Disseminated Coccidioidomycosis Presenting as Carcinomatosis Peritonei and Intestinal Coccidioidomycosis in a Patient with HIV

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Abstract
Coccidioidomycosis (CM) is a fungal infection endemic in southwestern regions of the United States, northwestern regions of Mexico, and some areas of Brazil and Argentina. Clinical presentation varies depending on the extent of the infection and the immune status of the host. The most common presentation ranges from flu-like symptoms to self-limiting pneumonia. Extrapulmonary presentations are uncommon and may involve the meninges, skin, and bone. Gastrointestinal and peritoneal involvement is extremely rare. Here we report a case of disseminated CM presenting as carcinomatosis peritonei as an AIDS-defining illness in a young male.

Introduction
Coccidioidomycosis (CM) has been recognized as a distinct disease since 1892 [1]. It is caused by a dimorphic fungus of which there are 2 subspecies, Coccidioides immitis and Coccidioides posadasii. In the United States, it is endemic to southwestern states, primarily affecting California, Arizona, and Texas with C. immitis infections being more common [2]. Up
to 60% of the patients remain asymptomatic with the remaining developing self-limiting flu-like symptoms. Less than 1% of the patients develop disseminated infection with the immunocompromised state being a major risk factor and carrying high mortality [3, 4]. The Centers for Disease Control and Prevention have identified CM as an acquired immunodeficiency syndrome (AIDS)-defining illness [5]. We report here a rare case of disseminated CM, presenting with carcinomatosis peritonei and CM of terminal ileum in an AIDS-defining illness.

Case

A 20-year-old Hispanic male with no significant prior medical history presented to the emergency department with complaints of nausea, vomiting, abdominal pain, and diarrhea for 3 weeks. History was significant for high-risk sexual behaviors, anorexia, 10-pound weight loss, and low-grade fever. Physical examination revealed a cachectic male not in any distress. Heart rate was 104/min, blood pressure was 124/88 mm Hg, respiratory rate was 18/min, oxygen saturation of 95% on room air, and temperature was 98.3°F. Abdominal examination was significant for tenderness without visceromegaly. The remainder of the physical examination was unremarkable.

Laboratory studies showed a WBC count 8.2/µL, hemoglobin 11 g/dL, platelets 458,000/µL, and normal renal and liver function. Chest X-ray showed minimal right-sided pleural effusion. Computed tomography (CT) scan of chest and abdomen without contrast was obtained and showed bilateral pleural effusions, diffuse mesenteric lymphadenopathy, mesenteric edema, minimal ascites, diffuse ill-defined omental hyperdensities, and regional lymphadenopathy suspicious for carcinomatosis peritonei (Fig. 1).

Colonoscopy showed evidence of terminal ileitis along with submucosal nodular lesions (Fig. 2). Biopsies of ileal lesions did not reveal any malignancy but did show numerous CM spherules (Fig. 3). HIV screening test was positive. The patient was started on amphotericin B, 5 mg/kg intravenously. Serum CEA, CA 19-9, interferon gamma release assay, serum serotonin, and 24-hour urine 5-HIAA were normal. Serum CM antibody titer by complement fixation was 1:2,048 (normal range <1:2). Immunodiffusion assay revealed CM IgG level of 9.4 (normal range <0.9). HIV RNA level was 48,000 copies/mL, wild-type genotype, and no mutations. CD4 count was 102/µL. On hospital day 10, the patient developed shortness of breath and chest X-ray showed worsening pleural effusions. Thoracocentesis showed the fluid to be exudative with a white cell count of 1,018 (48% lymphocytes, 42% mesothelial cells). Pleural fluid cultures were negative for bacterial, mycobacterial, and fungal growth. On hospital day 17, a repeat CT of the abdomen showed improvement and the patient was clinically much better. Oral fluconazole 800 mg was started after completion of 2 weeks’ therapy of amphotericin B. Trimethoprim-sulfamethoxazole 160/800 mg one tablet daily was added for Pneumocystis jirovecii pneumonia prophylaxis. The patient was subsequently discharged. At 5 weeks’ follow-up, the patient reported resolution of all his symptoms. Antiretroviral therapy was initiated. At 16 weeks’ follow-up, serum CM titer by complement fixation decreased to 1:256 and CD4 lymphocytes increased to 369/µL. Serum HIV RNA level was <20 copies/mL. The plan is to continue oral fluconazole for at least 1 year and lifelong antiretroviral therapy.
Discussion

CM is a fungal infection with annual incidence increasing from 5.3 cases per 100,000 in 1998 to 42.6 cases per 100,000 in 2011. 3,000 deaths were reported between 1990 and 2008 [6]. Of the estimated 150,000 infections per year, approximately two-thirds are subclinical.

