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Case Report

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# Differentiating between Intestinal Tuberculosis and Crohn's Disease May Be Complicated by Multidrug-resistant *Mycobacterium tuberculosis*

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Differentiating between intestinal tuberculosis (ITB) and Crohn's disease (CD) remains a challenge for gastroenterologists. In Asia, where the prevalence of tuberculosis is relatively high and the incidence of CD is rapidly increasing, this issue is crucial. Here we report a case that was initially misdiagnosed as CD, subsequently showed no response to empirical first-line anti-tuberculosis medication, and was finally diagnosed with multidrug-resistant ITB. This case reminds physicians that multidrug-resistant ITB may complicate distinguishing between ITB and CD. **(Ewha Med J 2021;44(3):93-96)**

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**Key Words**
Crohn's disease; Gastrointestinal tuberculosis; Multidrug-resistant tuberculosis

## Introduction

Differentiating between intestinal tuberculosis (ITB) and Crohn's disease (CD) remains challenging for gastroenterologists, although new technologies such as endoscopic molecular imaging have been developed for inflammatory bowel diseases [1]. In contrast to pulmonary tuberculosis (TB), the issue of drug resistance has rarely been addressed in ITB [2,3]. Apart from treatment difficulties, multidrug-resistant (MDR) *Mycobacterium tuberculosis* may complicate the differentiation between ITB and CD.

Here we report the case of a 50-year-old female who was initially misdiagnosed as CD, subsequently showed no endoscopic response to 11-week treatment with first-line anti-TB drugs, and was finally diagnosed with MDR ITB on a drug susceptibility test. In this case report, we aim to remind physicians that MDR ITB may complicate distinguishing between ITB and CD.

## Case

A 50-year-old female with a history of constipation lasting for more than a year visited an outpatient clinic. She had undergone a colonoscopy at another hospital and treatment with 5-aminosalicylic acid under the diagnosis of CD. Her symptom did not improve despite this treatment for about a year. She reported no gastrointestinal symptoms except constipation and denied any respiratory symptoms. She had no history of

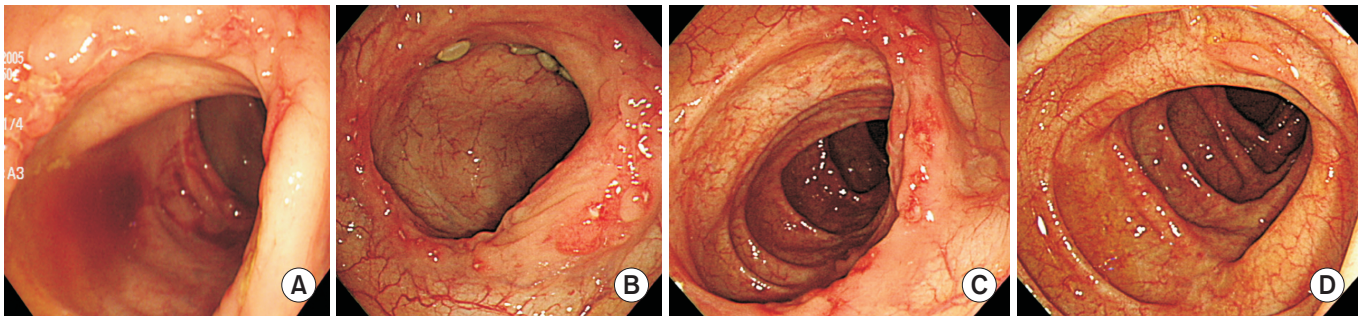


**Fig. 1.** Serial colonoscopy findings. (A) Initial colonoscopy performed in another hospital reveals multiple transverse ulcers in the ascending colon. (B) Follow-up colonoscopy performed 11 weeks after commencement of the first anti-tuberculosis therapy still shows multiple transverse ulcers in the ascending colon. (C) Follow-up colonoscopy performed 25 weeks after commencement of the first anti-tuberculosis therapy still shows multiple transverse ulcers in the ascending colon. (D) Follow-up colonoscopy performed 28 weeks after therapy for multidrug-resistant intestinal tuberculosis shows only scarring and no active ulcers. A written informed consent for publication and use of medical data and images was obtained from the patient.

pulmonary TB. A chest X-ray was unremarkable.

