

Case Report

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Fatal Case of Disseminated Tuberculosis in a 24-year-old Male Patient with Crohn's Disease: A Case Report

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Abstract

Introduction: Crohn's disease (CD) is an idiopathic disorder involving the GI tract. The differential diagnosis of CD is broad and includes infectious colitis, ulcerative colitis, intestinal TB (iTb), etc. Due to the lack of standards in a definitive diagnosis, discrimination between iTb and CD has long been a diagnostic challenge.

Case presentation: A 24-year-old male patient, known to have Crohn's disease, treated with daily prednisone 60 mg and mesalamine since 1 week (due to a flare-up), presented for 2 days history of severe exacerbating diffuse abdominal pain, along with generalized weakness, weight loss, watery diarrhea, vomiting, decreased oral intake, and high-grade fever (39 °C). An urgent abdominopelvic CT scan with IV contrast showed significant pneumo-peritoneum and minimal fluid distributed inside the abdomen, denoting bowel perforation. The patient underwent an urgent laparotomy. Intraoperative findings were an abdominal cavity full of fecal material, multiple small bowel perforations, and entero-enteric fistulas. 1.5 meters of the small intestine was resected. Pathology showed iTb. TB PCR of deep tracheal aspirate was positive as well. The patient was started on anti-TB treatment for disseminated tuberculosis affecting the lungs and GI tract. Unfortunately, the patient developed a septic pulmonary embolism on day 7 post-op and was pronounced dead on day 9.

Conclusion: Our case emphasizes that the two chronic granulomatous diseases (CD and iTb) have similarities that make the distinction between them difficult and yet crucial because of possible repercussions of a misdiagnosis. It also highlights the importance of latent TB screening before starting the confirmed CD immunosuppressive treatment especially in underdeveloped countries, as the patient could have a reactivation of latent TB upon initiation of immunosuppressive therapy.

Keywords: intestinal TB, Crohn's disease, concomitant diagnosis, active pulmonary TB, disseminated TB, iTb and CD, case report

Background

Crohn's disease (CD) is an idiopathic inflammatory disorder involving the gastrointestinal (GI) tract, transmurally, in genetically predisposed individuals [1]. It presents usually with chronic abdominal pain, weight loss, bloody or mucoid stools, and chronic diarrhea [2]. The differential diagnosis is wide and includes ulcerative colitis, infectious colitis, and intestinal tuberculosis (iTb). Due to the lack of standards in its definitive diagnosis, discrimination between CD and iTb constitutes a diagnostic challenge [3].

iTb is generally secondary, due to a disseminated primary pulmonary TB caused by *Mycobacterium tuberculosis*. However, it may also be primary and associated with *Mycobacterium bovis* instead [4].

iTb and CD have close mimicry 1) *clinically*, both presenting with abdominal pain, fever, fatigue, and weight loss; 2) *endoscopically*, showing similar mucosal inflammation that can affect any part of the GI tract and mainly involving the ileocolonic region; 3) *radiologically*, through similar intestinal findings on CT scan, [5] 4) *and histopathologically*, through their granulomatous formations [6].

CD differs mainly by having a longer duration of symptoms and perianal disease, symmetric wall thickening with mural stratification, fatty changes, and absence of lymphadenopathy or ascites on the CT scan. iTb is more characterized by strictures and hypertrophic lesions but rarer anorectal influences than CD, which has the pathognomonic cobblestone appearance. Furthermore, granulomas in iTb tend to be bigger in size better organized, caseated and near the affected mucosa [5, 7].

CD has an incidence ranging from 1.4 to 1.66/100,000 in Middle Eastern countries, whereas the incidence of TB in Lebanon has reached 20/100,000 (attributed to nonnational populations), and a study conducted in the Middle East showed that 15.8% of TB patients had gastrointestinal involvement [5].

In this article, we report the case of a 24-year-old male CD patient presenting with an acute abdomen. The patient underwent an urgent laparotomy, and was found to have iTb on pathology, however, despite starting anti-TB treatment, he developed complications and died postoperatively. This case emphasizes the importance of distinguishing between the two chronic granulomatous disorders because of the possible repercussions of a misdiagnosis. It also sheds the light on the importance of latent TB

screening before starting the confirmed CD immunosuppressive treatment, especially in high TB incidence populations.

