Management of severe gastrointestinal tuberculosis with injectable antituberculous drugs

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Abstract

Abdominal tuberculosis (TB) is generally responsive to medical treatment, and early diagnosis and management can prevent unnecessary surgical intervention. However, there is a need for intravenous therapy for severe forms of tuberculosis with extensive gastrointestinal involvement. The authors report an immunocompetent patient with gastrointestinal TB who was successfully managed with a combination of surgical intervention and anti-TB medications, and discuss the importance of injectable anti-TB medications in the management of severe gastrointestinal TB. The present case report illustrates a model for assessment and intervention in severe forms of gastrointestinal TB.

Keywords: tuberculosis, gastrointestinal tuberculosis, *M. tuberculosis*, injectable antituberculous drugs, management
Introduction

Tuberculosis (TB) is one of the leading global causes of morbidity and mortality. The World Health Organization (WHO) has estimated an approximately annual incidence of 8.6 million cases of TB globally [1]. According to the WHO report, 1.3 million people died from disease in 2012. Abdominal TB can be present in different clinical forms including peritoneal TB, tuberculous lymphadenopathy, gastrointestinal TB and visceral TB. This latter manifestation of TB, which is not commonly seen as pulmonary TB, can be a source of significant morbidity and mortality and is usually diagnosed late due to its nonspecific clinical presentation [2]. Abdominal TB is generally responsive to medical treatment, and early diagnosis and management can prevent unnecessary surgical intervention. However, there is a need for intravenous therapy for patients with severe forms of TB with extensive gastrointestinal involvement, who have impairment to take and absorb oral medications. Here in, we report an immunocompetent patient with gastrointestinal TB who was successfully managed with a combination of surgical intervention and antituberculous (anti-TB) medications. The authors emphasize and discuss the importance of injectable anti-TB medications in the management of severe gastrointestinal TB.

Case Report

A 13-year-old female adolescent was referred to our hospital with bloody diarrhea, anemia and a 5-kg weight loss over approximately 2 months. Blood examination data revealed a hemoglobin of 9.8 d/dL; hematocrit of 35%; white blood cell of 7.2 x 10^9/L, and platelets of 189 x 10^9/L. After admission, she had been initially treated with corticosteroids for 7 days following a colonoscopy suggestive of Crohn’s disease. The symptoms had progressively worsened during the last week so that she presented a
massive rectal bleeding upon arrival at ICU. She had repeated blood transfusions and a further colonoscopy showed fragile mucosa with multinodular appearance, circumferential deep ulcers, and hemorrhagic lesions predominantly in the cecum (figure 1). Histology of a biopsy fragment of the cecum showed the presence of acid alcohol fast bacilli. Laboratory tests revealed increased white blood cells and increased erythrocyte sedimentation rate and C-reactive protein levels. Chest X-ray showed a small circumferential lesion in the upper left lobe. She had a positive history of non-treated pulmonary tuberculosis in the family, with the uncle as the index case. She was not vaccinated with BCG. Gastric lavage fluid showed acid alcohol fast bacilli. Anti-HIV serology (ELISA) was negative and serum immunoglobulins were normal. Tuberculin skin test was negative. Physical examination revealed a marked skin pallor and abdominal distension with marked pain in all the abdominal quadrants. Corticosteroid was withdrawn and she started on intravenous regimen of levofloxacin (500 mg once a day), linezolid (600 mg every 12 hours), and streptomycin (750 mg once day) since the conventional oral treatment with rifampin, isoniazid and pyrazinamide was impaired due to the massive rectal bleeding. After 10 days of admission, a second colonoscopy showed the active bleeding coming from the upper small bowel through the distal ileum with no active bleeding in the colon. The first laparotomy performed in the following day showed friability and bleeding throughout the small bowel, no resection was done, lymph nodes were collected for culture and histology showed no granuloma. Culture of the mesenteric lymph node grew *Mycobacterium tuberculosis*. *M. tuberculosis* was sensitive to all four line anti-TB drugs (isoniazid, rifampin, streptomycin and pyrazinamide). Whilst on the IV treatment for tuberculosis, she did not ameliorate from the rectal bleeding and an abdominal angiotomography showed a bleeding site at distal ileum. She underwent a second
laparotomy 5 days after the first laparotomy and 30 cm of distal ileum, cecum and ascending colon were resected (figure 2). Histology of the resected intestine showed the presence of loose granulomas with acid alcohol bacilli (figure 3). Lower gastrointestinal bleeding stopped after the surgery and at that moment, she completed 40 days of IV anti-TB treatment. Enteral feeding was started and intravenous regimen of streptomycin (750 mg/day), linezolid 600 mg every 12 hours) and levofloxacin (500 mg/day) were then replaced by oral regimen of isoniazid (300 mg/day), rifampicin (600mg/day), pyrazinamide (1000 mg/day). The patient successfully completed a full 9-month’s course of oral anti-TB drugs without any additional intervention after 2 years of follow-up.

