

Diagnostic problem on patient with tuberculous colitis mimicking Crohn's disease



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ABSTRACT

Introduction: Tuberculous colitis and Crohn's disease (CD) are two disorders that possess similarities in clinical features and colonoscopy findings.

Case presentation: The patient had previously undergone colonoscopy and mucosal biopsy in this case report, indicating chronic diarrhea and hematochezia. Based on the results from the colonoscopy, the patient was suspected for Crohn's disease. Meanwhile, the collected mucosal biopsy stained with Hematoxylin-Eosin suggested the early diagnosis of CD. Hence, patient was prescribed with sulfasalazine 2x500 mg for 6 weeks, where no clinical improvement was found afterward. Patients still complained nausea, vomiting, frequent diarrhea and bloody stools. The patient was later suspected of intestinal tuberculous and prepped for interferon-gamma release assay (IGRA) and stool Xpert MTB/RIF test. Both of the additional tests suggested that the patient was positive tuberculous. According to the collective facts and findings, the patient was diagnosed with intestinal tuberculous and prescribed with category 1 anti-tuberculosis.

Conclusion: The patient was followed-up after nine months treated with anti-tuberculosis, where the negative result was obtained from the stool Xpert MTB/RIF test. In the following year after the therapy, the patient felt no complaints.

Keywords: Crohn's disease, diagnosis problem, IGRA, tuberculous colitis, Xpert MTB/RIF.

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INTRODUCTION

A public health threat, tuberculosis (TB), has been known the "great imitator" due to its clinical and serological manifestations. Tuberculosis affects 1/3 of the population across countries, mainly in emerging countries. If untreated within 10 years of diagnosis, TB mortality could be high (about 70%).¹ Among 20% of TB cases suffered by immunocompromised patients are extrapulmonary. Tuberculosis could occur at any age, but is rare in children. The disease is more common in young adults and peaks at age 20-40 years old. Around 12% of extrapulmonary TB occurred in abdominal area, where 10% of the cases were reported in population under 10 years old.² Although the ileum is the most frequently affected organ, TB enteritis could affect any organs in gastrointestinal tract.³ Tuberculous colitis was reported in 2% until 3% of patients with abdominal tuberculosis.⁴

Manifestations of tuberculous colitis could be nonspecific and similar to various conditions, including malignancies, making a definitive diagnosis more

difficult. The results of endoscopy and radiographic imaging could be misleading because the results are affected by the severity of the disease which could have been progressed since examination was performed. Therefore, diagnosis can be difficult. Until recently, there was no single method to diagnose intestinal tuberculosis accurately. Multiple investigative techniques have been proposed to facilitate the diagnosis of TB-associated colitis.⁴

Distinguishing between tuberculous colitis and Crohn's disease (CD) could be a serious diagnostic problem. Both of the diseases are chronic granulomatous disorders and share similar clinical manifestations and histopathological characteristics.⁵ Early diagnosis as well as TB treatment and surgical management are important to avoid morbidity and mortality.⁶

CASE PRESENTATION

An 18-year-old woman presented to the emergency department with chief complaints of diarrhea and vomiting, experienced for 3 days before hospitalized

without the presence of mucus and blood. Two weeks earlier, the patient was having nausea and vomiting, hindering the patient to eat and drink, which became worse since the last 7 days. Colic pain in lower stomach was felt by the patients 2 days prior to admission. She admitted for having frequent bloody diarrhea (sometimes only blood) 1.5 years ago, where she required hospitalization and blood transfusion due to anemia. Last bleeding occurred 1 week ago before admitted with around 100 mL blood was found in her stool. Patients also complained of pale, weakness, and fatigue since the last 2 weeks. Patients did not have fever, night sweats, and cough with mucus or blood. Since a year ago, the patient had appetite decreased and experienced 10-kg bodyweight reduction in 4 months.

The patient had past medical history of inflammatory bowel disease that was treated with sulfasalazine 1x500 mg/day and Omeprazole 1x20 mg/day. The conditions were not improved following the 6 weeks of treatment, where she still experienced nausea, vomiting, and bloody diarrhea or bloody stool. The patient received blood transfusion several times



Figure 1. Granulomatous appearance (cobblestone) on mucosal colon on colonoscopic images.