Case Report

A 24-year-old male Syrian refugee patient, known to have CD, diagnosed by colonoscopy and pathology 18 months ago, presented for 2 days history of severe diffuse exacerbating abdominal pain - that was present in the previous 20 days but milder. He also reported generalized weakness, non-documented weight loss (for 6 months), decreased oral intake, watery, non-bloody and bilious diarrhea 3-4 times per day, and high-grade fever of 39° C. He was on daily prednisone (60 mg) and mesalamine (a salicylate preparation) for 1 week before presentation due to exacerbation of symptoms that was diagnosed as a CD flare-up. He had no family history of CD and no TB-ill contacts.

The physical exam revealed a pale disheveled patient with tachypnea (22 breaths/min), tachycardia (107 beats/min), and hypotension (97/64 mm Hg; baseline of 120/85 mm Hg). The patient was afebrile (36.5°C). He had a rigid, mildly distended, and diffusely tender abdomen.

Labs showed a low hemoglobin level of 7 gm/dL (LLN 14 gm/dL), neutrophilia 93.4% (UNL 60%), and an elevated CRP 197 mg/L (UNL 3mg/L).

An urgent abdominopelvic CT scan with IV contrast (Fig. 1) showed significant pneumoperitoneum denoting bowel perforation. The stomach and small bowel loops, mainly the jejunum, were distended, reaching a diameter of 5 cm. A transition zone was noted around the proximal to mid-ileum. Mild mural thickening of the cecum and the distal ileal loops was noted along with fibro-stenotic changes, most likely causing proximal bowel dilation, in keeping with the patient's history of CD. Minimal fluid was seen in the peri-splenic, para-colic, and pelvic spaces, with extensive mesenteric congestion, fat stranding, and multiple sub-centimetric mesenteric lymph nodes.

Chest X-ray (Fig 2) done in the ER as a preoperative protocol showed bilateral multiple nodular opacities mainly in the upper lobes with possible cavitations, and a CT chest was recommended to exclude coexisting active TB.

The patient underwent urgent laparotomy. Intraoperative findings were an abdominal cavity full of fecal material, multiple small bowel perforations (Fig. 3), entero-enteric fistulas and adhesions. As such, 1.5 meters of small bowel was resected and sent to pathology, and an



Figure 1: Abdominopelvic CT scan with IV contrast: pneumo-peritoneum (red arrow), distended jejunum (yellow arrow), and thickened bowel wall (blue arrow)

ileostomy was performed. The patient was extubated, and left the operating room in a stable condition and was transferred to the intensive care unit (ICU) for observation and medical treatment. During his ICU stay, he was on tazocin (piperacillin/tazobactam) 4.5 g IV every 6 hours, enoxaparin 40 mg subcutaneous once daily and pain killers. His post-operative course was smooth, but he had a sudden respiratory deterioration on day 7, was intubated again, and an urgent CT chest angiography (Fig. 4) showed a septic pulmonary embolus and cavitory lesions on the upper lobes of both lungs.

Deep tracheal aspirate TB PCR was done and revealed positive. The pathology report showed diffusely ulcerated intestinal mucosa with multifocal caseation and few epithelioid with a

Ziehl-Neelsen stain presenting numerous acid-fast bacilli (AFB) and negative for Periodic Acid Schiff (PAS), Gracott's and Gram stains (Fig. 5A).

Final pathology revealed Small intestinal tuberculosis (Fig. 5B). The patient was started on anti-TB treatment. Unfortunately, he was declared dead on day 9 post-operation due to a septic pulmonary embolus.

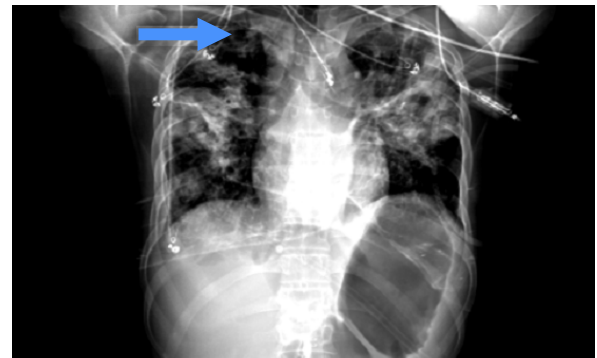


Figure 2: Chest X-ray showing bilateral multiple nodular opacities mainly in upper lobes with possible cavitations (blue arrow).

