Colon Perforation and Budd-Chiari Syndrome in Behçet’s Disease

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Patient: Female, 38
Final Diagnosis: Behçet’s disease
Symptoms: Severe abdominal pain • fever
Medication: —
Clinical Procedure: Parsiyel colectomy
Specialty: Surgery

Objective: Unusual clinical course
Background: Behçet’s disease is a chronic inflammatory disease involving multiple systems, with vasculitis being the most important pathological feature. Multiple colon perforations are thought to be secondary to vasculitis and they occur in patients with ulcers. These may be encountered within the entire colon but most commonly in the ileocecal region. Intestinal perforation and Budd-Chiari syndrome are infrequent in Behçet’s disease, and are associated with high mortality and morbidity. Budd-Chiari syndrome results from occlusion of either hepatic veins or adjacent inferior vena cava, or both.

Case Report: We report a patient with Behçet’s disease having multiple perforations in the transverse colon, descending colon, and sigmoid colon. The patient also had Budd-Chiari syndrome due to inferior vena cava thrombosis extending into the right and middle hepatic vein. Our observations are presented with a review of the literature.

Conclusions: In Behçet’s disease, treatment of colon perforation necessitates urgent surgery, whereas management of Budd-Chiari syndrome is directed towards the underlying cause. Behçet’s disease, as a chronic multisystemic disease with various forms of vasculitis, is resistant to medical and surgical treatment. Prognosis is worse in Behçet’s disease with colon perforation than that in Budd-Chiari syndrome alone.

MeSH Keywords: Behcet Syndrome • Budd-Chiari Syndrome • Colorectal Surgery • Intestinal Perforation

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Background

Behçet’s disease is a chronic inflammatory disease involving multiple systems, with vasculitis being the most important pathological feature. Multiple colon perforations are thought to be secondary to vasculitis and they occur in patients with ulcers. These may be encountered within the entire colon but most commonly in the ileocecal region. Intestinal perforation and Budd-Chiari syndrome are infrequent in Behçet’s disease, and are associated with high mortality and morbidity. Budd-Chiari syndrome results from occlusion of either hepatic veins or adjacent inferior vena cava, or both.

Case Report

A 38-year-old woman presented to our Emergency Department with severe abdominal pain. She had no history of drug use or constipation. She said that she had intermittent bloody diarrhea. Physical examination revealed rebound tenderness and guarding over the abdomen. Stool microscopy was negative for amoeba trophozoites or any parasites. Fecal occult blood was found. Sedimentation was 27 mm/s, CRP (nephelometry) was 65.6 mg/L (normal range 0–5), anti-nuclear antibody was 0.4 (0–0.8 negative), anti-ds DNA <10 (<20 negative), white blood cell count was 14.98 (normal range 4–10), hemoglobin level was 10.9, neutrophil count was 13.14, platelet count was 473 (100–300), urea level was 17 mg/dl, BUN level was 7.94 mg/dl, creatinine level was 0.56 mg/dl, AST was 20 U/L, and ALT was 24 U/L. HIV was negative. Abdominal ultrasound scanning showed free fluid at the right paracolic, perihepatic, left paracolic gutters and pelvis. Upon detection of air-fluid level and free air under the diaphragm on erect abdominal x-ray, emergency laparotomy was performed. In the operation, multiple perforation areas were found in the sigmoid colon, descending colon, and transverse colon. Wide resection of the transverse colon with descending and sigmoid colon resection was undertaken (Figure 1).

Pathergy test was positive. The patient had recurrent oral and genital aphthous ulcers 4–5 times within the past year. Eye

![Figure 1. (A, B) Perforation areas on the serosal surface of the colon and the macroscopic view indicative of peritonitis.](Image)

![Figure 2. (A) Thrombus within the inferior vena cava lumen extending through right and middle hepatic vein. (B) Absence of flow within the inferior vena cava lumen due to total occlusion.](Image)
examination results were normal. Computed tomography revealed extensive thrombus within the inferior vena cava extending through the right and middle hepatic vein (Figure 2).

The patient received corticosteroid, anticoagulant, and immunosuppressive therapy. Our patient is still alive and healthy 53 weeks later (Figure 3).

