

Intestinal Tuberculosis as First Manifestation of Human Immunodeficiency Virus (HIV) Infection. A Single History Snapshot

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Abstract

A 33-year-old man was admitted in 1999 because of abdominal pain, fever, and weight loss. After a presumptive diagnosis of acute complicated appendicitis, laparotomy was carried out. Since cecum and terminal ileum showed a 'carcinomatous appearance' ileocecal resection and right hemicolectomy were performed. Pathological assessment revealed the presence of acid-fast bacilli which were later identified as *Mycobacterium tuberculosis*. There was no evidence of neoplasia. As the patient had been intravenous drug user and had absolute lymphopenia, Human Immunodeficiency Virus serology was requested after surgery, with the result being positive. The patient was placed on standard antituberculous therapy and was discharged. However, he decided to stop quickly the treatment and was readmitted 3 month after discharge because of fever and cervical lymphadenitis. Culture of a neck lymph node sample grew *Mycobacterium tuberculosis*. This time, the patient took appropriately antituberculous drugs and also initiated antiretroviral treatment. Except for some diarrheic episodes, he has remained well throughout the follow-up period (from June, 1999 to December, 2013). It is well known that there is no such thing as an easy diagnosis of intestinal tuberculosis, even nowadays. We have just tried to remember it.

Keywords: Appendicitis; Intestinal tuberculosis; *Mycobacterium tuberculosis*; Crohn's disease; Human Immunodeficiency virus

Background

Intestinal involvement is a well known signature of *Mycobacterium tuberculosis* infection [1,2]. However, since clinical presentation of intestinal tuberculosis (TB) usually masquerades as other conditions such as Crohn's disease, malignancies, and several infectious entities, the diagnosis may become a true clinical challenge [1,3-6]. Additionally, it seems the incidence and severity of abdominal TB is increased in Human Immunodeficiency Virus (HIV)-positive individuals [1,2]. We describe a case of intestinal tuberculosis in a patient initially diagnosed with acute complicated appendicitis. Following surgical intervention, serologic testing for HIV infection revealed to be positive. Considering that the progress toward TB elimination will require ongoing surveillance and improved TB control, the present case could help clinicians to keep in mind such an objective.

Case Report

A 33-year-old man presented to the emergency department in June, 1999 for abdominal pain, daily fever, weight loss, anorexia, and fatigue over the last 3 weeks. He drank alcohol in moderated amount. On examination he was afebrile and had normal vital signs. There was increased pain upon palpation on the right lower quadrant of the abdomen, where a lengthened mass-like formation was appreciated. Slight parietal muscular spasm and rebound tenderness were evident in the same localization. Lymphadenopathy was absent. Laboratory values were relevant for a white blood cell count of 4,900/ μ L and a mild elevation of gamma-glutamyltransferase. Chest radiography displayed normal findings. A subsequent abdominal ultrasonography revealed appendicular and ileocecal mural thickening, a possible periappendiceal collection, and mesenteric lymph nodes enlargement. As the surgery consultant had a strong suspicion that acute complicated appendicitis could be present, the patient was brought to the operating room for urgent intervention. Surprisingly, besides macroscopic signs of appendicitis, the cecum and terminal ileum showed a 'clear

carcinomatous appearance'. This finding prompted the surgeon to perform ileocecal resection and right hemicolectomy with end-end ileocolonic anastomosis (Figure 1). Pathologic study confirmed the presence of non-perforated appendicitis but also revealed numerous ulceroinflammatory, stenosing lesions occurring in terminal ileum, cecum, and ascending colon. There was no evidence of neoplastic disease. However, multiple necrotizing granulomas with Langhans type giant cells and acid-fast bacilli were demonstrated in appendix, ileum, cecum, right colon, and mesenteric lymph nodes (Figures 2-5). Culture of intestinal tissues was not asked for. Then, an internal medicine physician was consulted about what to do next. Given that he

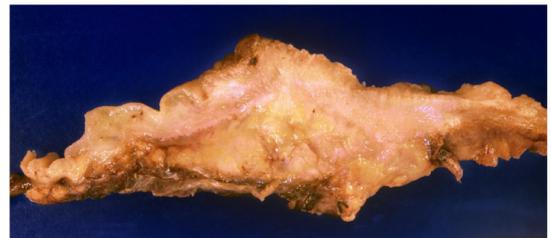


Figure 1: Macroscopic view of the resected intestinal segment (ileocolic specimen, 12 cm length).