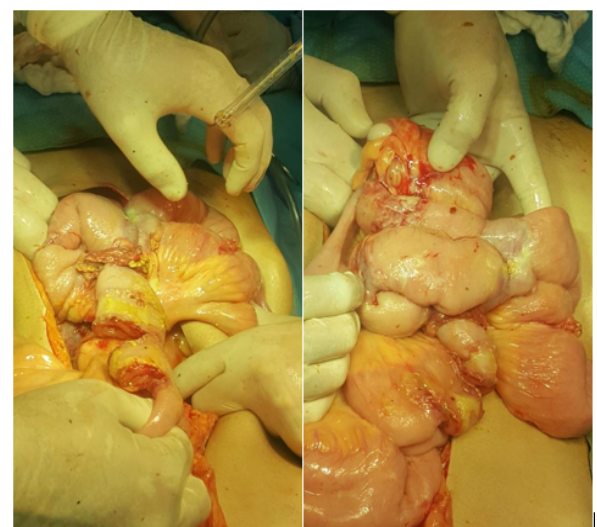


Figure 3: Multiple ileal perforations seen intraoperatively

Discussion

Tuberculosis (TB) infection affecting the GI tract is considered to be the sixth most common extra-pulmonary site of TB infection, with a significantly higher prevalence in men than women, whereby the ileocecal region is the most common site [5,10,11]. Abdominal Tuberculosis (aTB) must be considered in patients with pulmonary tuberculosis (pTB) and abdominal pain, knowing that it is common for aTB and pTB to coexist (67.1%) [11, 12]. CD is a chronic inflammatory and granulomatous disorder with transmural

inflammation of the GI tract, which shows similar clinical, endoscopic and histopathologic features to iTB, with misdiagnosis rates ranging from 50-70% due to the difficulty to differentiate between them, making it a diagnostic challenge to physicians [1, 4].

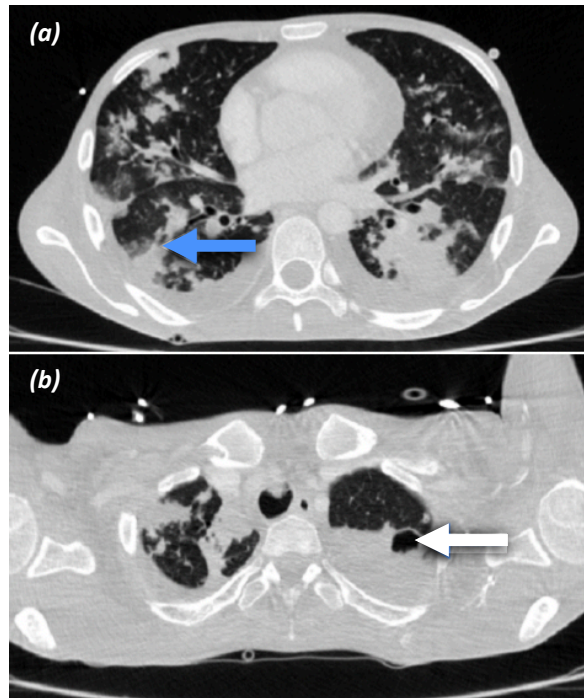


Figure 4: (a) CT chest showing the septic embolus (blue arrow) and the pleural effusion as well as (b) a cavitary lesion in the left upper lobe (white arrow)

This explains why our patient may have been misdiagnosed as having a CD flare, instead of an iTB. Performing a Ziehl Neelsen stain does not always help when seeking a diagnosis between CD and iTB, even in a high-incidence area of tuberculosis (TB), because only around 50% of tuberculosis cases will turn out positive for mycobacteria; and while a positive result confirms iTB, it doesn't rule out the presence of a concomitant CD [3].

The histological findings with Ziehl Neelsen stain in the case of our patient who was known to have CD (confirmed on pathology 18 months ago) confirmed the diagnosis of concomitant iTB (Fig.2).

To better assess and diagnose a patient with CD or iTB, the use of TB PCR in combination with histopathologic results and immunohistochemistry helps to raise the sensitivity in differentiating iTB from CD and aids in confirming the diagnosis [13, 14].

Oral prednisone is used for inducing remission in patients with moderate-to-severe active Crohn's disease as was the case in our patient before presenting to our emergency department, whereas intravenous corticosteroids are used in severe fulminant CD. In the absence of improvement, anti-TNF α (infliximab) is the next step in management [8]. Before starting infliximab or intravenous corticosteroids, latent TB must be ruled out, because immunosuppression resulting from CD treatment makes a patient more susceptible to new infections or reactivation of latent TB [9].

