

Crohn's Disease in a Patient with Tuberculosis: A Diagnostic and Therapeutic Challenge

Santiago Revelo-Moreno,¹ Luz Daniela Gómez-Suta,² Jairo Alfredo Guevara-Guzmán.³

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¹ Physician, Internal Medicine specialist, Universidad Tecnológica de Pereira, Colsubsidio SURA Medical Center (PAC). Bogotá, Colombia

² Physician, Internal Medicine resident, Universidad Tecnológica de Pereira. Pereira, Colombia.

³ Physician, Internal Medicine, Gastroenterology, and Digestive Endoscopy specialist, Universidad Militar Nueva Granada. Professor of Gastroenterology, Universidad Tecnológica de Pereira, Gastro Elite S. A. S. Pereira, Colombia.

Correspondence: Santiago Revelo-Moreno.
sanrevmor@gmail.com

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Abstract

Introduction: Crohn's disease (CD) is unusual in Colombia. Tuberculosis (TB) occurs more frequently, but intestinal involvement is rare. Differentiating these two entities and treating the cases in which they coexist is a challenge. **Clinical case:** A 28-year-old man with three months of constitutional, respiratory, and GI symptoms was initially diagnosed with pulmonary tuberculosis, and all the clinical manifestations were attributed to this entity. Given the absence of improvement with treatment and the sum of radiological, endoscopic, and pathological findings, CD was confirmed. Treatment was complex due to the coexistence of the two entities, although he finally went into remission with the use of biologicals. **Discussion:** Diagnosing CD requires the sum of clinical and paraclinical findings. A therapeutic test may be necessary to differentiate it from intestinal TB. The treatment of CD in a patient with TB has some limitations; steroids are not contraindicated, and biologicals must be initiated cautiously. **Conclusions:** Differentiating CD from intestinal TB is a diagnostic challenge. Therapeutic management when these two entities coexist requires an interdisciplinary approach.

Keywords

Crohn's disease, tuberculosis, differential diagnosis.

INTRODUCTION

Crohn's disease (CD) is part of the inflammatory bowel disease, and its manifestation is rare in Colombia: an incidence of 0.74 per 100,000 people per year⁽¹⁾. Meanwhile, tuberculosis (TB) is a more frequent entity, with an incidence of 22.6 to 28.9 cases per 100,000 inhabitants⁽²⁾, but intestinal involvement is uncommon; it only represents 3.5% of extrapulmonary tuberculosis cases⁽³⁾. Intestinal TB mainly affects the terminal ileum and cecum. It may result in the formation of ulcers and fistulas⁽⁴⁾, and in histopathological studies, granulomas can be found. It is one of the primary differential diagnoses in patients with suspected CD⁽⁵⁾.

Differentiating these pathologies represents a high level of complexity not only from a diagnostic point of view but also from a therapeutic one since some treatments, such as biologicals, may increase the risk of infections⁽⁶⁾. We present the case of a patient with pulmonary TB and CD.

CLINICAL CASE

A 28-year-old man presented with a 3-month clinical picture of abdominal pain and bloody, non-fatty diarrhea, which woke him up and persisted despite fasting. In the systemic inquiry, he reported occasional cough and involuntary weight loss of 30 kilograms in the last 3 years.

Personal and family history was negative. A chest X-ray and CT scan were performed, suggesting TB; this entity was confirmed by bronchoalveolar lavage samples with Ziehl-Neelsen stain, PCR, and positive cultures, with no evidence of drug resistance. Colonoscopy showed colitis and ileitis with histopathology findings of chronic nonspecific ileitis and chronic nonspecific colitis with a focal active component. Due to the clinical context of pulmonary TB and with a high index of suspicion, intestinal TB was diagnosed, so the patient was administered rifampicin, isoniazid, pyrazinamide, and ethambutol.

