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Case report

# Behçet's disease compared with inflammatory bowel disease. Differences in their clinical presentation

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## Abstract
Behçet's disease is a rare disease with systemic involvement whose main manifestations include the gastrointestinal, neurological, vascular, and articular systems, as well as the skin and eyes. Due to its multisystemic nature, it is often mistaken for other entities such as inflammatory bowel disease since they share multiple characteristics in their clinical presentation. A clinical case is described, and an epidemiological review of clinical manifestations is discussed to have better knowledge that allow identifying it on time.

## Keywords
Behçet's disease, Ulcerative colitis, Inflammatory bowel disease.

## INTRODUCTION

Behçet's disease is a rare type of vasculitis of unknown etiology characterized by the presence of recurrent oral aphthous ulcers and any of their systemic manifestations, including gastrointestinal alterations (1, 2).

The most common clinical presentation is the presence of recurrent mucocutaneous ulcers. However, up to 10% of patients have gastrointestinal manifestations that may be the first symptoms of the disease and, given its heterogeneous clinical presentation, differentiating it from inflammatory bowel disease (IBD) can be a diagnostic challenge to (1, 2).

The following is a case of Behçet's disease, which is discussed through a narrative review, in order to find out what differentiates it from inflammatory bowel disease in terms of clinical manifestations from an epidemiological standpoint and shed light on their unique characteristics.

## CLINICAL CASE

A 61-year-old female patient was admitted to the hospital due to a 6-month history of symptoms consisting of the appearance of erythematous non-pruritic lesions, initially on both knees, which later spread to the thighs, abdomen, and lumbar and gluteal region, that were episodic and

migrating. She also had rectorrhagia, fever, and vaginal bleeding over the same period of time, as well as yellowish liquid stools that became more frequent. All these symptoms worsened two weeks before the consultation. In addition, the patient reported a 4-month history of recurrent oral ulcers and functional class deterioration.

Her medical history included a diagnosis of ulcerative colitis (UC) two months prior to presenting the symptoms, for which she was receiving outpatient treatment with oral mesalazine. According to the patient, the diagnosis was made through colonoscopy; however, she did not have the pathology study available. Physical examination revealed an ulcer with a gray base and a peripheral erythematous halo on the mucosa of the lower lip and 2 ulcers with a gray base on the inner region of the labia minora on the vulva. In addition, erythematous papules and plaques were observed on both thighs. No ocular lesions or findings in the joints were documented.

She was assessed by the internal medicine and gastroenterology services considering an exacerbation of her UC (Truelove 19) with extraintestinal manifestations. A colonoscopy was performed and an edematous, friable, ulcerated mucosa with loss of glandular and vascular pattern and pseudopolyp formation was found in the sigmoid colon. However, while hospitalized, the patient presented hemicranial headache, so studies were performed, leading to the diagnosis of a lobar aneurysm of the right middle cerebral artery. Moreover, she reported chest pain and cardiomyopathy with left ventricular ejection fraction (LVEF) of 38% with healthy coronary arteries.

Considering her clinical progression, the approach to the case was reconsidered and a differential diagnosis of Behçet's disease was proposed, so an HLA-B51 test was ordered, which was negative, as well as a skin biopsy. During her stay, the colon pathology report was received, describing an ulcer with granulation tissue, lymphoplasmacytic and neutrophilic infiltrate with reactive epithelial changes, compatible with active chronic colitis. The biopsy report of the ulcers in the oral and vaginal mucosa described the presence of non-specific ulcers with severe acute and chronic inflammation. Skin biopsy reported interface dermatitis.

Given the clinical difficulty of the case, the dermatology, internal medicine, and gastroenterology services held a meeting, in which it was suggested that the diagnosis of Behçet's disease was more likely based on the patient's multisystemic involvement and the clinical and laboratory findings, which scored 6 points on the International Criteria for Behçet's disease (ICBD). Regarding the patient's progress, cerebral aneurysm was corrected with surgery, heart failure management was initiated and immunomodulatory management with prednisolone, colchicine, azathioprine and mesalazine was continued. This resulted in an adequate clinical evolution and resolution of diarrhea, skin lesions and mucosal lesions, with subsequent discharge. In the rheumatology outpatient follow-up, remission of the disease was observed, with a score of 0 points on the ICBD system.