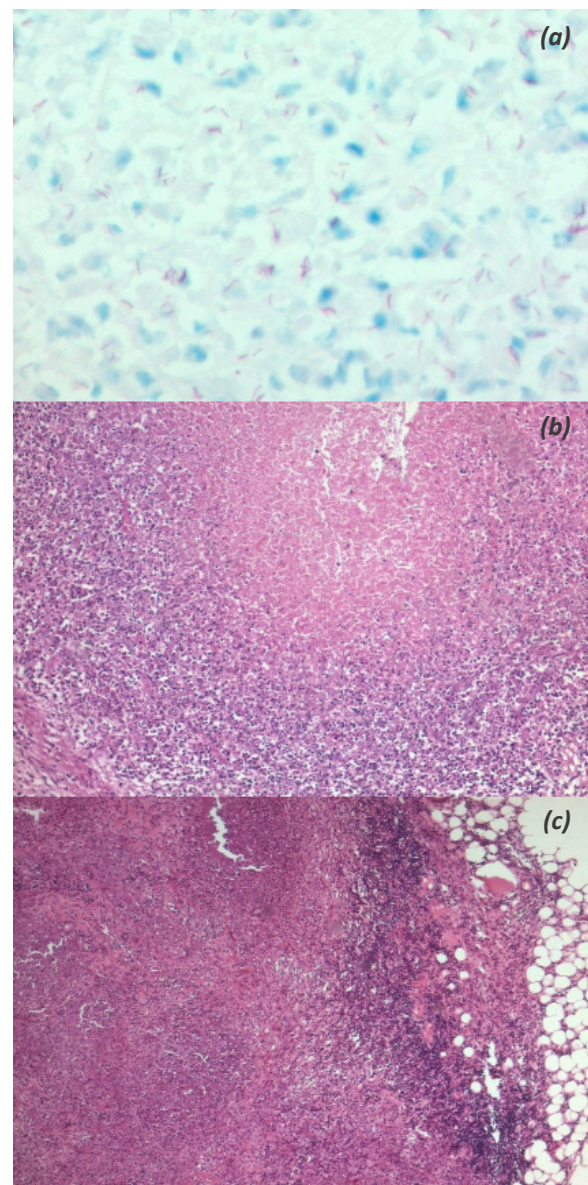


Figure 5: (a) Acid Fast Bacilli X40 (pink rods), (b) caseous necrosis X10, & (c) Involved mesenteric lymph node

Mesalamine, on the other hand, has showed benefits in ulcerative colitis maintenance of remission treatment; no great benefit was

reported in CD except in mild-to-moderate cases [8].

The misdiagnosis between CD and iTB may result in toxicity from unnecessary anti-TB treatment and delay in CD treatment. On the other hand, treating an iTB patient, misdiagnosed with CD, by steroids alone, exposes the patient to high rates of morbidity (obstruction, perforation, and hemorrhage) and mortality [15]. This describes what happened in the case of our patient who had a delay in diagnosis of disseminated concomitant TB, and ended up with multiple small bowel perforations and death. As such, a close follow-up for symptoms improvement and screening of TB before definitive CD treatment may help to differentiate iTB from CD flare-ups and decrease the consequent morbidity and mortality.

Conclusion

The diagnostic challenge between CD and iTB and their similarity is reiterated by the case of this 24-year-old patient who was misdiagnosed with a CD flare-up instead of iTB, which lead to multiple small bowel perforations complicated by a septic embolism and resultant mortality. This emphasizes the importance of ruling out iTB and performing latent TB screening before starting any CD immunosuppressive treatment, together with close follow-up of clinical symptoms improvement of a CD flare-up, especially in underdeveloped countries.

