Distal jejunal obstruction due to *Cryptococcus neoformans* and rifampicin-resistant *Mycobacterium tuberculosis* co-infection: A case report

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**Abstract**

Jejunal obstruction secondary to *Cryptococcus neoformans* and rifampicin-resistant *Mycobacterium tuberculosis* co-infection in HIV is not previously reported. This is a case of a 30-year-old HIV-positive male with severe headaches, a positive cerebrospinal fluid cryptococcal antigen assay, and elevated intracranial pressure requiring serial lumbar punctures and opioids. He developed constipation and abdominal distension, had partial jejunal obstruction and histopathology revealed Cryptococcus yeasts and caseous granulomas with *Mycobacterium tuberculosis* (TB). Post-operatively, rifampicin-resistant TB was detected in urine.

1. Introduction

*Cryptococcus neoformans* (*C. neoformans*) and *Mycobacterium tuberculosis* (*M. tuberculosis*) infections are prevalent among people living with HIV including those with a CD4 cell count of less than 200 cell/μL, antiretroviral therapy (ART)-naïve, and poor adherence and/or failing on ART [1–4]. We previously showed that 14% of cryptococcal meningitis patients have tuberculosis (TB) at the time of cryptococcal meningitis diagnosis and a further 9% are diagnosed with TB after two weeks of cryptococcal meningitis treatment [3]. People living with HIV co-infected with *C. neoformans* and MTB are at increased risk of mortality compared to those without any of the infections and those with only one of the two infections [1–3].

*C. neoformans*’ primary infection in the lungs mainly disseminates to the central nervous system as meningoencephalitis [5]. *M. tuberculosis* primary mediastinal infection (Ghon focus) is followed by dissemination, but to wider organ systems unpredictably [6]. However, both infections are rarely established in the intestinal wall and have not been reported as co-infection in the jejunum. The diagnosis of cryptococcal disease is rapid with IMMY cryptococcal antigen lateral flow assay (IMMY, Norman, OK, USA) which has a sensitivity of 99% [7]. However, TB diagnosis still lags, but the introduction of Xpert MTB/RIF Ultra assay (Cepheid, Sunnyvale, CA, USA) has improved TB diagnosis and rifampicin resistance detection in urine [8].

We present a novel case of co-current *C. neoformans* and rifampicin-resistant *M. tuberculosis* jejunal infection in HIV-associated cryptococcal meningitis. This case brings to light the approach to diagnosis and management of the patient which we believe will help clinicians attending to cryptococcal meningitis patients with a similar presentation in the future.

2. Case

A 30-year-old, HIV seropositive male on zidovudine, lamivudine, and nevirapine ART combination for one and half years with poor adherence and unknown viral load was admitted (day 0) with a month history of severe headache. He also had a history of confusion, generalized tonic-clonic seizures, and vomiting. His examination revealed hypothermic of 35.8 °C, elevated blood pressure of 163/123 mmHg, a heart rate of 86 beats per minute, oxygen saturation of 93%, confusion (Glasgow Coma Score rating of 14), a stiff neck, and left cranial nerve six palsy. His admission lumbar puncture cerebrospinal fluid (CSF) intracranial opening pressure was 42 cmH₂O (normal range 9-20 cmH₂O) with bedside CSF glucose of 66 mg/dL glucose and 2.6 mg/dL lactate. Two hours after this first lumbar puncture, he was groaning with a severe headache and received a second lumbar puncture which had a CSF opening pressure of 32 cmH₂O. He had a positive bedside serum and CSF IMMY cryptococcal antigen lateral flow assay and a negative Alere urine lipaobarinomannan (Abbott laboratories, Illinois, USA). Laboratory examination of his first CSF sample revealed it was turbid with a white blood cell count of <5 cells/mL, and 5,400,000 cryptococcus colony forming units (CFU)/mL of CSF after ten days of incubation. His baseline
CSF Xpert MTB/RIF Ultra was negative. His day 0 blood results including complete blood counts and renal and liver function tests were only remarkable for increased serum creatinine at 1.24 mg/dL (normal range 0.5–0.9 mg/dL) and serum alanine transaminase (ALT) at 167 U/L (normal range 5.3–39.9 U/L).

He was randomized on day 0 and treated under the AMBITION-cm clinical trial (TRIA2015-1092) [9]. He received a single dose of liposomal amphotericin B (Ambisome®, Gilead, Foster City, CA) at 10 mg/kg body weight, then fluconazole 1200mg/day and flucytosine 100 mg/kg/day in four divided doses. While hospitalized, he had persistent elevated intracranial opening pressures that required daily serial lumbar punctures and a codeine-bisacodyl combination to relieve his pain. On day 6, he developed constipation and abdominal distention. This was initially managed conservatively with intravenous fluid (4 L of normal saline per day) and the bisacodyl dose was increased to 10mg every night. However, the abdominal distension worsened, and on day 8, he

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**Fig. 1.** Biopsy staining showing *Cryptococcus neoformans* on Periodic acid–Schiff (PAS) and Hematoxylin and eosin (H&E) stain. White clearing represents cryptococcal polysaccharide capsule. (A) x40 objective magnification PAS-stained sections showing cystic areas containing *C. neoformans*. (B) x20 objective magnification H&E staining showing cystic areas containing *C. neoformans*. (C) x10 magnification H&E staining showing cystic areas containing *C. neoformans*.

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**Fig. 2.** Jejunal biopsy staining showing acid-fast bacilli staining, granulomas and giant cells, consistent with *Mycobacterium tuberculosis* infection. (A) x40 objective magnification Ziehl-Neelsen staining shows positively stained bacilli. (B) x10 objective magnification Hematoxylin and eosin (H&E) stain showing areas of necrosis and granuloma formation. (C) x20 objective magnification H&E stained sections showing granuloma formation with multinucleate giant cells.
developed vomiting. Due to concern for small bowel obstruction, a surgical consultation was requested. He was diagnosed with an acute abdomen, and an exploratory laparotomy was indicated. During surgery, the surgeon found a distal jejunal stricture without intussusception, resected it, and performed end-to-end hand-sewed anastomosis. Post-operative follow-up at the surgical center continued through day 12. During these four days of hospitalization, his oral antifungals (fluconazole and flucytosine) were held as the team awaited for his gastrointestinal function to normalize. On Day 13, his oral fluconazole and flucytosine were reinstated after passing stool and flatus despite persistent moderate abdominal pain. At this time extra-pulmonary intestinal TB was highly suspected with a plan to initiate anti-TB therapy. However, the decision to start anti-TB drugs was delayed due to ongoing and flucytosine were reinstated after passing stool and flatus despite gastrointestinal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perForations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11].

3. Discussion

Gastrointestinal cryptocoCCosis affects any part of the digestive tract from the esophagus to the colon [10,11]. Symptoms of gastrointestinal cryptocoCCosis include watery diarrhea, melena, burning epigastric pain, constipation, and abdominal distension [11]. Gastrointestinal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11]. Several case reports have described abdominal cryptocoCCosis lesions include ulcers, adenopolyps, strictures, and perforations [11].

Declaration of competing interest

“There are none.”

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