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CASE REPORT

Atypical Intestinal Behçet's Disease Complicated by Latent Tuberculosis Infection

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SUMMARY

Background: **When Behçet's disease is complicated with gastrointestinal ulcers, it is referred to as intestinal Behçet's disease (BD). Clinically uncommon, this condition can involve the entire gastrointestinal tract, often presenting diagnostic challenges in differentiation from Crohn's disease.**
Methods: **In this case, atypical BD was diagnosed through endoscopic examination, whereas latent tuberculosis infection (LBTI) was confirmed via T-SPOT and PPD tests.**
Results: **Methylprednisolone was administered during acute flare-ups to promote rapid ulcer healing. Adalimumab, meanwhile, provided swift treatment for intestinal BD and helped maintain long-term remission in affected patients. Additionally, isoniazid and rifampicin were used for the treatment of LBTI.**
Conclusions: **This case demonstrates the complex and variable clinical course of BD, characterized by highly atypical presentations. As symptoms continue to develop and worsen over time, TNF-α inhibitors play a pivotal role in achieving long-term remission during treatment.**
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KEYWORDS

atypical Behçet's disease, latent tuberculosis infection, endoscopic examination, TNF-α inhibitor

INTRODUCTION

Behçet's disease (BD) is a chronic systemic inflammatory disorder of the blood vessels, affecting multiple organs including the skin, eyes, blood vessels, nerves, gastrointestinal tract, kidneys, joints, and other systems. When BD affects the intestines, it is specifically referred to as intestinal BD [1].

The average annual incidence of intestinal BD in Korea was 0.18 per 100,000 people, with most patients presenting initially with episodic abdominal pain, mainly in the right lower quadrant, and a minority experiencing intestinal bleeding, perforation, perianal abscesses, and intestinal obstruction as initial symptoms [2]. Due to its rarity, distinguishing intestinal BD from inflammatory bowel disease is challenging, as clinical symptoms and

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imaging findings often overlap and specific laboratory tests are lacking.

Clinical manifestations of intestinal BD closely resemble those of Crohn's disease. Traditionally, it has been widely believed that intestinal BD is often misdiagnosed as Crohn's disease but not mistreated. However, intestinal BD carries a worse prognosis, with a higher incidence of complications such as intestinal perforation. Increasing clinical experience and evidence indicate that the diagnosis and pharmacological management of intestinal BD require specific considerations. Distinguishing it from intestinal tuberculosis, intestinal lymphoma, and other immune-mediated gastrointestinal disorders presents diagnostic challenges. In light of these factors, we present a case study detailing the diagnostic journey, clinical treatment plan, and outcomes of one patient with BD. Coupled with a review of pertinent literature, this report aims to enhance healthcare providers' awareness of intestinal BD, thereby facilitating early diagnosis and prompt intervention to aid patient recovery.

CASE PRESENTATION

The patient, a 54-year-old male, was admitted to the department of emergency due to "recurrent oral ulcers persisting for over 5 months, accompanied by fever and one day of abdominal pain." Initial laboratory tests showed a C-reactive protein level of 88 mg/L, hemoglobin level of 95 g/L, and a white blood cell count of 9.72×10^9. Upon hospitalization, additional biochemical tests revealed an erythrocyte sedimentation rate of 94 mm/hour, a ferritin level of 845.1 μg/L, and an albumin level of 29 g/L. An abdominal CT scan indicated inflammatory lesions in the ileocecal region, with multiple enlarged peripheral lymph nodes and an appendicolith present. Colonoscopy findings revealed massive deep ulceration at the terminal ileum and ileocecal valve swelling. Consequently, the patient was treated with acid suppression, antispasmodics for pain relief, and antibiotics for infection. While his abdominal pain has slightly improved compared to before, he continues to experience recurrent episodes of fever.