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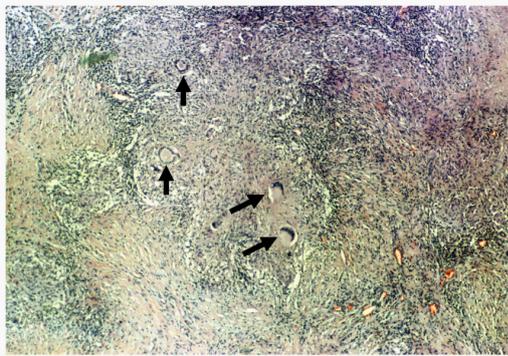


Figure 2: Bowel biopsy demonstrating granulomas with Langhans type giant cells (arrows) (hematoxylin-eosin staining, original magnification X40).

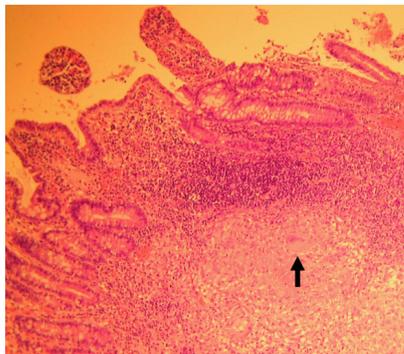


Figure 3: A more detailed view of intestinal biopsy showing a granuloma with a Langhans type giant cell (arrow) (hematoxylin-eosin staining, original magnification X400).

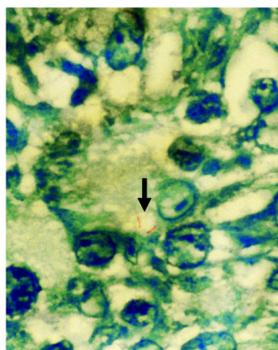


Figure 4: Two acid fast bacilli in a biopsy sample of intestinal tissue can be appreciated (arrow) (Ziehl-Neelsen staining, original magnification X1000).

had been an intravenous drug user and had absolute lymphopenia on admission (500 lymphocytes/ μL), HIV serology was requested with the result being positive. CD4+ cell count and HIV plasma RNA level were 10/ μL and 6,570 copies/mL, respectively.

Taking into account the concurrent clinicopathological features and that TB is a highly prevalent infection in Spain [7], the patient was placed on standard antituberculous therapy. The patient, however, demonstrated fluctuant reluctance to medical advice which raised some doubts about adherence to our preventive and therapeutic recommendations. That is why no planning of antiretrovirals (ARVs)

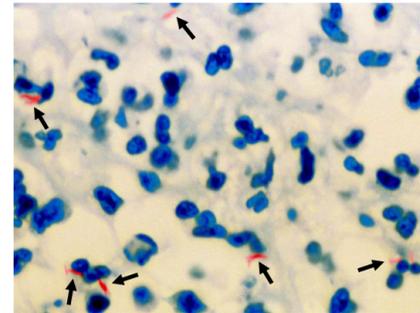


Figure 5: Intestinal biopsy revealing the presence of multiple acid fast bacilli (arrows) (Ziehl-Neelsen staining, original magnification X1000).

initiation added to antituberculous treatment was put forward before discharge. On this point, we had scheduled ARVs starting in an outpatient setting after confirming the appropriate adherence to antituberculous therapy. He was finally discharged on postoperative day 10. Unfortunately, he stopped treatment some days later and was readmitted 3 months after discharge because of fever and cervical lymphadenitis. Culture of a neck lymph node sample obtained through fine-needle aspiration grew *Mycobacterium tuberculosis*. On this occasion, he showed a positive attitude towards treatment adherence and eventually completed 9 months of antituberculous therapy besides starting on antiretroviral therapy. Acid-fast bacilli present in appendix and bowel tissues in 1999 were identified as *Mycobacterium tuberculosis* by PCR-ELISA assay in January, 2012. In spite of irregular observance of the antiretroviral regime, he has remained well since the second discharge. Currently, fourteen years later, the patient is asymptomatic, his CD4+ cell count is 199/ μL , and his HIV viral load is <20 copies/mL.

