Cavernous transformation and granulomatous epididymis in Behçet's disease

Short title: Cavernous transformation and granuloma in BD

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Conflicts of Interest and Source of Funding

Jun Wada receives speaker honoraria from Astellas, Boehringer Ingelheim, Daiichi Novartis, Sankyo, and Tanabe Mitsubishi, and receives grant support from Astellas, Bayer, Baxter,

Chugai, Daiichi Sankyo, Kissei, Kyowa Hakko Kirin, MSD, Novartis, Novo Nordisk, Ono, Otsuka, Pfizer, Teijin, Torii, and Takeda. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Abstract

Superficial vein thrombosis of the extremities and thrombosis of the deep veins of the lower extremities are common in BD; however, the formation of cavernous portal vein is rare. A 47-year-old man had been diagnosed with granulomatous epididymitis when he was 30 years old. He developed uveitis 4 years later and was treated with glucocorticoids based on a diagnosis of suspected sarcoidosis. Computed tomography performed when he was 40 years old revealed a cavernous transformation of the portal vein, but the etiology remained unknown. In January 2017, he experienced a relapse of the uveitis with high fever, and erythema nodosum and genital ulcerations developed. Human leukocyte antigen B51 was detected. Finally, he was diagnosed with Behçet's disease (BD), and vascular involvement was suspected. After admission to our hospital, his fever spontaneously resolved and treatment with colchicine was initiated to prevent relapse. Portal vein involvement is very rare in BD, and the presence of a granuloma might delay the diagnosis of BD.

Key Words: Behçet's disease, cavernous transformation, granuloma, epididymitis, vascular involvement, vasculitis

Background

Behçet's disease (BD) is a systemic disease characterized by acute inflammation of the oral mucosa, skin, eyes, external genitalia and vascular systems [1]. According to several reports, 7.8-27.7% of the BD patients have vascular involvement [1-3]. The vascular involvement is classified into two categories: venous occlusions and arterial aneurysms/occlusions [1]. Among these types of vascular involvement, superficial vein thrombosis of the extremities and thrombosis of the deep veins of the lower extremities are the most frequent manifestations; portal vein (PV) involvement is rare (approximately 1% of vascular involvement of BD) [1, 2]. The PV involvement is also thought that thrombosis firstly occurs, then hepatopetal collateral vessels enlarge in order to decompress the abdominal viscera, finally forming cavernous transformation [2]. Here, we report a case of BD with cavernous transformation and granulomatous epididymitis.

Case report

In 2000, a 30-year-old man with a right swollen, red and inflamed scrotum visited a community hospital. Because his symptoms did not improve despite treatment with several types of antibiotics, orchiectomy was performed and granuloma with multinucleated giant cells and epithelioid cells were detected in the resected specimen; a diagnosis of epididymitis and orchitis was made (Figure 1). In 2004, bilateral uveitis developed; the hypopyon was detected and the fluorescein angiography showed retinal vasculitis. There were no signs of tuberculosis infection and he was treated with glucocorticoid (GC) pulse therapy based on a diagnosis of suspected sarcoidosis. After increasing and decreasing the dosage of prednisolone (PSL) repeatedly, his uveitis was successfully treated with 7.5 mg of PSL in 2010. Contrast-enhanced computed tomography (CT) revealed a cavernous transformation of the PV at the same time.

In January 2017, he experienced relapse of the iritis accompanied by a high fever. He was admitted to the community hospital and was treated with several types of antibiotics (firstly, cefepime was used for 2 weeks, then it was changed to sulbactam/ampicillin), but his symptoms did not resolve. Non-tuberculous mycobacterial infection could not be excluded because he tested positive for serum anti-mycobacterium avium complex antibody, so he was also treated with rifampicin, ethambutol, and clarithromycin for a week. However, his symptoms still did not resolve. After that, erythema nodosum developed in his lower abdomen and genital ulcerations occurred; therefore, he was referred and admitted to our hospital in February 2017.

Laboratory examinations revealed an elevated leucocyte count of 9930 /μL (neutrophils, 73.0%; lymphocytes, 18.0%) and a C-reactive protein level of 16.96 mg/dL. His serum angiotensin-converting enzyme levels were within the normal range (6.6 U/L), and his immunoglobulin G level was 1513 mg/dL. The level of PT-INR was 1.14, APTT was 38.5 sec and d-dimer was 2.4 μg/mL. Human leukocyte antigens were A2, A11, B51 and B55, and results of the interferon gamma release assay (IGRA) were positive. Contrast-enhanced CT revealed the cavernous transformation, suggesting occlusion of the extrahepatic portal vein in the past (Figure 2). There were no signs and symptoms of tuberculosis infection. Ultrasonography detected fatty liver, and transient sonography showed a liver stiffness of 11.8 kPa, which was close to that of cirrhosis. Finally, he was diagnosed with BD based on the international criteria [4].

After admission, the patient's fever and the serum inflammatory markers spontaneously subsided. Treatment with colchicine (0.5 mg/day) was initiated on the ninth day to prevent relapse. The patient was discharged on the twenty-second day.

Discussion

Here, we report a patient with BD who had cavernous transformation of the PV, suggesting vascular involvement. It is known that cavernous transformation of the PV is formed as a bypass route between the splanchnic veins around the obstructed PV and intrahepatic PV; liver cirrhosis (LC), Budd-Chiari syndrome (BCS), and PV thrombosis could have been the probable causes of the transformation [5]. Venous occlusions have generally been seen as the vascular involvement in BD [1-3]. Among cases with venous involvement, thrombophlebitis was observed in 28.2% of cases, while inferior vena cava occlusion was observed in 12.8% [1]. Two reports have described PV involvement. One reported PV involvement in four of 728 vascular BD patients, and the other reported it in one of 66 patients [1, 2]. Therefore, PV involvement might be a very rare manifestation but could cause the transformation after a long-time course of BD.

Granulomas could form in BD. Although there are no specific histological findings in BD, common pathological findings include predominant neutrophil infiltration and perivascular lymphocytic cuffing, while granulomatous inflammation is rare [6-8]. On the other hands, granulomatous orchitis can occur in infectious diseases, such as tuberculosis, syphilis, and brucellosis, or non-infectious diseases, such as sarcoidosis, seminoma, lymphoma, and immunoglobulin G4-related disease [9, 10]. Although IGRA was positive in this case, there was no evidence of tuberculosis infection, and anti-tuberculosis drugs were ineffective. Moreover, there were no signs of other possible causes. Previous reports have suggested that non-caseating epithelioid granulomas were found in colon biopsies or surgical specimens in patients with intestinal BD [11-13]. Another report revealed that 8% of nodular skin lesions contained granulomas [7]. Because the most common findings from these skin biopsies were arterioles and venules inflammation, it appears that granulomas could be related to vascular involvement.

We experienced a patient with BD with cavernous transformation of the PV and granulomatous epididymitis. BD should be considered as a differential diagnosis in cases of refractory uveitis with cavernous transformation even if granulomatous inflammation is detected.

Key points

- In cases of cavernous transformation, Behçet's disease should be included in the differential diagnosis.
- Granulomatous inflammation might be related to vascular involvement in Behçet's disease.

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Figure Legends

Figure 1. Histopathology of epididymitis and orchitis

H&E staining shows the epithelioid granuloma. White arrows indicated multinucleated giant cells.

Figure 2. Cavernous transformation of the portal vein

Contrast-enhanced computed tomography of the portal vein (PV) shows transformation of the extrahepatic PV (white arrow).