After 6 months, his respiratory and constitutional symptoms improved, but he was admitted to the hospital due

to persistent abdominal pain and diarrhea. Adherence to antituberculous therapy was confirmed, and microbiological studies for TB were negative. The laboratory tests detected fecal calprotectin of 2,060 $\mu\text{g/g}$ (**Table 1**) and the magnetic resonance enterography (MRE), intestinal sub-occlusion in the ileum (**Figure 1**). A new ileocolonoscopy identified cecal folds, appendiceal orifice, and ileocecal valve with severe edema covered by ulcers, easy bleeding, and edema involving the proximal ascending colon. In addition, biopsies were taken that reported inflammatory bowel disease with chronic ulceration and granulomas (**Figure 2**). The diagnosis of CD was made with a Crohn's disease activity index (CDAI) of 421

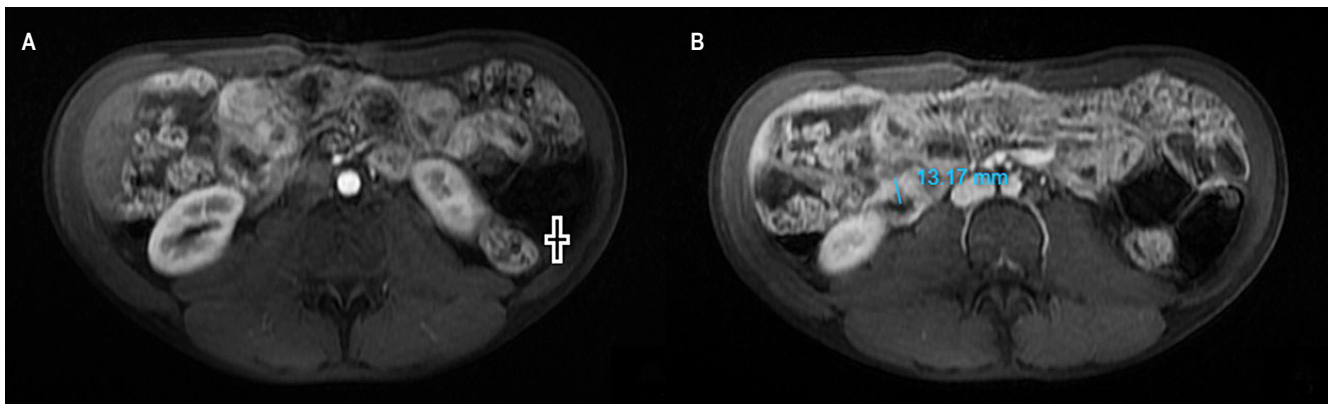


Figure 1. MRE with contrast. **A.** In the arterial phase: thickening of the ileus (+). **B.** In the portal phase: thickening of the ileum with a wall of 13 millimeters. Image owned by the authors.