Pathological findings

In macroscopy, the transverse colon was 50 cm and sigmoid and descending colon specimens were 27 cm in length. Specimens of both colon segments were 4 cm in diameter. Perforation areas were evident in the serosal surface. Colonic wall and bowel mucosa was edematous and hyperemic. Plicae were regular in their course. There were 3 roundish, punched-out perforations in the transverse colon and 4 in the descending and sigmoid colon, which were somewhat separate from the colonic wall, with the largest being 2 cm in diameter (Figure 4). There were multiple ulcers (the largest was 1 cm in diameter) in different locations, which were not merging together, and were somewhat separate from the surrounding mucosa via a certain limit, covered with exudate and surrounded by a hyperemic region. There were no macroscopic lymph nodes in the serosa. Numerous samples were taken from ulcerated and perforated regions and normal mucosa. The samples were submitted for routine microscopic tissue follow-up. Hematoxylin-eosin, tissue Giemsa and PAS-stained slides were prepared for examination.

In microscopic examination, there were neutrophil leukocyte and lymphocyte reaction around and within the walls and lumens of arterioles, and venules around the perforated and ulcerated lesions (Figures 5 and 6). There were well-organized thrombi and intimal proliferation within some vessels (Figures 7 and 8). There was marked acute peritonitis. Surface epithelium
and colonic crypts were regular within the colonic mucosa apart from the ulcerated or perforated lesions. Samples were free of parasites or their eggs.

Discussion

Since its first description by Hulusi Behçet in 1937 [1,2], criteria for diagnosis and classification of Behçet’s disease (BD)
BD is a chronic, inflammatory, multisystemic, and vasculitic disease [1,3–7]. Its exact etiology is unknown [1,8,9]. Considering its geographical distribution, the presence of a genetic predisposition has been suggested and there is strong evidence indicating that the disease is linked to human leukocyte antigen (HLA)-B51 gene locus [1,8,11,12]. Currently, the focus in pathogenesis of BD is on extrinsic factors such as bacterial and viral infectious microorganisms and on intrinsic factors such as abnormal immunological response, together with environmental factors [11].

The prevalence of BD in Turkey was reported to range from 20 to 421 per 100,000 adult population [13]. Gastrointestinal tract involvement is present in 10% to 50% of patients with BD [5,8,14], with the ratios being 70% in Japan, 50% in the United Kingdom, and 1.4% in Turkey [11]. GIS involvement is more common from the Far East to the Mediterranean region, along the historical “silk road” [3,4,11,12,14]. The ileocecal region is involved in 75% of patients [8]. Intestinal lesions are irregularly distributed over antimesenteric region [15]. Ulcerative changes are present in less than 1% of patients [5]. Longitudinal ulcers are rare [15,16]. Ulcerations may occur in 2 major types—localized and diffuse [5,17]. Intestinal ulcers are aphthous or deep punched-out lesions (Figures 4 and 5) and these ulcers are round and oval shaped, single or multiple lesions [11,15,16].

Localized lesions occur in the ileocecal region; they are deeply located and penetrate into the serosal surface [5,18], whereas diffuse lesions, as in our case, are located more diffusely and separately in the colon as multiple punched-out lesions [5]. Perforation, penetration, and bleeding occur in 50% of patients with ulcers [15,18]. Kasahara et al. [17] reported in their series of 136 patients that multiple ulcers were present in 73%, localized ulcers frequently located around the terminal ileum was present in 76%, and perforation or penetration was present in 56% of patients with enteric BD. The pathogenesis of mucosal ulcerations is not clearly understood [1] and the condition has been explained by lymphocytic venulitis [2,8,16] of submucosal veins in Behçet colitis [14].

Characteristic vasculitis is better evaluated in resection specimens, as in our case. Small calibrated veins, especially venules, are generally involved [6,8]. This pattern of vasculitis is characterized by intramural monoclonal cells and neutrophil infiltration; subsequently, fibrosis and luminal occlusion ensue [8].

