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INTESTINAL TUBERCULOSIS, A CHALLENGE IN CLINICAL PRACTICE: CASE REPORT

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Abstract: Introduction: Intestinal tuberculosis is an uncommon form of extrapulmonary presentation of the disease. Some groups of individuals are at greater risk of developing this pathology, and high suspicion must be maintained based on epidemiological risk factors associated with symptoms and complementary tests with a focus on early treatment. **Goal:** To report a case of intestinal tuberculosis and its diagnostic difficulty. **Case description:** This is a 62-year-old man, initially presenting with abdominal pain and weight loss, being diagnosed with human immunodeficiency virus infection. He evolved with diarrhea and hematochezia, which led to a lower digestive endoscopy. Initial findings compatible with cytomegalovirus infection, however, without improvement after treatment and in the control exam, it showed a change in the histopathological characteristic favoring the diagnosis of intestinal tuberculosis. **Conclusion:** The heterogeneity of the clinical presentation requires a high degree of suspicion combined with epidemiological risk factors for early diagnosis and treatment.
Keywords: Intestinal tuberculosis, extrapulmonary tuberculosis, mycobacterium tuberculosis, crohn's disease, diagnosis.

INTRODUCTION

Mycobacterium tuberculosis is the causative agent of tuberculosis (TB), an infectious disease that traditionally affects the lung parenchyma (pulmonary TB). However, this microorganism can also infect other tissues (extrapulmonary TB)[1]. According to data from the World Health Organization (WHO), in 2020 tuberculosis ranked 13th among the causes of death in the world, with 1.5 million deaths. In addition, 10 million cases were diagnosed[2].

It is estimated that extrapulmonary TB accounts for 20% of tuberculosis cases. And of these, 10% are cases of intestinal tuberculosis (TBI)[1]. Although a minority of patients develop the disease, approximately a quarter of the world's population has latent tuberculosis.[3] On the other hand, people living with the Human Immunodeficiency Virus (HIV), diabetics, smokers, high alcohol consumption, malnourished, have a higher risk of developing the disease.[2]

The diagnosis of TBI is a major challenge in medical practice, since it can mimic several intestinal conditions, such as inflammatory bowel diseases, lymphomas, solid tumors and even other infectious diseases. Therefore, the high degree of suspicion is essential for early diagnosis and reduction of morbidity and mortality.[1,4,5]

CASE REPORT

Male patient, 62 years old, started with abdominal pain, weight loss of 7 kg over 4 months. He sought care at a local emergency health unit, culminating on 12/08/20 in hospitalization for diagnostic investigation and symptom control. He had a history of systemic arterial hypertension and was a former smoker and former alcoholic, both habits stopped about 6 months before hospitalization.

He presented positive serology for HIV, diagnosed during his hospitalization. Antiretroviral therapy (ART) with tenofovir (TDF), lamivudine (3TC) and dolutegravir (DTG) was started on 12/16/20. During hospitalization, he reported constipated intestinal rhythm, with bowel movements every 3 days, dry stools (Bristol 2) and evacuation effort. He was evaluated by the coloproctology team, who identified a topical anus, extensive left lateral plicoma on physical examination, rectal examination with a normotonic sphincter, but with irregular mucosa and the presence of fresh blood. In view of this, he underwent flexible

rectosigmoidoscopy (RSCF) on 12/30/20: It was visualized in the rectum, at the level of the first valve of Houston, mucosal retraction covered by fibrin and friable to the touch of the device, affecting approximately 40% of the circumference. Biopsies were performed with cold forceps. Examination on 01/25/21 showed an HIV viral load of 47 copies; CD4 119 cells.

The patient was discharged due to stability and clinical improvement, being advised to return for follow-up and biopsy recovery in 30 to 45 days. However, due to the context of the COVID-19 pandemic, the patient did not follow up as instructed. Biopsy rescue in electronic medical record with histopathology evidenced: Ulcerated chronic granulomatous rectitis, presenting loose granulomas with multinucleated giant cells; cryptitis; ulceration; loss of parallelism; rarefaction of glands. Negative microorganism research. Coloration: HE, PAS, Grocott and Fite-Faraco.