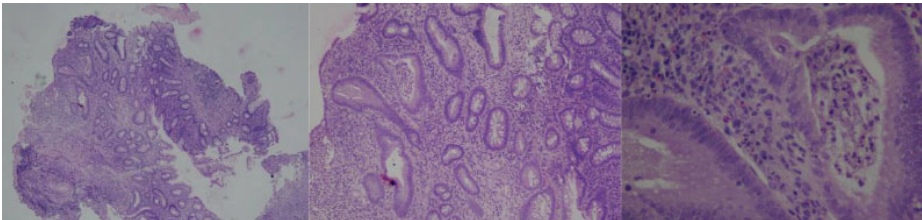


Figure 2. Histologic images with hematoxylin-eosin staining suggesting the presence of chronic colitis suppurative.

due to anemia. Patients declined to have had hypertension and diabetes mellitus. She did not smoke cigarettes, drink alcohol, or consume drugs other than those prescribed by the doctor. No family members had a history of illness similar to that in the patient.

At presentation, the patient was conscious and fatigued. Her vital signs were as follows: blood pressure of 110/70, heart rate of 96 bpm, respiratory rate of 20 cycles/minutes, and body temperature of 36.5°C. The laboratory analysis results were as follows: hemoglobin of 12.6 g/dL, white blood cells of 6790/ μ L, platelets of 297000/ μ L; random blood sugar of 72 mg/dL, serum creatinine of 0.22 mg/dL, blood urea nitrogen of 2 mg/dL, aspartate aminotransferase of 34 U/L, alanine transaminase of 10 U/L, albumin of 3 g/dL, sodium of 123 mmol/L; potassium of 3.6 mmol/L, chloride of 80 mmol/L, HbsAg was non-reactive and rapid human immunodeficiency virus was non-reactive. Electrocardiography suggested normal rhythm. Thorax photo was normal. Colonoscopic results suggested that the patient had inflammatory bowel diseases (Crohn's disease) as presented in [Figure 1](#). Meanwhile, the findings from histopathologic analysis revealed the presence of Colitis Chronic Suppurative ([Figure 2](#))

After receiving sulfasalazine 2x500 mg for 6 weeks, patients did not have any clinical improvement. The patient still complained of nausea, vomiting, frequent diarrhea and bloody stools. She was repeatedly admitted to the hospital and to receive blood transfusion because of anemia. The patient was suspected of intestinal TB and prepped for additional examinations using interferon gamma release assay (IGRA) and stool Xpert MTB/RIF. Results revealed that the patients were positive with TB infection. Based on clinical data, laboratories, and endoscopic results, the patient was diagnosed with tuberculous colitis treated with antituberculosis - category 1. The patient underwent stool Xpert MTB/RIF analysis following the nine-month therapy and declared TB-negative. The patient felt no complaints until 1-year post-therapy.

DISCUSSION

Mycobacterium tuberculosis (TB) remains common in many countries, in which it is capable of affecting multiple organs in the body.⁷ TB could be distributed to the abdomen as well as gastrointestinal tract through a variety of pathways, including gastrointestinal, hematogenous, and directly spreading from other nearby infected structures.² Typically, gastrointestinal tuberculosis might have clinical manifestations such as stomach

pain, weight reduction, diarrhea, fever, or anorexia. Other than that, hematochezia was also found as its manifestation though less common. The ileocecal junction has been reported as the most frequent location for TB-related gastrointestinal involvement and bleeding.^{8,9}

The clinical and colonoscopy indicators of both tuberculous colitis as well as Crohn's disease (CD) are similar. Despite the similarity, their pathogenesis and treatment are different. Appropriate anti-tuberculosis treatment (ATT) could provide a full recovery of tuberculous colitis. However, ATT is ineffective for a progressive and recurrent disease, CD. Therefore, it is important to distinguish tuberculous colitis from other disorders for proper management of the disease.⁹

CD and tuberculous colitis belong to the group of granulomatous enteritis, even though the formation mechanism of granuloma is different from one case to another. Tuberculosis colitis promotes the utilization of lymphocytes and macrophages to escape the host immune system. Nonetheless, a decrease in the intestinal barrier and an increase in antigenic permeability in dendritic cells could trigger excessive immune response concomitant to granuloma formation. The observable caseous granuloma has been assigned as the gold standard for confirmation of tuberculous colitis. Yet, the aforementioned symptoms are observed in only a small percentage of patients (22%), where non-necrotic granulomas could also be found. Therefore, it is necessary to focus on other features that might be more distinctive, such as their distribution, size, as well as number. In particular, tuberculous colitis is observed with multiple granulomas (five or more per site) that are confluent and have large sizes (>400 μ m). As for CD, it appears disorganized, nonconfluent, and small (< 200 μ m) granulomas affecting the mucosa. Other diagnostic indicators tuberculous colitis include irregular inflammation of the superficial submucosa and the appearance of clusters of epithelial cells. Particularly, a study using epithelial cell clusters has a high diagnostic specificity of 94%. Last but not least, methods such as immunohistochemistry (IHC) is reported helpful as it could identify CD73

