, Rivaroxaban and Corticosteroids

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ABSTRACT Budd-Chiari syndrome (BCS) is a clinical state with thrombosis in major hepatic veins which may be related with myeloproliferative diseases, hypercoagulopathy states, oral contraceptives and secondary to compressing tumors. As a rare etiology, Behçet's disease may be responsible from this thrombotic cascade. Behçet's disease-related BCS has a number of treatment modalities including anticoagulants, immunosuppressives, immunomodulators, biological agents and alkylating anti-neoplastic agents such as cyclophosphamide. In this case report, we aimed to emphasize the importance of early initiation of immunosuppressives and anticoagulant treatment with a combination of cyclophosphamide, corticosteroids and rivaroxaban in a Behçet's disease-related BCS case with multiple thrombotic venous vessels.

Keywords: Behçet's disease; Budd-Chiari syndrome; cyclophosphamide

Behçet's disease (BD) is a chronic relapsing vasculitic disease which is characterized by recurrent oral and genital aphthous ulcers, skin lesions, uveitis, arthritis and vasculitis.¹ Thrombosis as a result of vasculitis and lower extremity deep vein involvement as the leading finding may be present. Budd-Chiari syndrome (BCS) is caused by obstruction of major hepatic veins. These patients may progress to liver failure and portal hypertension over time.² BCS is related with BD in 5% of cases in western countries, while 9% in Turkey and 13% in Egypt.^{3,4} However, misdiagnosis or delay of diagnosis is common in patients with BD-related BCS.⁵ Some of the patients may be asymptomatic, while abdominal pain, jaundice, emesis, hepatomegaly and ascites are frequently present. In these patients, incomplete diagnostic criteria of BD should not delay the treatment. Here, we present a patient hospitalized for elevated liver en-

zymes and history of lower extremity thrombosis diagnosed later as BD-related BCS responding to combination therapy.

CASE REPORT

A 30-year-old male patient was referred to our clinic with elevated transaminases. His medical history revealed swelling of the right leg two months ago. An angiographic intervention was performed and same symptoms developed also in the other leg. Meanwhile the patient himself began a herbal mixture. Due to elevation of liver enzymes, he was referred to our tertiary center. The laboratory results were AST 300 IU/L, ALT 800 IU/L, high CRP (x16 of normal) and elevated erythrocyte sedimentation rate (93 mm/h). Other related laboratory parameters were in normal range. Viral hepatitis serology and autoimmune liver markers were found negative. No thrombotic lesions

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were detected in portal doppler ultrasonographic examination, thus contrast enhanced abdominal computed tomography (CT) was planned due to clinical suspicion of BCS. CT findings were compatible with thrombosis of inferior vena cava extending from iliac veins to the right atrium (Figure 1, Figure 2). Before treatment, liver biopsy was performed and sinusoidal dilations, ground-glass appearance and eosinophilic infiltration suggesting a diagnosis of congestive ischemic liver disease were found (Figure 3). Heparin infusion was initiated immediately. After one week, ALT value increased to 1500 IU/L, while coagulation tests and bilirubin levels remained stable. Heparin-induced liver toxicity was thought and heparin was shifted to rivaroxaban.

Genetic tests, antiphospholipid antibodies, Factor V Leiden mutation, protein-C and protein-S levels, anti-nuclear antibody (ANA), complement and paroxysmal nocturnal hemoglobinuria (PNH) panel were negative. The patient had a history of recurrent oral aphthous ulcers, but no genital ulcers, arthritis or ophthalmic symptoms. The pathergy test was 3/6 positive. Rheumatology consultation agreed with incomplete BD diagnosis. Afterwards, immunosuppressive treatment was initiated with 1 gr/day intravenous methylprednisolone pulse treatment for three days and followed with 80 mg/day oral steroid. Due



FIGURE 1: Contrast CT image of thrombosis of inferior vena cava in coronary plane.

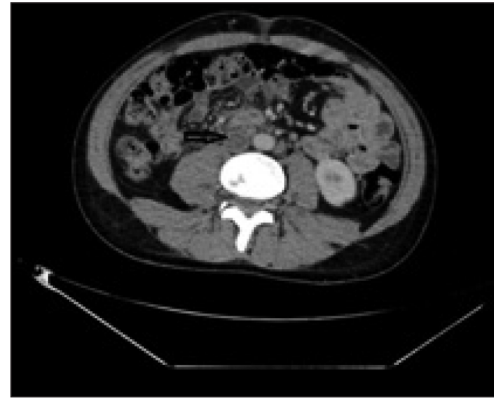


FIGURE 2: Axial plane of contrast CT image of thrombosis of inferior vena cava.

to persistent elevation of ALT up to 1100 IU/L, intravenous cyclophosphamide bolus treatment was administered as 1000 mg/month. Meanwhile, steroid was tapered to 4 mg/day. After the first dose of cyclophosphamide, ALT began to decrease gradually to normal levels. Control CT with contrast at the fourth month of the treatment demonstrated a complete resolution of the thrombus (Figure 4). The patient is under follow-up in sixth month with treatment of cyclophosphamide, colchicine, rivaroxaban and 4 mg/day methylprednisolone. It is planned to introduce azathioprine and cease the cyclophosphamide treatment. A written informed consent was obtained from the patient for this case report.