Still analyzing the electronic medical record, a new passage was observed on 07/07/22 with a description of urinary focus sepsis in dialysis urgency (Cr 4.78; K 7.8; Ur 160; Hb 8.2; Leukocytes 27,000 with a 14% deviation from rods; platelets 543,000). He was then transferred to the intensive care unit (ICU) on 7/8/22. As it is from a private network unit, associated with the public sector, we do not have access to the medical records of this period. The patient was discharged from the ICU on 8/2/22, returning to the hospital of origin. He evolved with diarrhea and hematochezia on 08/08/22, when the RSCF biopsy taken in 2020 was rescued.

Therefore, a new opinion from Proctology was requested. When evaluated on 08/11/22, the patient was already using metronidazole due to possible pseudomembranous colitis (recent hospitalization, age over 60 years and use of broad-spectrum antibiotic therapy). He had watery diarrhea, without mucus, with hematochezia, with about 3 episodes a day. On physical examination: anoscopy showed mucosa with edema, friability and hyperemia.

A new RSCF was performed on 08/12/22 up to the descending colon, which macroscopically showed no alterations. Rectum with great friability to the passage of the device, presence of large ulcerations covered by fibrin, with loss of the submucosal vascular pattern. Conclusion: Severe distal colitis. Dosage of HIV viral load with 255 copies and CD4 210 cells (08/16/22). In view of the new endoscopic evaluation, hydrocortisone 100mg was prescribed every 8 hours from 08/21 to 08/26, with improvement in symptoms.

Only on 08/27/22 was the patient transferred to the infectology care unit of our unit, in which we, the gastroenterology team, began the joint follow-up of this patient.

Complementary exams collected on 08/29/22 showed: negative viral hepatitis serologies; negative VDRL; Leishmaniasis negative; Histoplasmosis negative; Negative cryptococcus; PCR for cytomegalovirus (CMV) 2686 copies and RSCF histopathology performed on 08/12 (09/16/22): marked neutrophilic activity; ulceration; cytopathic changes consistent with viral action by CMV; foreign body giant cells. Coloration: HE. He also underwent contrast-enhanced computed tomography of the abdomen: Thickening with parietal hyperenhancement of the rectum and sigmoid colon and small amount of free fluid. Other structures without relevant findings.

A few days after transfer, the patient had a recurrence of diarrhea, on average 6-8 episodes per day, Bristol 7, hematochezia and abdominal pain 7 out of 10. With positive PCR for CMV and compatible pathology, ganciclovir was started on 09/15 and performed 14 days of medication. However, the symptoms persisted despite the

instituted treatment. In view of the clinical maintenance, he underwent a colonoscopy on 10/14/22: Examination performed after digital dilation of stenosis in the lower rectum, up to the terminal ileum, in good preparation conditions (Boston 9), whose macroscopic appearance has signs of villous atrophy. The ileocecal valve is unchanged. Presence of scar-like nodulation measuring approximately 4 mm, smooth surface, reddish color and radial neovascularization in the ascending colon (Figure 1), biopsy was performed. Presence of diverticular ostia in the cecum and ascending colon, wide base, without signs of inflammation or bleeding. The mucosa of the entire rectum has an intense inflammatory process (Figure 2), circumferential, extending for about 15cm, with the presence of a mucosal lesion characterized by ulcers, friability and bleeding when passing the device.

Based on the findings, the infectology team recommended empirical treatment for lymphogranuloma venero with doxycycline, performed for 21 days without improvement. Close to the end of the instituted treatment, the histopathological result of the colonoscopy was ready: ileus with usual-looking mucosa; ascending with architectural distortion, loss of parallelism and glandular rarefaction in addition to intense inflammatory infiltrate with a predominance of mononuclear cells and frequent plasmocytes; descendant with the presence of large granulomas, multinucleated giant cells, epithelioid histiocytes and lymphocytes; normal-looking mucous sigmoid; rectum with architectural distortion, loss of parallelism, ulceration with exuberant granulation tissue and numerous plasma cells. NOTE: Microorganism research using special stains was negative. Coloration: HE, PAS, Grocott, Fite-faraco.

On this occasion, after persistence of symptoms despite the treatments instituted, the gastroenterology team recommended empirical treatment for intestinal tuberculosis. Then, on 11/11/22, the RIPE regimen (rifampicin + isoniazid + pyrazinamide + ethambutol) was started. IGRA was also performed on 11/15/22 with a negative result. In the first 10 days, hematochezia reduced, persisting with diarrheal bowel movements with Bristol 6. Between the 14th and 18th day, there was a reduction in the frequency of bowel movements from 6-8 bowel movements per day to 4 bowel movements a day. He was discharged on 12/24/22, with 2 bowel movements a day, bristol 5, no blood or mucus.

