Abdominal Tuberculosis: A Report Outlining Surgical and Unique Pharmacologic Management in the Absence of Enteral Access

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ABSTRACT

Abdominal tuberculosis (TB) occurs only in a subset of TB-infected persons. With a higher incidence in the immunocompromised population, successful treatment includes early diagnosis and initiation of anti-TB medications. This case report discusses a 22-year-old immunocompetent male diagnosed with advanced duodenal and peritoneal TB after perforation requiring emergent surgery and intravenous anti-TB treatment secondary to lack of enteral access.

Keywords: Abdominal tuberculosis, intravenous management of tuberculosis, peritoneal tuberculosis, surgical infection.

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I. INTRODUCTION

Tuberculosis (TB) is a curable and preventable infection caused by *Mycobacterium tuberculosis*. It most commonly infects those who are immunocompromised and is more prevalent in endemic areas. While primarily affecting the pulmonary system, isolated extra-pulmonary disease is identified in up to 20% of active TB cases [1]. Abdominal TB is the sixth most frequent extra-pulmonary site, accounting for 6-38% of infected persons, and is associated with high mortality. Infection may include tubercular lymphadenopathy, peritoneal, gastrointestinal (GI), or visceral sites; meanwhile duodenal TB is significantly rare

and represents only two percent of all intrabdominal cases [2].

Pharmacologic management with anti-TB medications is often sufficient for treatment of abdominal TB; a four-drug combination of rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE) remains the standard of care [3]. Intravenous (IV) anti-TB medications may be considered in patients with extensive intestinal involvement, limited enteral access, those who have failed oral treatment or those with multidrug resistance. Surgery is reserved for those who present with or develop perforations, small bowel obstruction, abscess or fistula. Here, we report a case of a patient with a history of latent TB who presented with

significant peritoneal and GI TB and required extensive surgical and pharmacologic intervention with IV anti-TB medications.

II. CASE REPORT

A 22-year-old male presented to the emergency department (ED) with palpitations, a two-month history of nausea, vomiting, diarrhea, and 90-pound weight loss over the last four months. Past medical history was notable for hyperthyroidism, autism, microcytic anemia, gastritis, gastric ulcers, gastroesophageal reflux disease (GERD) on antacids, sliding hiatal hernia, and latent TB. It was undetermined if the patient completed treatment for latent TB prior to admission.

Upon review of patient's electronic medical records (EMR), the patient had presented to the ED 54 days earlier with nausea, vomiting and abdominal pain and was discharged with a diagnosis of dyspepsia due to lack of remarkable radiological findings. The patient subsequently returned to the ED twice for evaluation at 31 days and 37 days later. He was noted to have tachycardia, nausea, vomiting, abdominal pain and diarrhea and was admitted to the medical service. He was diagnosed with hyperthyroidism on this third ED visit. He underwent a computed tomography (CT) of the abdomen, which showed possible small bowel obstruction and pneumatosis of the duodenum. Upon surgical evaluation, there were no clinical findings of peritonitis, small bowel obstruction (lack of flatus, lack of bowel movement) or laboratory findings suggestive of pneumatosis. Endoscopic, rather than surgical, intervention was deemed more appropriate. During hospitalization he was initiated on methimazole and propranolol for a new diagnosis of hyperthyroidism. He was discharged on hospital day five. Plans for esophagogastroduodenoscopy (EGD) were postponed secondary to the novel coronavirus 19 (COVID-19).

At 54 days from initial presentation and 11 days following discharge, the patient returned again with decreased appetite, diarrhea, fevers, and tachycardia. Due to concerns for worsening symptoms, he was admitted to the medical intensive care unit for evaluation of sepsis and thyroid storm. On hospital day one, he subsequently suffered a cardiac arrest and underwent four rounds of cardiopulmonary resuscitation (CPR) with return of spontaneous circulation; however, full consciousness was not regained due to anoxic brain injury. A CT scan of abdomen and pelvis obtained on hospital day two showed pneumoperitoneum suggestive of hollow viscus rupture. Surgery was consulted and an emergent exploratory laparotomy was performed.

