Case report

Disseminated tuberculosis and gastric mucormycosis coinfection

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ABSTRACT

Tuberculosis and mucormycosis coinfection has rarely been reported in the medical literature. We present a case of gastrointestinal (GI) mucormycosis in a diabetic patient with disseminated tuberculosis. Early diagnosis, addressing the risk factors for mucormycosis, surgical debridement, and timely antifungal treatment are the mainstay of care.

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Introduction

Mucormycosis (Zygomycosis) can present with a variety of clinical syndromes. Gastrointestinal (GI) infection remains a rare manifestation and it represents 7% of cases of mucormycosis [1]. Few cases of non-GI mucormycosis and tuberculosis (TB) coinfection have been reported in the medical literature. Herein, we present a case of life-threatening GI mucormycosis in a patient with disseminated tuberculosis.

Case presentation

A 54-year-old Latin American female, with history of type 2 diabetes mellitus and end-stage renal disease presented to the emergency department with a 10-day history of headache and photophobia. She complained of chronic cough, weight loss, and low-grade fever. She reported close contact with a person with pulmonary tuberculosis three years prior to her admission. On physical examination, she was febrile (38.5°C), tachycardic and had mild impairment of alertness. Pulmonary auscultation revealed diffuse crackles mainly of the left lung. Initial laboratory studies showed white blood cell count (WBC) 4800 cells/µL; absolute lymphocyte count 816 cells/µL; hemoglobin 10.3 g/dL; and blood sugar 111 mg/dL. Liver function tests were normal, creatinine 7.2 mg/dL; and blood urea nitrogen 59 mg/dL. The chest x-ray showed bilateral interstitial infiltrates and brain magnetic-resonance images showed multiple ring-shaped lesions in posterior areas of both hemispheres. Acid-fast bacilli sputum culture was positive on Ziehl-Neelsen stain and grew \textit{Mycobacterium tuberculosis} complex (MTB) with no evidence of antibacterial resistance. HIV1/2 and toxoplasma serologies were negative. On lumbar puncture, the opening pressure was 30 cm H$_2$O. Analysis of the cerebrospinal fluid (CSF) showed red blood cell count 1000 cells/µL; WBC 114 cells/µL; lymphocytes 92%; glucose 30 mg/dL; and proteins 181 mg/dL. CSF neurocysticercosis serology and cryptococcal antigen were negative. CSF \textit{Mycobacterium tuberculosis} stain and culture and adenosine deaminase were negative, whereas a polymerase chain reaction (PCR) was positive for MTB.

Anti-TB therapy was started with rifampin, isoniazid, pyrazinamide, ethambutol and pyridoxine with adjunctive dexamethasone planned for 8 weeks. A few days later, her mental status rapidly deteriorated requiring admission to the intensive care unit and initiation of hemodialysis for uremia, which resulted in clinical improvement. After three weeks of hospitalization, she developed acute abdominal pain and hematemesis. A computerized tomography (CT) of the abdomen revealed a loculated multiseptated gas and fluid collection along the posterior aspect of the gastric fundus with free intra-abdominal air consistent with gastric perforation (Fig. 1a). An exploratory laparotomy demonstrated complete stomach necrosis (Fig. 1b). She underwent a total gastrectomy with intestinal discontinuity followed by cervical esophagostomy and jejunostomy tube (J-tube) placement. Oral anti-TB therapy was switched to intravenous treatment with amikacin, linezolid,
levofoxacin and rifampin. The patient developed septic shock, requiring intubation and mechanical ventilation. Empiric broad-spectrum antibacterial therapy was initiated with piperacillin-tazobactam for intra-abdominal infection.

Histopathology of gastric tissue on hematoxylin and eosin (Fig. 1c) and Grocott-Gomori methenamine silver stains showed broad, irregularly branched, rarely septate hyphae consistent with angio-invasive gastric mucormycosis. The acid-fast bacilli stain and culture were negative. Liposomal amphotericin B 7.5 mg/kg daily was initiated and TB treatment with levofoxacin, rifampin, isoniazid, and linezolid was maintained for one more month. Then, isoniazid plus rifampin were continued by jejunostomy tube to complete 12 months of treatment. Liposomal amphotericin B was switched to posaconazole as oral suspension 200 mg/6 h per-tube. Upon clinical stabilization and improvement, she returned to her country of origin in Latin America to finalize her treatment.

Discussion

Although GI mucormycosis represents 7% of all mucormycosis infection [1], mortality rate can reach 85% [2]. Gastric infection accounts for 57.5% of all GI mucormycosis followed by colon, 32.2%; and small bowel, 9.1% [3,4]. In medical reports between years 1960 and 2000, GI mucormycosis was primarily observed in malnourished children and premature low-weighted infants [3]. It was also encountered in solid organ and hematopoietic stem cell transplantation, hematological malignancies, in adults with diabetes, or patients receiving corticosteroids therapy [1,3]. Special situations, such as the ingestion of naturistic medications and nosocomial transmission by tongue depressors have also been reported [3]. The pathogenesis and mechanism of infection is mainly by ingestion of the fungal spores. In our patient, diabetes, uremia, and the adjunctive use of corticosteroids for tuberculous meningitis might have played a role in the infection, however, active tuberculosis per se could have also predisposed to invasive fungal disease. In patients with tuberculosis, an increased activity of regulatory T cells (Treg) is associated with inhibition of T effector cells and antigen presenting cells, decreasing bacterial clearance [5]. Moreover, M. tuberculosis promotes a down-regulation of immune mediators to counteract Th1-type cells and innate immunity response [6].

Only three cases of Mucorales infection in patients with active TB have been reported in the literature, affecting the orbit [7], lung [8] and kidney [9]. Gastrointestinal mucormycosis may manifest with abdominal pain, fever, vomiting, diarrhea, melena or hematochezia and peritoneal signs [3]. CT scan of the abdomen usually shows thickening of the GI wall, collections or bowel perforation. Obtaining a tissue sample and performing hematoxylin and eosin, periodic acid-Schiff (PAS) and Grocott-Gomori methenamine silver (GMS) stains are of paramount importance for hyphal identification on the histopathology [9]. Fungal cultures might not be sensitive enough and techniques based on molecular biology are not completely standardized [9] or widely available.

Surgical debridement and systemic antifungal therapy with Liposomal amphotericin B (dose of 5–10 mg/kg/day) are the
cornerstone of treatment [1,10]. Controlling associated risk factors is also recommended. Posaconazole and isavuconazole have proven activity against *Mucorales* at optimal serum concentrations.

In conclusion, gastrointestinal mucormycosis is infrequently associated with disseminated tuberculosis. The immunosuppressive effect of disseminated tuberculosis and maybe the coexistence of uremia, uncontrolled diabetes mellitus, and systemic corticosteroid therapy may represent risk factors for the coinfection.

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**Ethical approval**

This research does not need an IRB approval.

**CRediT authorship contribution statement**

Alexandre Malek: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. Alejandro De la Hoz: Conceptualization, Writing - original draft, Writing - review & editing. Roberto Arduino: Conceptualization, Writing - original draft, Supervision, Writing - review & editing. Gabriel M. Eisenberg: Conceptualization, Writing - original draft, Supervision, Writing - review & editing.

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