## DISCUSSION

### General epidemiology

Among inflammatory bowel diseases, UC is the gastrointestinal inflammatory disorder with more extraintestinal manifestations similar to those presented in Behçet's disease (1). Its incidence varies depending on the region, being higher in England, North America and northern Europe, with predominance in individuals aged 15 to 29 years, with no differences between sexes (1, 2). In contrast, Behçet's disease is found primarily along the Silk Road, especially in Turkey, and usually affects young adults between the ages of 20-40 (1).

### Epidemiology of clinical findings

Ocular manifestations are observed in 25-75% of patients with Behçet's disease, (3) with uveitis being the most common in its bilateral and episodic presentation (4). Likewise, 3% of these patients present with conjunctival ulcers (5, 6). On the other hand, in patients with IBD, the most frequent ocular condition is bulbar conjunctivitis, which occurs in 2-5% of patients, and is exacerbated when the disease is active (7). As for uveitis, it may occur in 0.5 to 3% of patients with IBD and more often in women (8).

Regarding manifestations in the joints in patients with Behçet's disease, non-erosive and asymmetric arthritis is observed in 50% of patients (9). In contrast, arthritis is the most common extraintestinal manifestation of IBD, with 3% -10% of them presenting with ankylosing spondylitis. Arthritis in IBD differs from Behçet's disease by the presence of sacroileitis and entesitis (10-12).

With respect to mucocutaneous manifestations, in Behçet's disease up to 50% of patients develop erythema nodosum or erythema nodosum-like lesions (13), which is similar to what happens in IBD, where 40% of patients may present with erythema nodosum as an extraintestinal manifestation (14). Also, in Behçet's disease, most patients develop extensive and multiple oral aphthous ulcers on the tongue, lips, and oral mucosa and, therefore, present with recurrent aphthous stomatitis, with a frequency estimated between 97% and 100%. This contrasts with IBD, in which recurrent aphthous stomatitis has an incidence of 10 % in patients with Crohn's disease (CD) and 4 % in UC (14, 15). Concerning the involvement of the genital mucosa in Behçet's disease, ulcers tend to leave scars, occur in 56.7 %-

97 % of cases and their presence is common in the vulva, vagina and cervix (16). In contrast, IBD does not affect the genital mucosa, and only vulvar involvement has been observed, which appears as erythema, edema, discomfort, and pruritus in the vulva, with only 200 cases described in CD patients (17).

In turn, cardiomyopathy, which can affect any of the heart›s layers, is found in 6% of Behçet›s disease patients. Only 6 cases of myocarditis were reported in a Danish cohort of 15 572 patients with IBD, and epidemiological studies estimated an incidence of cardiomyopathy of 8.3 for CD and 2.6 for UC; in the latter, a significant percentage was associated with mesalazine-induced toxicity, highlighting the fact that cardiac involvement is more common in Behçet›s disease than in IBD (18).

Vascular involvement is one of the leading causes of morbidity and mortality in Behçet›s disease, with a prevalence of 14.3 %, and it is more common in men. Commonly affected arteries are the carotid, pulmonary, iliac and aorta, while involvement of the renal and cerebral arteries is less frequent (4). A 2014 meta-analysis on IBD found a slightly increased risk of stroke (*odds ratio* [OR]: 1.18) with a more evident increase in risk in women and young patients. Cerebral venous thrombosis has also been reported, which is more common in UC patients than in CD patients. The preceding data reveal that IBD has a slight association with thrombotic (arterial or venous) events in the central nervous system, whereas Behçet's disease tends to involve large vessels and has a higher tendency to produce aneurysms (19).