Discussion

The most common site of gastrointestinal involvement in tuberculosis is the ileocecal segment which is involved in approximately 64% of cases [3]. In particular, the terminal ileum is more commonly involved because of the various contributing factors like stasis, presence of abundant lymphoid tissue, increased rate of absorption at this site and closer contact of the bacilli with the mucosa [4]. Concomitant jejunal involvement may be seen in the form of single or multiple short or long segment strictures. Isolated jejunal involvement is rare, and if present, may mimic Crohn’s disease. Isolated involvement of colon is 10.8% [5]. The incidence is increased in the immunocompromised patients and patients with AIDS. The cecum is the most common site of involvement of colon but it is usually involved in contiguous involvement with the terminal ileum and ileocecal junction [6].

Our patient was successfully managed similarly to a previous report describing an HIV-infected patient, who presented severe disseminated tuberculosis with extensive intestinal involvement [7]. Although our patient did not have any detectable underlying
immunosuppression, the presence of numerous acid alcohol fast bacilli with loose granulomatous lesions reflects the immunocompromised status of the host. In addition to surgery, this patient was successfully treated with an initial combination regimen of injectable and oral anti-TB agents. As observed in our patient, with advent of anti-TB therapy, surgery is usually reserved for those cases where it is absolutely indicated as in cases of non resolving intestinal obstruction, gastrointestinal bleeding, perforation and abscess fistula formation [8].

Injectable anti-TB drugs is essential for treating different categories of TB patients including patients with severe disseminated and gastrointestinal TB where solely oral anti-TB agents might be not effective. In some cases, this is caused by quick decomposition of the drugs during their relatively slow intake from the gastrointestinal tract and, in others, by the impossibility of increasing the dose. In the case of intravenous administration, the drugs are easily absorbed, which leads to the creation of higher concentrations in the infected tissues [9]. Unfortunately, current guidelines for the management of tuberculosis have not addressed this issue.

Fluorquinolones including levofloxacin are injectable anti-TB drugs that have been shown to have early/extended bactericidal activity and are well tolerated. They are concentrated in macrophages and other phagocytic cells, bronchial mucosa and epithelial lining fluid where levels are higher than those found in the serum [10]. Linezolid has also an injectable formulation which has good activity against drug-susceptible and drug-resistant *M. tuberculosis* strains in vitro and animal studies [11]. Interestingly, we have not observed the reported toxicities of linezolid in our patient, including primarily myelosuppression and neuropathy. Aminoglycosides have excellent bactericidal activity and long-post-antibiotic effect that has proved valuable after once a daily administration [12, 13]. Additional potential antituberculous drugs such as
Imipenem, meropenem and ampicillin-sulbactam, are active against *M. tuberculosis* considering that resistance can be overcome by inhibiting the β-lactamase or by use of an antibiotic that is not a substrate for this enzyme [14].

Most of the TB guidelines do not address the use of injectable anti-TB drugs in patients with severe forms of tuberculosis that unable to take oral medications. In many countries such as Brazil, first line injectable anti-TB drugs such as rifampim and isoniazid are not available. Considering that clinical trials are difficult to perform in this type of clinical setting, further case reports and case series addressing the efficacy of adjunctive injectable anti-TB drugs have an important function illustrating models for assessment and intervention, describing new clinical challenges and phenomena for the management of severe forms of gastrointestinal TB.

The authors declare no conflict of interest

References


Figure 1. Colonoscopy revealing deep ulcerated lesions in the cecum
**Figure 2.** Laparotomy showing extensive hemorrhagic areas of the intestine.
Figure 3. (A). Histology of resected colon fragment showing loose granulomatous lesions (HE stain) with the presence of acid alcohol fast bacilli (ZN stain) (B).