Incidence of extrapulmonary complications has been estimated to be less than 1% in immune-competent patients and increases to 30–50% in immunosuppressed patients such as those with AIDS or lymphoma or recipients of solid-organ transplant or rheumatologic therapies [7]. Of the various extrapulmonary sites for disseminated CM, gastrointestinal tract is rare and involvement is thought to occur by hematogenous transmission following a primary infection of the lung [8]. However, swallowing of pulmonary secretions has also been considered as a possible route of transmission [9].

Peritoneal seeding is an uncommon site for CM. There are approximately 35 cases of peritoneal seeding but there are only 4 reported cases in the literature of CM to the terminal ileum [10]. Out of these 4 reported cases, only 2 patients had HIV [11]. The remaining cases were associated with malignancy or immunosuppressive therapy. One highly cited case report involves a 71-year-old female who had peritoneal CM after having chemotherapy for non-Hodgkin's lymphoma [12]. Another interesting case is a 27-year-old immunocompetent male with spontaneous disseminated CM leading to eosinophilic ascites [13]. However, neither of these patients had HIV.

There are only 2 articles on literature search of patients with HIV and peritoneal CM. Jamidar et al. [14] described a case of a 42-year-old Caucasian male who presented with a 3-week history of increasing abdominal girth, anorexia, diarrhea, and generalized lethargy. Eighteen months prior to his admission, he was diagnosed with HIV-1 infection. Laparoscopy showed evidence of numerous large white plaques on the peritoneum. Biopsy of these plaques was consistent with C. immitis infection and serology was positive for CM. The patient was treated with 2 weeks of IV amphotericin and the 6-month follow-up showed the patient to be stable and asymptomatic [14]. In retrospect, this is considered to be the first case of CM peritonei as an AIDS-defining illness. Byrne and Dietrich [15] reported another case of a 57-year-old male with prior history of HIV infection with disseminated CM with involvement of lung and meninges. Two years after his initial presentation, he developed ascites. Abdominal paracentesis was performed and ascitic fluid culture was positive for C. immitis. The patient was treated with amphotericin B for 1 month and follow-up cultures became negative [15].

Our case is the third documented case of disseminated CM with peritoneal involvement in a patient with HIV infection. However, this is the first case where both peritoneal and terminal ileum involvement has been reported. It is also the first case in which HIV was tested and diagnosed on the basis of peritoneal involvement of CM.

In summary, CM involvement of the gastrointestinal tract and peritoneum presenting as carcinomatosis peritonei is extremely rare. We recommend that it should be kept in the differential diagnosis of patients with abdominal pain and HIV/AIDS risk factors.

Statement of Ethics

Informed consent was obtained from the patient to allow publication of this manuscript. Manuscript is a case report on a rare condition and did not involve research on human or
animal subjects. Case report was approved by the Texas Tech University Health Sciences Center Internal Medicine Department.

**Disclosure Statement**

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Fig. 1. CT of the abdomen and pelvis of the patient on admission. The abdominal image (a) shows mesenteric lymphadenopathy. The pelvic image (b) shows terminal ileum thickening suggestive of a possible mass. The CT report suggested possible neoplasm. However, after further studies, we know these changes occurred due to coccidioidomycosis infection.

Fig. 2. Endoscopic images of the abnormal mucosa noted in our patient. a Erythematous swollen ileocecal valve, denoted by an asterisk. b Inflammatory nodular mucosa in the upper half of terminal ileum, denoted by an arrow. This contrasts with the normal mucosa noted in the lower half of the same image.
Fig. 3. Histology from the ileal biopsy. It reveals 3 coccidioidomycosis spherules, denoted by arrows. The spherule on the right-hand side is actively releasing endospores.