(a biomarker that is not common in the CD).¹

Though nonspecific, laboratory indicators could have some changes including acute phase reactants (C-reactive protein or erythrocyte sedimentation rate), hemoglobin, albumin, or transferrin saturation. A more recently developed technique, IGRA could detect the interferon gamma produced by lymphocytes following the *M. tuberculosis* infection. It has sensitivity and specificity of 81% and 85%, respectively, with low false-negative when used to analyze samples from immunocompromised patients.¹ However, this test could not distinguish active and latent infections as the consequence of immunosuppressive treatments.¹

Histological diagnosis with Ziehl Nielsen staining revealed the presence of acid-fast bacilli and granulomas, however, less than 30% of biopsies showed bacilli. On the other hand, the sensitivity of real-time polymerase chain reaction (PCR) assay when analyzing colon tissue samples only reached 40-75%.¹⁰⁻¹³ Cultures of colonic biopsy specimens have drawbacks for being financially burdening, while the yielding is low.⁷ In a published report, all cultures were found TB-negative.⁷ Another study also reported a low number of positive results (3 out of 50 intestinal biopsies).⁷

Alternatively, PCR assays for *M. tuberculosis* (PCRMTB) could be performed on intestinal mucosa samples or stool samples. Some studies have investigated the diagnostic performance of PCRMTB, but received different results depending on the type of the sample. In one study, the sensitivity and specificity of PCRMTB on fecal sample reached 79% and 88%, respectively.¹⁰ However, in another study using intestinal mucosal samples, these numbers were dramatically different, where the sensitivity and specificity were 6.1% and 100%, respectively.¹¹

When it comes to imaging diagnosis of CD, computed tomography (CT) is recommended to evaluate its intra and extraluminal pathology. Regardless the dilatation of proximal intestine, thickened concentric wall of ileocecal junction in CT images is the widely utilized as a CD characteristic. In the case of TB,

lymphadenopathy in the abdomen could be observed in CT images that primarily involved the mesentery, superior and inferior regions of the paraaortic, peripelvic, and pancreaticoduodenal regions.¹²

In determining TB colitis, at least one of these followings should be found: (1) evidence of acid-fast bacteria (AFB) on smear or histology; (2) microbiologically or histologically confirmed tuberculosis at extraintestinal organs; (3) culture positive for acid-fast bacilli; (4) presence of granulomas on histopathology (intestinal, peritoneal, colon or lymph nodes); and (5) positive PCRMTB results.^{5,13} High suspicion should be put on cases where results from laboratory, endoscopy, and histological examinations suggest the TB colitis with addition of sensitivity against anti-tuberculosis drugs.^{5,13}

ATT is highly efficacious to treat patient with intestinal tuberculosis. In order to get the successful outcome from the treatment, patient's compliance is required. Usually, the treatment takes 9 months to complete, though recent findings revealed that 6-months treatment is sufficient.^{14,15} However, the 9-months treatment duration is recommended.¹⁴ There is an increased trend of drug-resistant *M. tuberculosis* contributing to the high rate of recurrency and persistence. A published case series reporting 30 TB colitis patients found a high prevalence of multi drugs resistant TB (13% of the total patients).¹²

CONCLUSION

It has been reported, an 18 years old female patient with chief complaints of chronic diarrhea and recurrent hematochezia. Initial diagnose for this patient was inflammatory bowel disease (Crohn's disease). No clinical improvement was observed following the 6-weeks treatment with sulfasalazine 2x500 mg. After that, the patient underwent several examinations namely colonoscopic with biopsy, histologic analysis, IGRA test, and stool Xpert MTB/RIF. Based on the clinical feature, physical examination, laboratories, colonoscopic and histologic findings, patient was then diagnosed having tuberculous colitis. The patient was treated with first-line ATT for nine

months. The patient experienced clinical improvement after the therapy and no complain after 1-year post-therapy.

PATIENT CONSENT

The patient had agreed and signed informed consent regarding publishing this clinical case in an academic journal without exposing the patient's identity.

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DISCLOSURE OF CONFLICTS OF INTEREST

The authors declare no conflict of interest regarding the manuscript.

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AUTHOR CONTRIBUTION

Both authors contributed equally to the study.

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