Finally, gastrointestinal involvement in Behçet's disease occurs in approximately 10% of patients and varies according to the region. It can cause abdominal pain, diarrhea, and bleeding, and it is frequently mistaken for IBD. It mainly affects the ileocolonic region, especially the ileocecal area, but it can involve any part of the gastrointestinal tract. However, it always respects the rectum, unlike UC, in which involvement of the rectum is frequent (20).

The international criteria (ICBD) (**Table 1**), the Japanese criteria (**Table 2**), or the criteria of the International Study Group for Behçet's disease (ISG) can be used to diagnose this condition, among other diagnostic criteria described (**Table 3**) (21-23). t should be noted that the three groups emphasize clinical manifestations and not laboratory test results. With respect to tests such as HLA-B51 and pathergy testing, neither is specific or sensitive enough to rule out or confirm the disease. Even the performance of the pathergy test varies depending on ethnicity or geographic location, with a better performance in the Middle East and a performance of only 5% in Caucasian patients (24, 25).

**Table 1.** International Criteria for Behçet's Disease (ICBD) (21)

| Findings | Points |
|---|---|
| Oral aphthosis<br>Genital aphthosis<br>Ocular lesions | 2 points |
| Skin manifestations<br>Neurological manifestations<br>Vascular manifestations<br>Positive pathergy test | 1 point |

Diagnosis with ≥ 4 points

**Table 2.** Japanese Criteria (22)

| | |
|---|---|
| **Major criteria** | |
| Recurrent oral aphthous ulcerations | |
| Skin lesions | |
| Eye injuries | |
| Genital ulcers | |
| **Minor criteria** | |
| Arthritis without deformity or ankylosis | |
| Gastrointestinal lesions attributed to ileocecal ulcers | |
| Epididymitis | |
| Vascular symptoms | |
| Symptomatic nervous system lesions | |
| Positive pathergy test | |
| Pathergy test with prick test for dead Streptococci | |
| Positive HLA-B51 | |
| Laboratory tests consistent with an inflammatory response | |
| **Classification** | |
| Complete | 4 major criteria |
| Incomplete | 3 major criteria |
| | 2 major criteria and 2 minor criteria |
| | Typical recurrent eye symptoms plus a major criterion or 2 minor criteria |
| Suspicion | ≤ 2 major symptoms |
| | Minor criteria that reoccur or worsen in severity |

**Table 3.** Criteria of the international study group for Behçet's disease ISG (23)

| |
|---|
| Recurrent oral aphthosis: major or minor aphtha or herpetiform ulceration observed by the physician or patient, which has recurred at least 3 times in a year |
| Plus 2 of the following: |
| - Recurrent genital aphthosis: Ulceration or scarring observed by the physician or the patient. |
| - Eye lesions: Anterior or posterior uveitis or cells in the vitreous on slit-lamp examination or retinal vasculitis observed by an ophthalmologist. |
| - Skin lesions: Erythema nodosum observed by the physician or patient, pseudofolliculitis or papulopustular lesions, or acneiform nodules observed by the physician or patient in post-adolescent without cortical treatment. |
| - Positive pathergy test |

With regard to similarities in their pathophysiology, it has been reported that when the IL23R and IL12Rb2 regions are expressed on chromosome 1p31.1, the predisposition to develop Behçet's disease increases. These same regions are involved in patients with IBD, and variations of such regions have been linked to the development of IBD. Additionally, both diseases have elevated Th1, Th17, CD4 + and CD8 + activity, suggesting a role of the innate and adaptive immune system in their pathophysiology (1).

## CONCLUSIONS

Since Behçet's disease shares many characteristics with IBD, diagnosing it can be challenging for any physician. As a result, it is critical to know the most common clinical symptoms of these diseases in order to guide it. The presence of ulcers in the genital mucosa, cardiac involvement, respect for the rectum and involvement of large vessels tip the balance toward Behçet's disease in patients with gastrointestinal symptoms in whom it is not clear whether they have IBD.

Given that there is yet no pathognomonic sign that accurately guides its diagnosis, it is critical that publications such as this promote research in this area to find new methods that lead to a faster and more efficient diagnostic approach. Medical history and physical examination continue to play an essential and explanatory role in both disorders.

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