Further tests revealed positive results for T-cell-based spot (T-SPOT) and purified protein derivative (PPD) skin tests. Additionally, capsule endoscopy indicated ileocecal valve swelling and multiple ulcerative lesions at the terminal ileum (Figure 1). Subsequently, the patient developed nodular erythema on the lower limbs, impairing mobility, and experienced chills and fever around 4:00 PM daily. Consequently, the treatment regimen was adjusted to methylprednisolone injection 40 mg bid IV drip and anti-tuberculosis therapy with rifampicin and isoniazid was initiated. Concurrently, adalimumab injection 160 mg was administered subcutaneously. Following treatment adjustment, the patient's temperature normalized, and abdominal pain improved, leading to discharge.

DISCUSSION

Intestinal BD is a form of vasculitis involving the digestive tract, characterized by distinct lesions. Typically occurring within several years after the onset of BD, its prevalence within BD patients ranges widely from 0% to 60% [3]. The most commonly affected areas include the ileocecal region and colon, followed by the lower esophagus and stomach fundus, with lesions appearing as focal, segmental, or diffuse patterns. The hallmark symptom of intestinal BD is the presence of intestinal ulcers, which can manifest as aphthous, irregular, or solitary large ulcers, either singularly or in multiple formations. These ulcers typically display round or oval shapes, with a clean base and surrounding mucosa that is not swollen, featuring clear boundaries [4]. In some cases, ulcers may appear irregular and longitudinal. Clinical symptoms of intestinal BD often include gastrointestinal manifestations such as nausea, vomiting, anorexia, abdominal pain, bloating, diarrhea, and weight loss. The case discussed in this article involves a 50-year-old male patient presenting with fever, right lower abdominal pain, and other symptoms consistent with intestinal BD. Notably, while intestinal BD symptoms commonly emerge 4 to 5 years after the onset of oral ulcers in BD patients, this case exhibited intestinal manifestations only six months after repeated oral ulcers, which is unusual. The patient's medical history revealed a unique disease progression from anal fistula to carotid artery stenosis, cerebral infarction, oral ulcers, intestinal ulcers, and erythema nodosum. This atypical sequence suggests that anal fistula and vascular disease could also be considered as early manifestations of BD in this case, challenging the conventional pattern where oral ulcers typically precede gastrointestinal symptoms. This variability underscores the need for clinicians to maintain a high index of suspicion for BD and pursue further research into its diverse clinical presentations. In conclusion, this case highlights the variable course of BD and emphasizes the importance of recognizing early signs, conducting thorough evaluations, and initiating timely interventions to effectively manage intestinal BD and improve patient outcomes.

Based on distinctive pathological features, the diagnostic criteria for intestinal BD have been outlined [5]. These criteria emphasize that intestinal BD manifests systemic BD characteristics alongside distinct endoscopic features. In the specific case discussed, oral ulcer symptoms were evident, with subsequent abdominal pain revealing intestinal BD involvement, including a solitary large ulcer in the ileocecal area. Further examinations showed multiple ulcers and inflammatory changes in the terminal ileum, with adjacent mesenteric lymph nodes mildly enlarged. Local ulcers were also observed in the pharynx and left piriform fossa, accompanied by acute and chronic mucosal inflammation. Distinguishing intestinal BD from Crohn's disease and ulcerative colitis presents challenges due to overlapping clinical features such as anal fistulae, ileocecal ulcers,