Colonoscopy conducted at the other hospital revealed multiple transverse ulcerations in the ascending colon and no remarkable findings in the rest of the colon (Fig. 1A). Since endoscopic findings corresponded to typical endoscopic features of ITB, empirical anti-TB treatment was initiated with isoniazid 300 mg/day, rifampin 600 mg/day, pyrazinamide 1.5 g/day, and ethambutol 1.0 g/day. At 11 weeks after the commencement of the first-line anti-TB drug treatment, a colonoscopy was performed to evaluate the endoscopic response. Multiple transverse ulcerations were still visible in the ascending colon, suggesting no endoscopic improvement (Fig. 1B). A colonoscopic biopsy was conducted for acid-fast bacilli (AFB) smear, *Mycobacterium* culture, and a PCR test for TB. The AFB smear and TB PCR test results were negative, but 8 weeks after the follow-up colonoscopy, the *Mycobacterium* culture was positive. The first-line anti-TB drugs were continued, and a follow-up colonoscopy was re-implemented for an endoscopic response assessment 25 weeks after the initiation of the anti-TB drugs. Transverse ulcerations were still observed without significant changes in the ascending colon (Fig. 1C).

The *Mycobacterium tuberculosis* drug susceptibility test results reported 26 weeks after the initiation of treatment revealed MDR ITB that was resistant to both isoniazid and rifampin. Treatment for MDR ITB was initiated with a combination of pyrazinamide 1.5 g/day, cycloserine 250 mg/day, moxifloxacin 400 mg/day, prothionamide 250 mg/day, p-aminosalicylic acid 3.3 g/day, and streptomycin 750 mg/day. Her constipation was relieved within weeks of the commencement of treatment for MDR ITB. A follow-up colonoscopy was performed 28 weeks from the initiation of treatment for MDR ITB, and showed only scar change in the ascending colon (Fig. 1D). The treatment continued for 24 months and she was declared completely cured.

## Discussion

ITB and CD are chronic granulomatous diseases that affect the gastrointestinal tract. Since they share similar clinical features and endoscopic findings, differentiating between them remains challenging. As the incidence of inflammatory bowel disease, including CD, is rapidly increasing in Asian countries [4,5], where the prevalence of TB is relatively high, distinguishing ITB from CD is becoming a more crucial issue in Asia. The clinical significance of differentiating between ITB and CD is relatively low in Western countries because ITB is very rare in this area. However, since ITB can develop in immigrants or immunocompromised patients such as those with HIV/AIDS, western physicians should be aware of the issue.

The two diseases require different treatments. Patients with ITB should receive at least 6 months of anti-TB therapy [6], whereas those with CD should receive anti-inflammatory drugs, immunosuppressants, or biologic agents for life [7]. When a confirmative diagnosis is delayed, the treatment failure or chronic complication rates may increase. Although there are several differences in clinical, endoscopic, histologic, radiologic,

and serologic findings between ITB and CD, the only certain ways to diagnose ITB are to identify a caseating granuloma on colonoscopic biopsy, confirm a positive AFB smear, or achieve a positive *Mycobacterium* culture. However, the exclusive features of ITB are observed in limited patients only [2]. To overcome this limitation, diagnostic prediction models by colonoscopic findings were developed, or an interferon-gamma release assay test was used to make the differential diagnosis between ITB and CD [8-11]. However, this test can provide false-negative results and its performance can be decreased by other medications such as immunosuppressants [12]. Despite these diagnostic efforts, in cases in which it is difficult to distinguish ITB from CD, it is considered appropriate to administer empirical anti-TB drugs and evaluate the clinical/endoscopic response in 2 to 3 months [13]. In this way, a differential diagnosis between ITB and CD involves a tough decision-making process.

The emergence of drug-resistant ITB may complicate distinguishing ITB from CD. According to a Korean study of the drug resistance patterns of ITB, 17.6% of patients with ITB displayed resistance to at least one anti-TB drug and 2.7% had MDR ITB [2]. If no response is seen to the empirical administration of the first-line anti-TB drugs, the diagnosis of CD is usually made, but the possibility of MDR ITB remains. Thus, one should not exclude the possibility of MDR ITB, even when the diagnosis of CD is most likely based on no response to the empirical first-line anti-TB therapy. Unfortunately, cases of ITB misdiagnosed as CD have been increasing [14]. Therefore, clinicians must become acquainted with the differences between ITB and CD, and when ITB is suspected, *Mycobacterium* culture of colonoscopic biopsy specimens should routinely be conducted [15].

In summary, differentiating between ITB and CD remains challenging for physicians and may be more complicated by the emergence of MDR ITB. Therefore, for gastroenterologists, it is necessary to figure out the differences between the two diseases. If ITB is suspected, *Mycobacterium* culture of biopsy specimens should be routinely conducted to prevent a diagnostic delay.

## Conflict of Interest Statement

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