Patient returned for consultation on 01/24/23, using medication regularly, reporting 1-2 bowel movements a day, bristol 4, without blood or mucus. The infectology team changed the ART regimen to zidovudine (AZT) + 3TC + DTG, due to the HIV/TBI co-infection and, at first, maintenance of the TB treatment with a planned duration of 9 months. Endoscopic reassessment scheduled in 3 months.

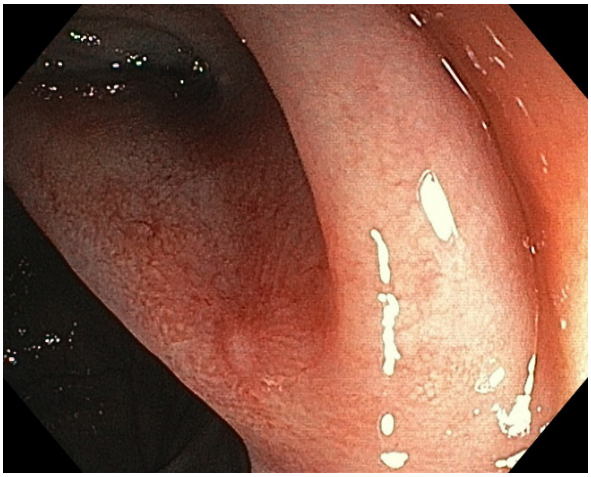
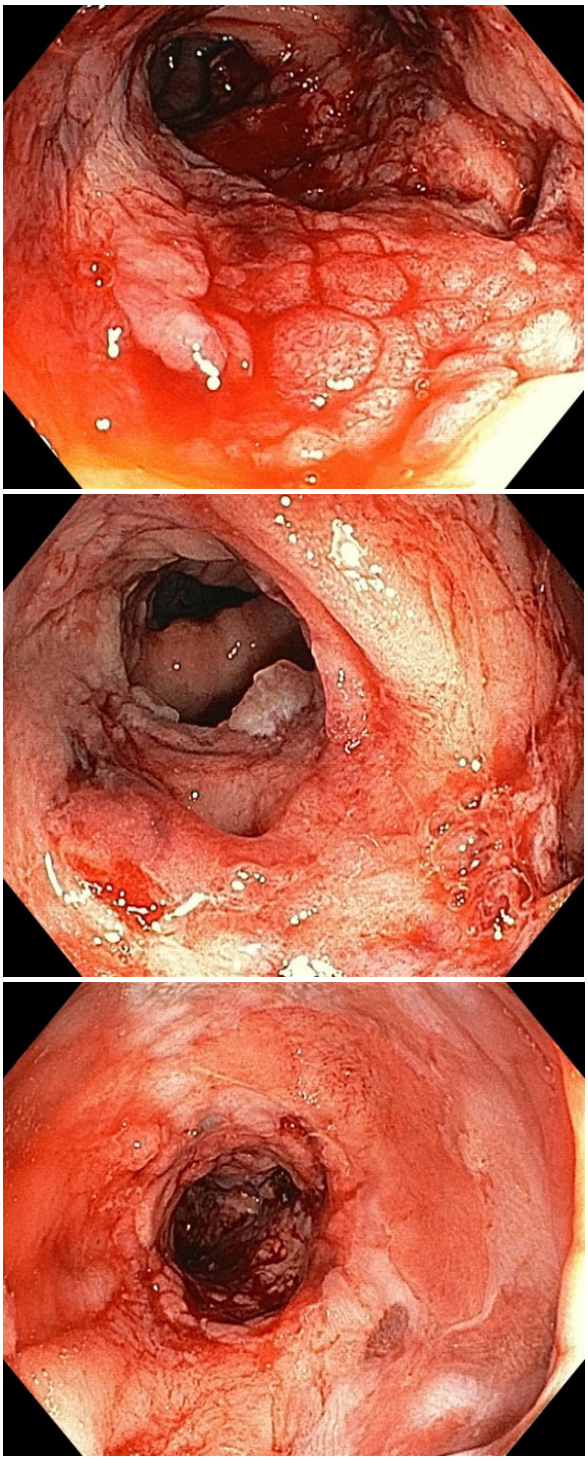


Figure 1. Area of isolated hyperemia in the cecum.