A. Surgical Intervention

Fluid aspirated upon entering the abdomen was turbid and murky. The small bowel was noted to be globally edematous and hyperemic with dense interloop adhesions and several perforations within the proximal small bowel. Multiple foci of small white chalky caseating granulomas were identified on the bowel, peritoneum, and omentum. Fluid samples were taken for cytology and nodules were biopsied. The specimens were also sent for acid-fast bacilli testing given the patient's history and the appearance of the intestines and peritoneum leading to high suspicion of abdominal TB. Multiple attempts

at adhesiolysis were unsuccessful due to these dense adhesions and fear of causing multiple enterotomies. The ascending colon, hepatic flexure, and descending colon were unable to be visualized due to dense adhesions. An intraoperative EGD was performed, which demonstrated viable esophageal, gastric, and proximal duodenal mucosa without any signs of ischemia, necrosis, ulceration, or perforation. After mobilization of the ligament of Treitz, an En-bloc resection of the proximal small bowel was performed, encompassing the fourth portion of the duodenum and proximal jejunum where the perforations were noted. Increased intra-operative requirements of vasopressors and persistent metabolic acidemia with pH <7.1 were noted throughout the procedure. The decision was made to leave the patient's small bowel in discontinuity and a vacuum-assisted closure was placed into the abdomen, with plans for abdominal closure following repeat exploration.

The patient returned to the operating room for re-exploration once deemed stable for surgery on hospital day nine, post-operative day seven. No further ischemia was noted. At this time, attempts were made to re-anastomose the two ends of the small bowel but were deemed unfeasible due to ongoing bowel edema and friability of the entirety of the distal small bowel. No attempts were made to resect additional small bowel distally for fear of developing short-gut disease. A venting gastrojejunostomy tube was placed with its jejunal limb terminating in the blind duodenal loop, two Malecot drains in the open lumen of the distal duodenum and another in the proximal jejunum, a feeding jejunostomy distal to the Malecot, and two Blake drains in bilateral colonic gutters were placed. Primary closure was not achievable at this point due to severe bowel edema and distension; therefore, the abdominal incision was closed with Vicryl mesh and an abdominal vacuum-assisted closure was placed over the skin.

B. Diagnosis/Differential Diagnosis

Due to concerns for immunosuppression, the patient was evaluated for human immunodeficiency virus, hepatitis, lupus and tuberculosis. While all were found to be negative, the QuantiFERON®-TB Gold was indeterminate. Additionally, COVID-19 testing was completed and also deemed negative. On hospital day 23, *M. tuberculosis* was identified in peritoneal tissue, confirming abdominal TB diagnosis and a four-drug RIPE regimen was initiated. The peritoneal TB culture demonstrated susceptibility to with no resistance.

C. Pharmacologic Infection Intervention

Intravenous rifampin was used in conjunction with enteral solutions of pyrazinamide, isoniazid, and ethambutol compounded by pharmacy for administration via jejunostomy tube. On RIPE day two (hospital day 25), the jejunostomy was displaced and enteral access was lost. Due to the hostile nature of his abdomen, it was unfeasible to replace the feeding jejunostomy tube. Upon discussion with the infectious disease consultant and the clinical pharmacist, and due to lack of enteric access for medications administration, decision was made to transition to an IV anti-TB regimen. Agents were selected from the World Health Organization recommendations for multidrug resistant *M. tuberculosis* [4]. Despite no antimicrobial resistance, the multidrug resistant

regimen was the only adequate option as it provided IV alternatives. The patient was initiated on a combination of amikacin, levofloxacin, linezolid, and meropenem. Adjustments for hepatic or renal dysfunction and monitoring for adverse drug events (i.e., thrombocytopenia, nephrotoxicity) were completed daily. Following two months of quadruple therapy, anti-TB medications were de-escalated to IV levofloxacin and linezolid to complete the six-month treatment duration. Had an enteric access been re-established, the regimen was to be transitioned back to oral medications for completion. The patient completed his six-month course with IV anti-TB therapy.

The hospital course was complicated by several other infections. *Stenotrophomonas maltophilia* ventilator associated pneumonia on hospital day three was treated with levofloxacin. Mold identified in the same sputum specimen brought forth concerns for *Aspergillus*. A bronchoalveolar lavage galactomannan antigen test confirmed the presence of *Aspergillus* (0.71; reference range 0.00-0.49) on hospital day seven for which the patient received a six-week course of isavuconazonium. Methicillin-resistant *Staphylococcus epidermidis* bacteremia developed on hospital day 22 requiring treatment with linezolid. *Candida glabrata* was isolated in blood cultures on hospital day 42 and warranted treatment with micafungin. Recurrent *Stenotrophomonas maltophilia* ventilator-associated pneumonia and *Candida glabrata* candidemia occurred on hospital day 103 and were treated accordingly. *Candida parapsilosis* was identified in blood cultures on hospital day 155 and 186 and was treated with micafungin on both occasions.