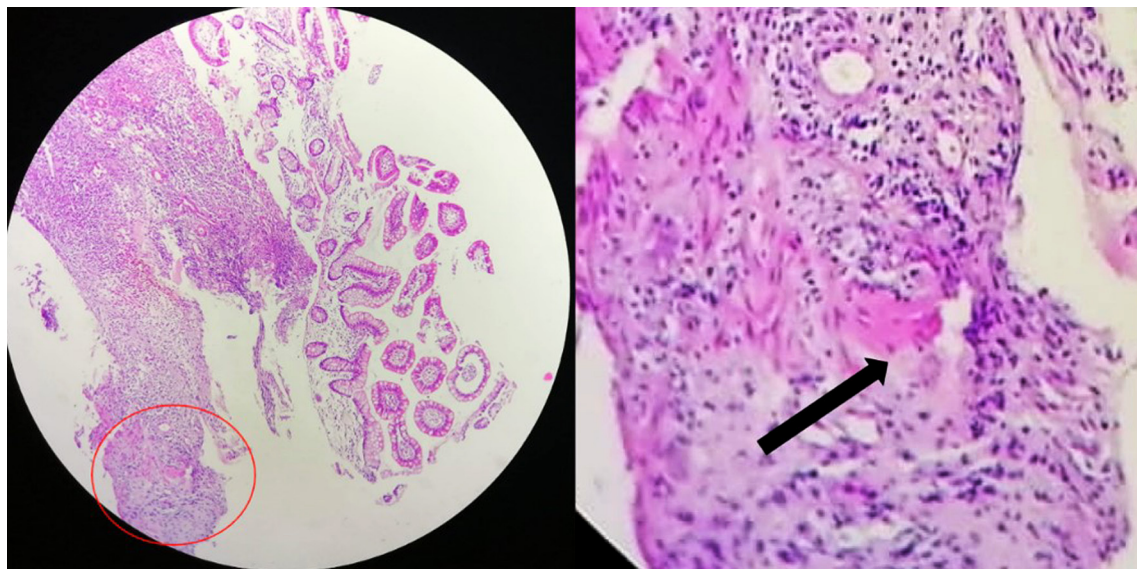


Figure 2. Biopsy: colon mucosa; in the submucosa, there is a non-necrotic, non-caseating granuloma with incipient multinucleated giant cells. Circle: granuloma. Arrow: giant cell. Image owned by the authors.

Table 1. Patient laboratory findings

Study	Result
Blood count	Leukocytes: 9.98×10^3 IU/L, neutrophils: 8×10^3 IU/L, lymphocytes: 1.2×10^3 IU/L, hemoglobin: 9.2 g/dL, MCV: 89 fL, RDW: 19.1 %, PLT: 503,000
Albumin	2.82 g/dL
Fecal calprotectin	2,060 $\mu\text{g/g}$
HIV 1 and 2 antibodies	Negative

PLT: absolute platelet count; RDW: red cell distribution width; MCV: mean corpuscular volume; HIV: human immunodeficiency virus. Table owned by the authors.

points. Controversially, corticosteroids were postponed, starting treatment with azathioprine.

A month later, he consulted for abdominal pain, so a new CT scan was performed, which reported enteritis in the jejunum, pneumoperitoneum, and collections. He was taken to a laparotomy, noting obstruction of the proximal and distal small intestine, granulomas in the middle of the small intestine, perforation of the middle jejunum with a plastron that compromised the distal ileum, and a fistulous tract. An intestinal resection and anastomosis were performed. Once TB treatment was completed, biological therapy was started with adalimumab up to a maintenance dose of 40 mg subcutaneously every 2 weeks. The clinical

evolution was favorable; 1 year later, he attended an outpatient gastroenterology check-up on clinical remission and without complications, and a new colonoscopy showed no alterations (**Figure 3**).

DISCUSSION

CD usually occurs between the second and fourth decades of life, as in the present case⁽⁷⁾, with a certain predominance in women⁽⁸⁾. The patient had no risk factors, such as family history or smoking⁽⁹⁾.

In the case presented, the constitutional and respiratory symptoms led to a rapid diagnosis of TB, which could explain the gastrointestinal findings as an extrapulmonary manifestation. However, given the persistence of symptoms despite having implemented anti-tuberculosis therapy, CD was considered a differential diagnosis.

Although controversial and reserved for very selected cases, when there is confusion between CD and TB in countries where TB is frequent, some authors recommend a therapeutic trial with anti-tuberculosis drugs to corroborate the clinical improvement at 3 months and healthy mucosa at 6 months in almost 100% of patients with TB⁽¹⁰⁾, which did not occur in this patient. In addition, the MRE, histopathology, and laboratory findings, such as elevated fecal calprotectin (with approximate sensitivity and specificity of 90% and 80%, respectively)^(11,12) allowed the diagnosis of CD.

The patient had a moderate CDAI; steroids would be indicated⁽¹³⁾, but they were not started since the patient was finishing the second phase of treatment for TB. It