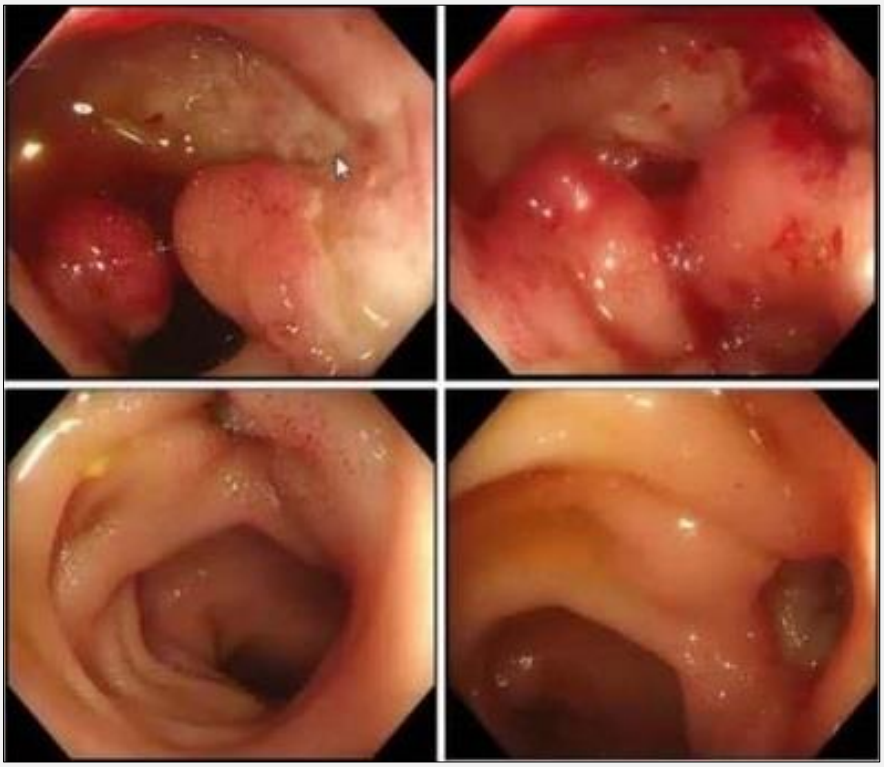

Figure 1. The presentation of capsule endoscopy examination.

oral ulcers, and lower limb erythema nodosum. However, distinctive findings on endoscopy, such as the characteristic solitary large ulcer in the ileocecal area, are indicative of intestinal BD. Additionally, extraintestinal manifestations like vulvar ulcers and skin lesions differentiate intestinal BD from Crohn's disease, with the former showing a predilection for recurrent vulvar ulcers, pseudofolliculitis, acneiform folliculitis, and superficial thrombophlebitis. A retrospective study from Peking Union Medical College Hospital [6,10] highlighted the sensitivity and specificity of vulvar ulcers (85.7% and 94.3%, respectively) and skin lesions (77.1% and 93.4%, respectively) in distinguishing intestinal BD from Crohn's disease. Both conditions primarily affect the ileocecal region, with differences in ulcer characteristics aiding differential diagnosis. Classic intestinal ulcers in intestinal BD are solitary annular ulcers > 2 cm in diameter with distinct margins and occasional ileocecal valve deformities, whereas Crohn's disease ulcers often exhibit a scattered distribution, aphthous or longitudinal shapes, and surrounding mucosal swelling.

Due to unclear pathogenesis, frequent postoperative complications, and high recurrence rates, the primary treatment approach for intestinal BD revolves around medication. These medications aim to manage acute episodes, alleviate inflammation, prevent relapses, and minimize organ damage. Glucocorticoid therapy is considered the frontline treatment during acute phases of intestinal BD, typically starting with an initial dose of prednisolone at 0.5 - 1.0 mg/kg/day. The dosage is gradually tapered by 5 mg per week based on clinical symptoms, with complete discontinuation within three months [7]. Immunomodulatory drugs are employed when patients develop steroid dependence or resistance, aiming to enhance steroid efficacy and reduce dependence [8]. However, the effectiveness and appropriate patient populations for different immunosuppressants vary, and their clinical benefits remain contentious, necessitating further research for clarification. Tumor necrosis factor-alpha (TNF-α) antagonists represent a promising area of research in the pharmacological treatment of intestinal BD. Agents such as infliximab, adalimumab, etanercept, and golimumab have all demonstrated efficacy and safety in the treatment of intestinal BD [9,10].

This case suggested that the clinical manifestations of intestinal BD and laboratory findings are less specific compared to inflammatory bowel disease. The clinical

course is often variable, with patients typically developing gastrointestinal symptoms after recurrent oral ulcers. Endoscopic findings include aphthous ulcers, irregular ulcers, or solitary large ulcers. The possibility of intestinal BD should be considered, and general practitioners need to increase awareness of this condition.

Declaration of Interest:
The authors declared no competing interest.

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