Involvement of large calibrated vessels may result in intestinal ischemia and infarction [14]. In our case, we observed neutrophilic vasculitis, perivenular lymphocyte reaction, and focal luminal occlusion of small calibrated venules in the colonic wall, especially around ulcers and perforations. Among the other histomorphological findings of BD, near-normal mucosa is observed in regions away from the lesions, and lymphoid aggregates or granulomas are not found [8,15]. In general, mortality of colonic perforation ranges from 35% to 47% [19]. Kasahara et al. [17] reported that postoperative ulcer recurrence within 6 months occurred in 22 of 34 patients (65%), whereas recurrence did not occur in 5 patients after more than 3 years of treatment.

In our case, in addition to colonic ulcer and perforations, we also detected presence of diffuse thrombus in the inferior vena cava and hepatic veins in computed tomography.

Budd-Chiari syndrome (BCS) is characterized by obstruction of hepatic venous flow (due to any cause) from the level of hepatic venules and large hepatic veins through the inferior vena cava and the right atrium [20–23]. The most common causes are hypercoagulation states [21]. The frequency of vascular involvement (superficial and deep venous thrombosis, arterial aneurysms, and occlusions) in BD ranges from 7% to 29% [24].

Incidence of BCS in patients with BD was reported at between 1.1% and 5.8% [7,20,24,25]. Uskudar et al. [22] reported in their series of 75 patients that web was 16%, hydatid cyst was 12%, and BD was 9% responsible in BCS etiology in Turkey. Desbois et al. [26] reported that among a total of 807 BD patients, venous thrombosis occurred in 586 cases, inferior vena cava thrombosis occurred in 7.5% (n=44), and BCS occurred in 2.4% (n=14). Bayraktar et al. reported in their series of 493 BD patients that there were 14 patients (26.4%) with BCS among 53 patients with large vein thrombosis. Ten (60%) of those 14 patients died within an average of 10 months [27]. Davatchi et al. [7] included a total of 6500 BD patients within a period of 35 years and reported that vascular involvement occurred in 8.3% of patients, whereas large vein (vena cava) thrombosis occurred in 1.1% of patients. Arterial thrombus occurs more infrequently [1,6,7].

The pathogenetic mechanism underlying the formation of thrombus is unclear [6,26]. However, it is attributed to vascular inflammation and endothelial ischemia similar to that is seen in pathogenesis of colonic ulcers [6,20]. High levels of endothelial products, such as Von Willebrand factor, contribute to the development of endothelial injury-related vasculitis [28]. In Okuda H et al. study [23] on 157 patients, etiology was idiopathic in 141 patients, protein C deficiency in 2 patients, protein S deficiency in 2 patients, and antithrombin deficiency in 1 patient. Ozoran et al. [9] reported that genetic prothrombotic factors such as Prothrombin 20210 G-A mutations are
associated with a marked increase in risk of thrombosis. Gül et al. [10] reported that factor V gene mutation was present in 15 of 64 BD patients with venous thrombosis. Orloff et al. [29] reported that hepatic vein occlusion resulted in liver fibrosis within a period of 6 months and centrilobular congestion and necrosis were found in microscopic examination of liver biopsies. They also reported that 1 patient with BCS due to BD died of colon infection secondary to diffuse vasculitis. Liver congestion that occurs due to occlusion of hepatic veins may lead fibrosis and resultant liver cirrhosis [1,10,29].

Urgent surgical intervention is essential in management of colon perforation. BD, as a chronic, multisystemic, and vasculitis-related disease, is resistant to medical and surgical treatment [20]. Besides the specific treatment of vasculitis, treatment options for BCS include corticosteroid, immunosuppressive, anticoagulation, thrombolytic, and radiological interventions, as well as surgical decompression, placement of surgical shunts, and surgical correction of the lesion [13,23].

In this paper we reported a patient with BD accompanied by BCS. Our case was interesting because it was complicated with multiple colon perforations and hepatic vein and inferior vena cava thrombosis. We described the histomorphological findings observed and discussed the findings in light of the literature.

Conclusions

In conclusion, our histomorphological findings support the view that colonic small vessel vasculitis may act as precursor lesions in ulcer pathogenesis. Patients with BD not only suffer from disease recurrence, but also become at high risk of mortality when the disease is associated with BCS. Therefore, BD should be taken into consideration in patients with colon perforations, ulcers, or large vessel thrombus and BCS, and in those with histological signs of vasculitis. Thus, appropriate treatment should be based on a multidisciplinary assessment.

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