Figures 2A, 2B and 2C. Deep rectal ulcerations, semicircumferential and transverse aspect, colonic.

DISCUSSION

Intestinal tuberculosis is an uncommon presentation of extrapulmonary TB. The signs and symptoms, in general, are nonspecific and depend on the location, with the main manifestations: abdominal pain (76%-88%), weight loss (50%-80%), fever (43%-80%), diarrhea (11%-37%) and hematochezia (5%-15%) [1,6,7]. The most common site of involvement is the ileocecal region (25%-90%), followed by the small intestine (6%-67%) and colon (2%-32%).[7].

There are multiple complementary exams available to aid in the diagnosis of TBI, however, all of them have limitations. Among the options, with their respective sensitivities (S.) and specificities (E.), we have: the culture of *M. tuberculosis* (S. 9.3% and E. 100%); staining of acid-alcohol-fast bacilli (AFB) by the Ziehl Neelsen method (S. 17.3%-31% and E. 100%); histopathological (S. 68% and E. 77.1%); Biopsy tissue GeneXpert (S. 81%-95.7% and E. 91%-100%); interferon-gamma release assay known as IGRA (S. 74%-88% and E. 74%-87%); polymerase chain reaction (S. 21.6%-65% and E. 93%-100%); multiplex-polymerase chain reaction (S. 77.5%-87.5% and E. 96.4%-100%)[1,8,9].

One of the biggest challenges in the gastroenterologist's clinical practice is the differentiation between Crohn's Disease (CD) and TBI. And this distinction is of paramount importance, as sometimes the treatment of CD involves the use of immunosuppressive medications that have the potential to spread the infection. Several studies have already been carried out exposing the most common clinical, radiological, endoscopic and histopathological findings of each of the two pathologies in order to assist the differential diagnosis, in an assertive way. [5,8,10-13].

Morphologically, intestinal tuberculosis has the potential to present ulcerative and ulcerohypertrophic lesions, and the two types may coexist[14]. Among the endoscopic findings that favor TBI, cecal involvement, transverse ulcers and patulous ileocecal valve

stand out, while the presence of longitudinal ulcers, aphthous ulcers, parallelepiped appearance, luminal stenosis, jumpy lesions, rectal and sigmoid involvement collaborate for dc [8,11,15].

Histopathological findings such as the presence of confluent, large and multiple granulomas, caseous necrosis; submucous granuloma; ulcer lined by histiocytes and epithelioids are more characteristic of ITB. In CD, the findings draw little attention, highlighting architectural distortion distant from granulomatous inflammation and intensified focal colitis [8-13].

The combination of nonspecific clinical presentation, tests with low sensitivity and also the limited availability of diagnostic modalities, contribute to the great challenge that is TBI. In our case, the infectology team recommended the use of an antituberculin regimen for 9 months. There are studies that demonstrate the equivalence of treatment times of 6 and 9 months, with no difference in disease recurrence. However, we still lack studies to support and validate the ideal treatment time [16,17].

The clinical response after initiation of antituberculostatic therapy is usually rapid, around 4 to 8 weeks. However, at the beginning of therapy, there may be a worsening of the stenoses and, consequently, of the symptoms due to the formation of scar tissue in response to the treatment. After this period, the lack of response must lead to a strenuous investigation to exclude other pathologies. As for the endoscopic response, a period of 8 to 12 weeks seems to be necessary for early evaluation and confirmation of a presumptive diagnosis. [18,19]. Delay in diagnosing TBI increases the risk of complications requiring a surgical approach, such as the intestinal obstruction, perforation, fistula, major bleeding [4,14,20].

In the case of our patient, some limitations contributed to the delay in diagnosis and early initiation of appropriate treatment. Among the factors we can mention: the time to be referred to our service, which has multidisciplinary professionals; confounding factor for CMV infection; indisponibilidade de alguns exames complementares e demora na liberação de resultados devido a grande demanda que o serviço público possui.

CONCLUSION

Intestinal tuberculosis is a challenging condition that has the ability to mimic several intestinal pathologies, especially in immunocompromised patients. Added to this, we still have limitations regarding complementary diagnostic tests and their low availability. Therefore, high suspicion is essential for early diagnosis and treatment in order to reduce the morbidity and mortality of these patients.

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