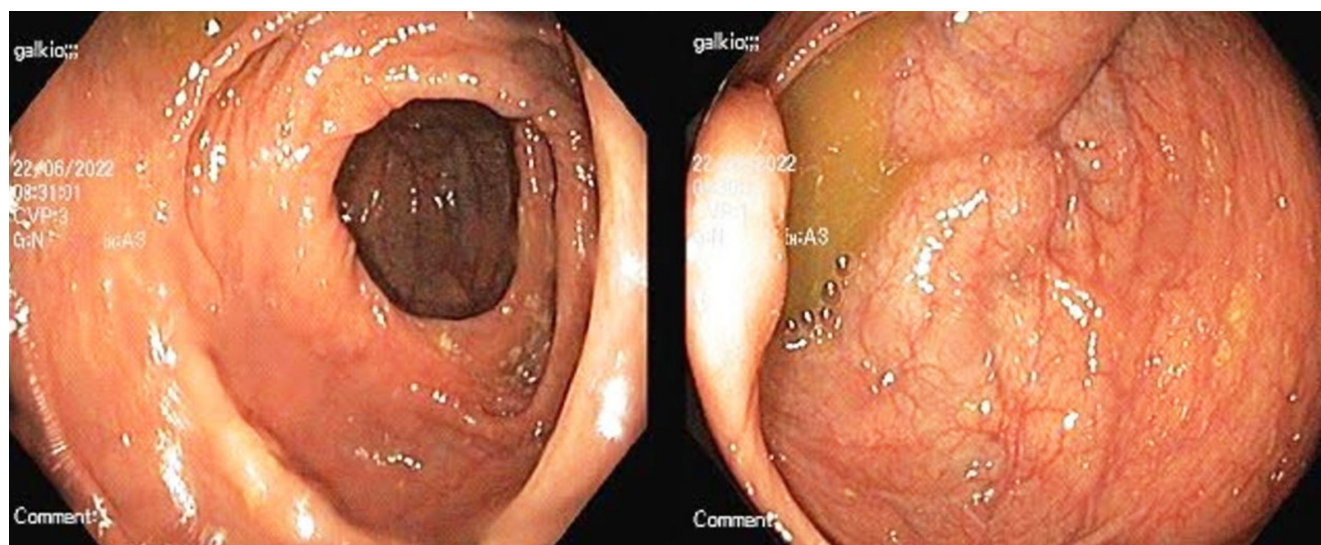


Figure 3. Colonoscopy images of the patient without evidence of disease activity. Image owned by the authors.

should be clarified that steroids in doses greater than 15 mg of prednisolone each day confer an odds ratio of 7.7 for infections. However, this is not an absolute contraindication to starting them in cases like this⁽¹⁴⁾. Azathioprine is an alternative, although it does not induce remission of an active disease. Another option to consider, since it is a man under 35 years of age, would have been methotrexate to avoid the increased risk of hepatosplenic lymphoma due to thiopurines, but it is not recommended for the induction of remission of the disease⁽¹³⁾.

The patient had a stenosing and penetrating complication of CD. This event and being under 30 are risk factors for recurrence, which occurs in up to 84% of post-surgical cases⁽¹⁵⁾. It was decided to start biological therapy; vedolizumab, an antibody against $\alpha 4\beta 7$ integrin, has shown benefit in CD⁽¹⁶⁾ and even good tolerance without an increase in the risk of opportunistic infections compared to placebo⁽¹⁷⁾. Even so, no evidence supports it as a first-line medication since it does not seem superior for the induction or maintenance of remission compared to other biologics⁽¹⁸⁾. Thus, and adding to the complications and high risk of the patient, anti-tumor necrosis factor (anti-TNF) was started, which

was a difficult decision since infliximab, for example, has shown a relative risk of 18.6 for TB activation⁽¹⁹⁾. There is no clarity on when to start anti-TNF in TB. Still, case series show safety in those with an evident clinical response, drug susceptibility results, and who have completed the first two months of the intensive anti-tuberculosis phase^(19,20).

Patients like this require multidisciplinary management where not only the gastroenterologist but also other specialties such as pulmonology, infectious disease, internal medicine, and coloproctology supervise their treatment.

CONCLUSION

The diagnosis of CD in a patient with TB is difficult due to the similarity of intestinal involvement between these two entities. The difficulty is also therapeutic since beneficial treatments for CD, such as steroids, can be omitted, and the start of biological therapy can be delayed. Considering the contraindications of these drugs and applying algorithms that allow the two entities to be differentiated is of great clinical use to improve outcomes and avoid complications.

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