DISCUSSION

Vascular involvement in BD may result in thrombotic and aneurysmatic lesions disturbing blood flow.⁶ Lower extremity deep vein and large artery thrombosis are commonly seen as vascular manifestations.⁷ In BD, venous involvement is more common than arterial involvement and is one of the earlier symptoms of the disease. Also, occlusion of superior and inferior vena cava, BCS, dural sinus thrombosis and other venous obstructive lesions may also be seen. Repeating attacks of thrombosis of the lower extremities may result in post-thrombophlebitic syndrome.^{8,9}

In a study of 493 patients with Behçet's syndrome, 53 patients presented with one or more extensive vascular thrombosis, 14 patients had hepatic vein thrombosis, 8 had inferior vena cava thrombosis, 4 had both inferior vena cava and portal vein throm-

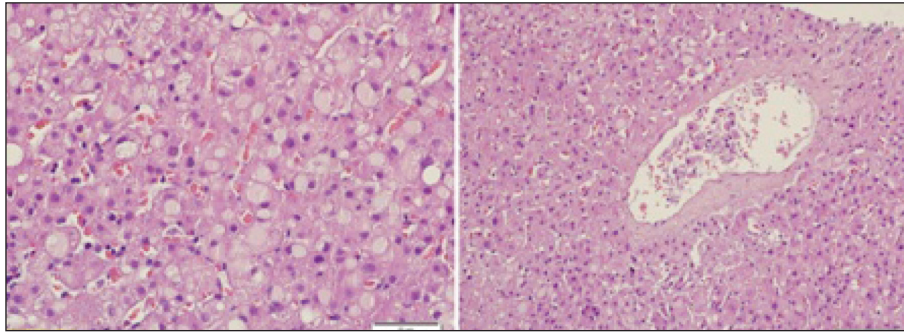


FIGURE 3: Central liver lobules demonstrating dilation and congestion of central vein and sinusoids and minor hemorrhage, parenchymal pseudo ground-glass appearance.



FIGURE 4: Coronal plane of contrast CT image of recanalised inferior vena cava after fourth month of treatment.

bosis.¹⁰ In our case, multiple vasculer involvement was seen in bilateral lower extremity veins and inferior vena cava which was occluded within last two months. In another study involving 73 patients, it was shown that individuals with Behçet's disease had developing venous thrombosis 14-fold higher than the control group.¹¹

Since BCS may be asymptomatic for years, it is possible for some patients diagnosed with different degrees of liver cirrhosis.¹² The percentage of hepatic vein occlusion and the development of collateral vessels correlate with the clinical severity of presentation.¹³ In countries with high incidence of BD, as in Turkey, awareness of etiology of BD in BCS is essential to diagnose earlier may improve poor prognosis and high mortality. Despite the antithrombotic treatment and therapeutic interventions,

vascular complications may be progressive in BD, thus early potent immunosuppressive treatment may reverse the thrombotic occlusion. As in our case, immunosuppressive treatment accompanying anticoagulation should be initiated without delay in BD-related BCS.

Due to lack of randomized controlled trials, treatment of BD related BCS is not established as an algorithm, but trials include corticosteroids, cyclosporine, azathioprine, thalidomide and anti-TNF blockers.¹⁴ The therapeutic outcome with immunosuppression in BD-BCS is superior to anticoagulation monotherapy, surgery or endovascular interventions.^{4,15} The 2008 EULAR guideline does not support the use of anticoagulants in BD, since there is an increased risk of aneurysmatic rupture.¹⁵ As in our case, early initiation of immunosuppressive treatment, anticoagulation and corticosteroid combination may improve clinical, laboratory and imaging parameters.

In conclusion, BCS is a rare but potentially life-threatening complication of Behçet's disease. Incomplete Behçet's disease may lead to misdiagnosis or delayed diagnosis if the criteria are not fulfilled. In the treatment of BCS related with Behçet's disease, combination of anticoagulants, cyclophosphamide and corticosteroids may be effective in thrombotic vascular lesions.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise,

working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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