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Clinical report

Intestinal Behcet's disease with severe pulmonary arterial involvement mimicking ulcerative colitis

Muhammed Sait Dag[a], Zeynel Abidin Ozturk[b], Irfan Koruk[a], Bunyamin Kisacik[c], Ozan Gerenli[d], Musa Ayd nli[a], Abdurrahman Kadayifci[a]

[a]Department of Gastroenterology, [b]Department of Geriatrics, [c]Department of Rheumatology, [d]Department of Internal Medicine, Gaziantep University, Faculty of Medicine, Gaziantep 27100, Turkey

Background: Behcet's disease (BD) is a chronic inflammatory systemic vasculitic disorder and affects multiple organ systems. Although the prevalence of the disease is high in Turkey, intestinal involvement is rare.
Objective: To report a case highlighting the high risk of mortality as a result of vascular involvement in BD, and suggest classification as a differential diagnosis in intestinal disease and inflammatory bowel disease (IBD).
Method: We report a case of BD in a patient who had symptoms of IBD and was misdiagnosed as having IBD, but later diagnosed as having BD with aneurisms on pulmonary vessels.
Results: A 23-year-old woman was diagnosed with and followed for ulcerative colitis (UC) by another center for one year. She was admitted to hospital with bloody diarrhea, abdominal pain, and weight loss symptoms. There were erythema nodosum-like lesions (ENLL) at pretibial sites and pustular lesions on her upper extremities. Colonoscopy showed nonspecific ulcerations on the colon and terminal ileum and the histopathology was nonspecific. During this period she complained of hemoptysis. Computed tomography (CT) of her thorax showed vascular dilatations in the parenchyma of the lung. CT angiography showed multiple pulmonary arterial aneurisms. She reported a history of recurrent oral aphthous and genital ulcers. A pathergy test was positive and she was diagnosed as having BD with severe pulmonary arterial involvement. Prednisolone (1 mg/kg/day), and cyclophosphamide (750 mg/m^2/month) was administered. At the end of the second week of treatment she showed significant clinical improvement.
Conclusion: IBD symptoms and signs may be the first presentation of BD. Because of the high risk of mortality as a result of vascular involvement, BD must be classified as a differential diagnosis in intestinal disease and IBD.

Keywords: Inflammatory bowel disease, intestinal Behcet's disease, pulmonary aneurism

Behcet's disease (BD) is a systemic, chronic inflammatory vasculitic disease that affects multiple systems and organs [1]. The etiology of BD is not well defined. It is most commonly seen in Mediterranean, far and middle-eastern patients. The highest prevalence is reported from Turkey as being 80–370/100,000 population [2]. Recurrent oral and genital aphthous lesions and uveitis are the classical triad of the disease [1]. As a systemic disease, it can also involve visceral organs such as the gastrointestinal tract, pulmonary, musculoskeletal, and neurological systems. This syndrome can be fatal, as a result of ruptured vascular aneurysms, or severe neurological complications. The classification of BD is mainly dependent on the organs and systems involved, such as intestinal BD or ocular BD. The incidence of intestinal BD is rare in Turkey, as it is in other Mediterranean countries, and is about 1% [3]. Vascular involvement is approximately 25%–30%, but is the major cause of mortality [4]. The dermatological existence of disease varies in a wide spectrum [5]. In this paper we report a case of intestinal BD, which was initially misdiagnosed as ulcerative colitis (UC) with skin signs and symptoms, and had severe intraparenchymal pulmonary arterial aneurysms.

Correspondence to: Zeynel Abidin Ozturk, Universite Bulvary Sahinbey, Gaziantep 27100, Turkey. E-mail: zaodr79@yahoo.com

Case report

A 23-year-old woman was admitted to hospital with fatigue, abdominal pain, and bloody mucous diarrhea with 6–7 movements/day and weight loss. She had a history of bloody and mucous diarrhea for two years and one year ago a colonoscopy was

performed in another center and she was diagnosed as having UC. On admission she was using no medications for UC. Physical examination at the anterior sites of the lower extremities showed nodular, reddish, palpable and painful erythema nodosum like lesions (ENLL) 2–3 cm in diameter. She also had pustular lesions on her the upper extremities and axillary fossae. The pathological laboratory findings were as follows: WBC: 21400/mm^3, Hb: 8 g/dl, platelets: 541,000/mm^3, CRP: 171 mg/l, ESR: 57 mm/h, albumin: 2.5 g/dl. Serum anti-neutrophil cytoplasmic antibody (p-ANCA) and anti-*Saccharomyces cerevisiae* antibody (ASCA) tests were negative. Stool microscopic analysis was normal and there was no bacterial growth in the samples from pustular lesions. Upper gastrointestinal (GI) endoscopy was normal and in lower GI endoscopy terminal ileum and whole colon mucosa were inflamed and edematous, and there were millimetric ulcerations. Biopsies taken from the terminal ileum and rectum were nonspecific and there was no crypt abscess or granuloma formation. Methyl prednisolone was applied at 1 mg/kg/day dose. During her hospital stay the patient had hemoptysis, and thorax X-ray images showed nodular opacities. The computed tomography (CT) of her thorax showed thickened walls of systemic arteries and bilateral saccular and fusiform aneurysmatic dilations in the intraparenchymal pulmonary vascular structures (**Figure 1**). There was partial thrombosis in her axillary veins and wall thickening in the bilateral saphenous veins in the Doppler ultrasound images. She was questioned regarding the other symptoms and signs for BD and we learned that she had arthralgia for six years and recurrent oral aphthous lesions. A pathergy test was positive and ophthalmic examination was normal. The final diagnosis was BD with intestinal and pulmonary arterial involvement. Cyclophosphamide (750 mg/m^2/d) was added to the therapy and symptoms improved in two weeks. She is now asymptomatic and in a follow-up program for at least 9 months.