D. Outcome

During hospitalization, our patient developed acute kidney injury requiring continuous veno-venous hemofiltration and hemodialysis for 49 days following his first surgical procedure. His renal function recovered, and has not required renal replacement therapies since. He has had multiple episodes of sepsis secondary to pneumonia, bacteremia and candidemia requiring intensive care monitoring and remains ventilator dependent. His course has since been further complicated by extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* pneumonia and bacteremia on two separate occasions. On hospital day 109 he returned to the operating room for sacral ulcer excisional debridement. He has been and remains dependent on total parenteral nutrition as surgical intervention for re-establishing enteric feeding access has been deemed of high risk during multiple surgical conferences with the family. He is in a persistent vegetative state with Glasgow Coma Scale < 8 secondary to cardiac arrest-associated anoxic brain injury. Currently, he is awaiting placement at a long-term care facility.

III. DISCUSSION

Extra-pulmonary TB affects less than 20% of TB infected patients with abdominal TB seen in 6-38%. It is thought to reach the abdomen via hematogenous spread, ingestion of infected sputum, or contiguous spread of adjacent organs [5]-[7]. Presentation often includes abdominal pain, nausea and vomiting, meanwhile severe disease is associated with GI bleeding or constitutional symptoms (fever, night sweats, and

weight loss). The vague symptomatology makes timely diagnosis and treatment difficult as it mimics other disease entities [7].

Peritoneal TB, as seen in our patient, is defined by one or a combination of ascites, thickened fibrosed or adhered bowel loops, or peritoneal studding [7]. Gastrointestinal TB presentation includes thickened bowel loops, bleeding, fistulas, or perforations most commonly occurring at the ileocecal region, although seen in the distal duodenum in our patient. The cause is attributed to stasis, abundant lymphoid tissue, and increased absorption at this segment of the small intestine [7]-[9]. Intestinal TB is classified as ulcerative, hypertrophic, and ulcero-hypertrophic. Ulcerative, often located in the terminal ileum, can form single or multiple ulcers. Ulcers may scar down during the healing process, leading to the formation of strictures, bleeding, perforations, and/or fistulas. Caseating granulomas remain a marker differentiating ulcerative intestinal TB from Crohn's disease. Hypertrophic and ulcero-hypertrophic subtypes often present as masses or perforations with matted caseating lymphadenopathy [7], [10].

Duodenal TB is found in a small percentage of intestinal TB patients. The gastroduodenal region is protected by higher acidity, the rapid transit of food, thicker mucosal lining, and fewer lymph nodes [11]. Long-term histamine-2 receptor blockers and proton pump inhibitors use has been associated with increased incidence of duodenal TB due to changes in pH. Histamine-2 receptor blockers competitively inhibit histamine release from gastric parietal cells, thus inhibiting gastric acid secretion and increasing the pH of gastric contents. Of note, our patient was prescribed histamine-2 receptor blockers and proton pump inhibitor for at least six weeks prior to hospitalization for treatment of gastritis, however, he did not have other risk factors for such severe disease [12]. Most patients with gastroduodenal disease are found to have other sites of TB infection [13]. Our patient was found to have peritoneal TB, which attributed to the formation of severely dense adhesions

Although most cases of abdominal TB respond to oral anti-TB agents, the severity of disease in this case prevented the safe anastomoses and placement of long-term enteral access necessary for use. Currently, RIPE remains the standard of care in drug-susceptible TB and should be used when enteral access is available. When administering via jejunostomy, alterations in drug absorption and serum concentrations must be considered. This case was complicated by a lack of enteral access throughout hospitalization. Our patient completed six months of a combination of amikacin, levofloxacin, linezolid, and meropenem. Although these agents are reserved for multidrug resistant TB, they may be considered when oral therapy is not feasible. Use of empiric anti-TB medications in the setting of drug-susceptible TB can be cumbersome and the risk for antimicrobial resistance should be acknowledged. In addition, patients must maintain IV access and monitoring for serious adverse reactions is required. While rare, our patient appeared to tolerate this combination with no adverse drug events. Furthermore, the acute kidney injury requiring renal replacement therapy occurred prior to initiation of aminoglycosides and thus was determined not to be a medication related adverse reaction.

IV. CONCLUSION

Abdominal tuberculosis is a rare entity, which can have devastating consequences especially when complicated by intestinal perforation. Standard of care treatment includes enteric RIPE therapy in combination with surgical intervention when warranted. This case report highlights successful use of IV anti-TB medications in a patient without enteral access using a six-month of combination of amikacin, levofloxacin, linezolid, and meropenem, a treatment modality usually reserved for multidrug resistant TB.

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