References

1. Cho JH. The genetics and immunopathogenesis of inflammatory bowel disease. *Nat Rev Immunol*. 2008 Jun;8(6):458-66. <https://doi.org/10.1038/nri2340> . PMID: 18500230.
2. Tontini GE, Vecchi M, Pastorelli L, Neurath MF, Neumann H. Differential diagnosis in inflammatory bowel disease colitis: state of the art and future perspectives. *World J Gastroenterol*. 2015 Jan 7;21(1):21-46. <https://doi.org/10.3748/wjg.v21.i1.21> PMID: 25574078; PMCID: PMC4284336.
3. Zhou D, Ouyang Q, Xiong M, Zhang Y. Crohn's disease with positive Ziehl-Neelsen stain: Three case reports. *Niger J Clin Pract*. 2018 Oct;21(10):1387-1390. PMID: 30297577.
4. Ng SC, Hirai HW, Tsoi KK, Wong SH, Chan FK, Sung JJ, Wu JC. Systematic review with meta-analysis: accuracy of interferon-gamma releasing assay and anti-Saccharomyces cerevisiae antibody in differentiating intestinal tuberculosis from Crohn's disease in Asians. *J Gastroenterol Hepatol*. 2014 Sep;29(9):1664-70. <https://doi.org/10.1111/jgh.12645> . PMID: 24910240.
5. Almadi MA, Ghosh S, Aljebreen AM. Differentiating intestinal tuberculosis from Crohn's disease: a diagnostic challenge. *Am J Gastroenterol*. 2009 Apr;104(4):1003-12. <https://doi.org/10.1038/ajg.2008.162> . Epub 2009 Feb 24. PMID: 19240705.
6. Ma JY, Tong JL, Ran ZH. Intestinal tuberculosis and Crohn's disease: challenging differential diagnosis. *J Dig Dis*. 2016 Mar;17(3):155-61. <https://doi.org/10.1111/1751-2980.12324> . PMID: 26854750.
7. Patel N, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S, Gupte P. Gastrointestinal luminal tuberculosis: establishing the diagnosis. *J Gastroenterol Hepatol*. 2004 Nov;19(11):1240-6. <https://doi.org/10.1111/j.1440-1746.2004.03485.x> . PMID: 15482529.
8. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018 Apr;113(4):481-517. <https://doi.org/10.1038/ajg.2018.27> . Epub 2018 Mar 27. Erratum in: *Am J Gastroenterol*. 2018 Jul;113(7):1101. PMID: 29610508.
9. Miller M, Vu KN, Zemek A, Shelton A, Kin C. TB or Not TB: Crohn's Disease, Peritoneal Tuberculosis, or Both? *Dig Dis Sci*. 2019 Jun;64(6):1432-1435. <https://doi.org/10.1007/s10620-018-5334-7> . PMID: 30334111.
10. Marshall JB. Tuberculosis of the gastrointestinal tract and peritoneum. *Am J Gastroenterol*. 1993 Jul;88(7):989-99. PMID: 8317433.
11. Cheng W, Zhang S, Li Y, Wang J, Li J. Intestinal tuberculosis: clinico-pathological profile and the importance of a high degree of suspicion. *Trop Med Int Health*. 2019 Jan;24(1):81-90. <https://doi.org/10.1111/tmi.13169> . Epub 2018 Nov 8. PMID: 30338607.
12. Papadakis KA, Targan SR. Tumor necrosis factor: biology and therapeutic inhibitors. *Gastroenterology*. 2000 Oct;119(4):1148-57. <https://doi.org/10.1053/gast.2000.18160> . PMID: 11040201.
13. Ince AT, Güneş P, Senates E, Sezikli M, Tiftikçi A, Övünç O. Can an immunohistochemistry method differentiate intestinal tuberculosis from Crohn's disease in biopsy specimens? *Dig Dis Sci*. 2011 Apr;56(4):1165-70. <https://doi.org/10.1007/s10620-010-1399-7> . Epub 2010 Sep 8. PMID: 20824497.
14. Jin XJ, Kim JM, Kim HK, Kim L, Choi SJ, Park IS, Han JY, Chu YC, Song JY, Kwon KS, Kim EJ. Histopathology and TB-PCR kit analysis in differentiating the diagnosis of intestinal tuberculosis and Crohn's disease. *World J Gastroenterol*. 2010 May 28;16(20):2496-503. <https://doi.org/10.3748/wjg.v16.i20.2496> . PMID: 20503449; PMCID: PMC2877179.
15. Seo H, Lee S, So H, Kim D, Kim SO, Soh JS, Bae JH, Lee SH, Hwang SW, Park SH, Yang DH, Kim KJ, Byeon JS, Myung SJ, Yang SK, Ye BD. Temporal trends in the misdiagnosis rates between Crohn's disease and intestinal tuberculosis. *World J Gastroenterol*. 2017 Sep 14;23(34):6306-6314. <https://doi.org/10.3748/wjg.v23.i34.6306> . PMID: 28974897; PMCID: PMC5603497.