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A Rare Cause of an Ileocecal Fistula in an AIDS Patient

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A 31-year-old Hispanic man presented with 5 days of right lower quadrant (RLQ) abdominal pain. His past medical history was notable for acquired immunodeficiency syndrome (AIDS), antiretroviral medication non-compliance, multiple opportunistic infections (e.g. pulmonary tuberculosis, oral candidiasis, herpes zoster), and polysubstance abuse (methamphetamine and alcohol). The patient was an unemployed construction worker who emigrated from Veracruz, Mexico nine years ago. His physical exam was notable for mild to moderate RLQ abdominal tenderness. Laboratory results revealed a white blood cell count of 5600 cells/ μ L with 63% neutrophils and 4% eosinophils, but were otherwise normal. CD4 count was 38 cells/ μ L and HIV viral load was 175,232 copies/mL. An initial computed tomography (CT) of his abdomen showed thickening of the terminal ileum and base of the cecum (Fig 1, arrow). A colonoscopy revealed a terminal ileum that was diffusely ulcerated and inflamed for 5 cm with a fistula of the terminal ileum to the cecal base (Fig 2, arrowhead points to fistula, arrow points to appendiceal orifice). Blood, urine, and stool bacterial and fungal cultures were negative. Serologic testing was negative for Aspergillus Galactomannan antigen, Coccidioides complement fixation and immunodiffusion, Cryptococcal antigen screen, Toxoplasmosis IgG and IgM antibody, Entamoeba histolytica antigen, and rapid plasma reagin. Urine Histoplasma antigen screen, stool ova and parasite, stool stain for Cryptosporidium and Isospora, and stool and sputum acid-fast bacilli smear and mycobacterium tuberculosis direct test were negative. A cytomegalovirus shell vial culture and a general viral culture were negative. Pathological specimens showed granulomatous ileitis/colitis with budding fungus (Fig 3, Gomori's Methenamine Silver [GMS] stain under 40 $\times$, inset shows a close up of the organism). Since the fungal infection could not be identified, the patient was empirically treated with fluconazole. However a month later, patient's symptoms did not improve.

What is the etiology of the ileocecal fistula and how would you make the diagnosis?

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Author Contributions: AZ evaluated the patient, obtained the colonic specimen, and drafted the manuscript. GL performed pathological analysis of the colonic specimen, and provided critical revision of the manuscript for important intellectual content. JTL evaluated the patient, obtained ITSPS testing, and provided critical revision of the manuscript for important intellectual content.

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Answer: Gastrointestinal infection by *Histoplasma capsulatum* infection identified with internal transcribed spacer primer sets (ITSPS).

Because the patient's symptoms did not improve with fluconazole treatment, a colonoscopy was repeated a month later with pathology samples sent for fungal DNA detection by internal transcribed spacer primer sets (ITSPS) which revealed *Histoplasma capsulatum*. The patient responded well to treatment with intravenous amphotericin followed by oral itraconazole.

Histoplasmosis is a common opportunistic infection of immunosuppressed or immunocompromised patients and in HIV-infected patients it presents in the disseminated form in 95% of cases.¹ Since the organism can spread hematogenously, the disease is manifested in many varieties, including infection of the gastrointestinal tract where it presents with fever, diarrhea, abdominal pain, bleeding, weight loss, and, rarely, bowel perforation.² It most commonly affects the ileocecum (~30%) or colon (~60%).² The urine *Histoplasma* antigen screen has a sensitivity of 91.8%, and specificity of 99%, in the setting of disseminated histoplasmosis and is the most commonly used test for diagnosis.

Our case is interesting for two reasons. First, there is no evidence of disseminated disease in this patient, as evidenced by a negative urine *Histoplasma* screen. Second, the patient presented acutely with fistulizing disease. There have been no reported case studies of gastrointestinal histoplasmosis causing fistulizing disease and reports of gastrointestinal histoplasmosis without disseminated disease are extremely rare. Our diagnosis was made by direct microscopic examination and DNA testing with ITSPS. Staining with GMS can aid in diagnosis but errors in identification of the organism are common. ITSPS, where polymerase chain reaction with primers specific to *Histoplasma* is used, was needed in this case since an organism could not be identified with standard serological testing and cultures.³

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Figure 1.

Figure 2.

Figure 3.