Discussion

There were no specific laboratory or histopathological findings. The diagnosis of BD depends on clinical symptoms, signs, and findings. The International BD Study Group criteria for the disease are highly sensitive and specific, involving recurrent oral aphthous lesions as a *sine qua non* and positivity of two of the four following items: recurrent genital aphthous lesions, ocular findings, skin lesions, and pathergy test positivity [1]. The GI tract is involved in a wide range (5%–60%) of BD and the main histopathological change is vasculitis of the intestinal wall venules. These changes vary from chronic inflammation to severe ulcers penetrating the serosa or causing perforations [6]. Most commonly, the terminal ileum and cecum are involved, but the other parts of the GI tract can also be affected. The differential diagnosis of BD and inflammatory bowel disease (IBD) is sometimes difficult because of the lack of specific laboratory and clinical findings. It is important to have exact diagnosis for appropriate management of the patient and system involvement. Although ASCA positivity has been reported as 50%–80% in Crohn's disease (CD) and p-ANCA positivity as 60%–80% of patients with UC [7], Filik et al. studied serum p-ANCA and ASCA levels in patients with BD diagnosis and all were negative [8]. Shin et al. showed anti-alpha enolase antibody (AAEA) positivity in 67.5% of patients with BD diagnosis [9]. Lee et al. studied the morphological pattern of the intestinal ulcers and concluded that round ulcers are supposed to be secondary to BD, and longitudinal ulcers are suggestive of CD. Irregular/geographic-shaped ulcers and focal distributions are suggestive of BD, while segmental/diffuse lesions suggest CD [10]. In BD, crypt abscess and granuloma formation are not seen histopathologically, as are seen in UC and CD respectively. In our case both antibodies (p-ANCA and ASCA) were negative and there were no crypt abscess or granuloma formation in pathological specimens. Some of the parameters and variables that can be used for differential diagnosis are listed in **Table 1.**

BD is a unique vasculitis disease and affects different sizes of both arterial and venous vessels. It is commonly seen as aneurysms in the arterial system and thrombosis in the venous system. Eighty-five percent of vascular involvement occurs in the venous system and arterial involvement is relatively rare. The most common type of venous involvement is thrombophlebitis of the superficial and subcutaneous veins. In the arterial system the most common affected vessels are the aorta and then pulmonary arteries. Arterial complications are the major cause of mortality in patients with BD [2,4]. In our patient there was thrombosis in axillary veins and aneurysms in intraparenchymal pulmonary arteries.

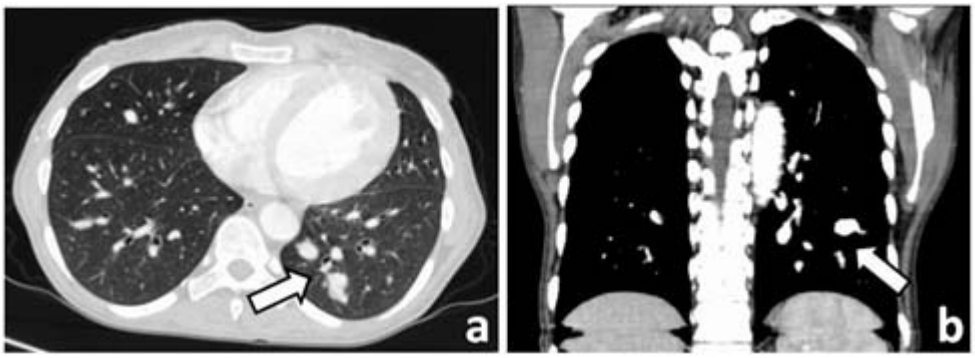

Figure 1. Thorax CT showing bilateral saccular and fusiform intraparenchymal aneurysmatic dilations of pulmonary vascular structures (white arrow) (a) sagittal plane and (b) coronal planes.

Table 1. The parameters and variables used in the differential diagnosis between Behcet's disease and inflammatory bowel diseases

Specifications	Behcet's Disease	Ulcerative Colitis	Crohn's Disease
Bloody diarrhea	±	+	±
p-ANCA	–	+	–
ASCA	–	–	+
AAEA	+	–	–
HLA-B51	+	–	–
Histopathology	Venulitis	Crypt abscess	Granuloma
Endoscopic findings	Round shape, focal ulcers	Granularity, fragility	Longitudinal, segmental ulcers
Involvement (common)	Ileocecal region	Rectum	Terminal ileum

p-ANCA: anti-neutrophil cytoplasmic antibody; ASCA: anti-*Saccharomyces cerevisiae* antibody; AAEA: anti-alpha enolase antibody

Skin lesions are seen in 80% of patients. Erythema nodosum like lesions (ENLL) are submucosal, reddish, palpable, and painful nodular lesions, which are localized on the anterior site of lower extremities. Pustular skin lesions can also be seen in BD and they are all sterile (11). In our patient there were erythema nodosum like lesions; aseptic, sterile, pustular lesions, and pathergy positivity. Pathergy positivity is found in about 60%–70% of patients in Turkey and Japan, which is higher than in patients from other locations [5].

In conclusion, as a vasculitic disease, BD can affect multi systems and organs. Intestinal involvement is relatively rare but it is important—and sometimes difficult—to differentiate from IBD. Because of the higher risk of mortality as a result of vascular involvement, BD must be classified as one of the differential diagnoses in intestinal disease and IBD.

The authors have no conflict of interest to declare.

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