Discussion

The key clinical feature in this case was establishing the diagnosis of the cause of abdominal pain in a man who presented with fever and abnormal ileocecal and appendicular findings. The differential diagnosis is quite broad and includes acute complicated appendicitis, Crohn's disease, colon cancer, lymphoma, intestinal TB, actinomycosis, and other infectious disorders. Although the chronicity of symptoms should have brought up appendicular abscess/mass instead of acute complicated appendicitis as the main presumptive diagnosis, this was the first diagnostic possibility considered by the surgeon. If we have kept such a feature in the case presentation it has been due to our wish to describe accurately what had happened. Moreover, although a conservative management is still a highly acceptable approach for an appendix mass, surgical approach can be reasonable in patients with persistent pain in the right lower abdominal quadrant, as occurred in our patient. Distinguishing among all the aforementioned conditions would require doing appropriate and careful pathologic assessment of the involved areas after surgical intervention, which was the preferred course of action.

TB still remains a major global health problem. In 2011, there were an estimated 8.7 million new cases of TB worldwide (13% co-infected with HIV) and 1.4 million people died from TB (30% HIV-associated) [8]. Additionally, there is an increased susceptibility of HIV-infected people to develop the disease and to present with non-pulmonary manifestations [3,9]. Extrathoracic TB accounts for 20% of cases in immunocompetent individuals and 50% of cases in HIV-positive patients [1,3]. The core message in this case is that diagnosing intestinal TB both entails a clinical challenge and should hinge on bearing a great

awareness of the disease by physicians, particularly in nonendemic regions. TB can affect the entire gastrointestinal tract, the ileocecal area being the most common site of involvement [1-3,10]. Since clinical manifestations, laboratory tests, imaging techniques, and endoscopy are nonspecific [1,3,4], a definitive diagnosis is based on histological evidence of caseating granuloma with acid-fast bacilli stained by Ziehl-Neelsen and culture/PCR positivity. Nevertheless, if there is a reliable presumptive diagnosis of the entity, empiric antituberculous therapy is warranted to optimize clinical outcome [11]. Although intestinal TB treatment is medical, surgery may be required if the diagnosis is doubtful, there is a concern about malignancy, or complications are present (mainly, perforation, obstruction, or hemorrhage) [1,11].

We believe the clinical management of the patient in this case deserves some criticisms. First of all, HIV serology should have been requested just after admission and before the operation, remembering his past medical history. Secondly, the signs and symptoms and even the ultrasonography findings reported would have raised doubt regarding the existence of a typical case of acute appendicitis, even if it had been a complicated one.

Thirdly, it seems the “carcinomatous appearance” of the ileocecal region would not have justified per se the surgical procedure that was actually performed and that it might have been more appropriate to have some more clear diagnostic evidence to justify such surgery. However, it is worth pointing out this intervention was carried out in a centre without possibility of doing intraoperative biopsy studies. Finally, in terms of follow-up, it certainly seems there is no way after 14 years of antiretroviral treatment that CD4 counts are still below 200 cell/ml. Nevertheless, patient’s follow-up has been markedly difficult, with frequent missed consultations and several periods of imprisonment. Since he has remained usually asymptomatic and his viral load has been set < 20 copies/mL on average, the low CD4 count has not been considered an extremely alarming event. Furthermore, it could be considered as a no little surprise the prolonged, fairly uneventful follow-up of the patient so far.

This case and the course that it subsequently took might be irrelevant to the modern era because virtually everyone with medical training is familiar with the appearance of TB. It is also very likely that it will not change current practice regarding patients with acute abdominal pain as appendicitis and inflammatory bowel disease are so much more common than terminal ileal TB. However, it is well known that there is no such thing as an easy diagnosis of intestinal TB, even nowadays, and that both the incidence of TB and the frequency of extrathoracic TB are increased in HIV-positive patients. Even it is very old, the real interest of this case may be its presentation and the lesson about performing HIV testing in some emergency conditions.

So, besides its possible historical relevance, we believe our case could help clinicians to keep in touch with intestinal TB, another great mimic that sometimes works with a hidden allied.

Suggested Take Home Messages

1. Extrathoracic tuberculosis (TB) is currently rising and accounts for 20%-50% of all TB cases.

2. TB can affect the entire gastrointestinal tract. Intestinal area is the most common site of involvement and is difficult to diagnose because its manifestations are nonspecific.

3. The crux of the matter in diagnosing intestinal TB consists of a permanent awareness of the disease by clinicians.

4. The incidence, morbidity, and mortality of TB as well as the frequency of extrathoracic TB are increased in HIV-positive patients.

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