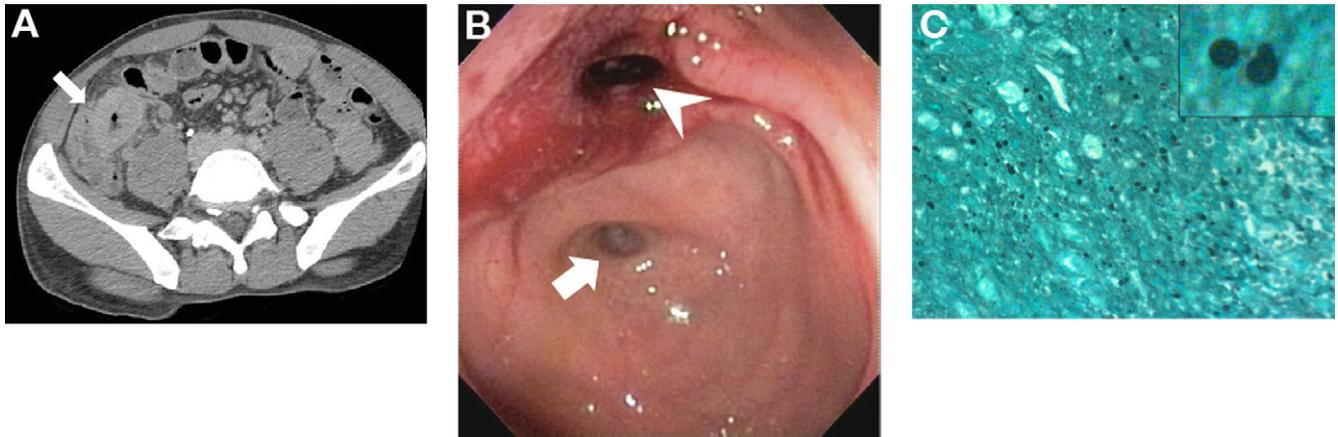


## A Rare Cause of an Ileocecal Fistula in an AIDS Patient

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**Question:** A 31-year-old Hispanic man presented with 5 days of right lower quadrant abdominal pain. His past medical history was notable for AIDS, antiretroviral medication noncompliance, multiple opportunistic infections (pulmonary tuberculosis, oral candidiasis, herpes zoster), and polysubstance abuse (methamphetamine and alcohol). The patient was an unemployed construction worker who emigrated from Veracruz, Mexico, 9 years earlier. His physical examination was notable for mild-to-moderate right lower quadrant abdominal tenderness. Laboratory results revealed a white blood cell count of 5600 cells/ $\mu$ L with 63% neutrophils and 4% eosinophils, but were otherwise normal. CD4 count was 38 cells/ $\mu$ L and HIV viral load was 175,232 copies/mL. An initial computed tomograph of his abdomen showed thickening of the terminal ileum and base of the cecum (Figure A, arrow). 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 (Figure B, 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* immunoglobulin (Ig)G 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. Pathologic specimens showed granulomatous ileitis/colitis with budding fungus (Figure C, Gomori's methenamine silver stain; original magnification,  $\times 40$ ; inset shows a close up of the organism). Because the fungal infection could not be identified, the patient was empirically treated with fluconazole. However, 1 month later, patient's symptoms did not improve.

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

**Look on page 857 for the answer and see the GASTROENTEROLOGY web site ([www.gastrojournal.org](http://www.gastrojournal.org)) for more information on submitting your favorite image to Clinical Challenges and Images in GI.**

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mucosa carry the risk of distant metastasis years after complete resection. Radical esophagectomy with 3-field lymphadenectomy is the treatment of choice when feasible. The effectiveness of adjuvant chemotherapy, radiotherapy, and immunotherapy is controversial. The mean survival time after operation is 10–14 months.<sup>1</sup>

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## Answer to the Clinical Challenges and Images in GI Question: Image 3 (page 696): Lansoprazole-induced Microscopic Colitis

Microscopic colitis (MC) is characterized by chronic, watery diarrhea. Typically, colonoscopy reveals normal-appearing colonic mucosa. Biopsy findings may indicate either lymphocytic colitis (LC), with increased intraepithelial lymphocytes (>20 lymphocytes per 100 surface epithelial cells), or collagenous colitis (CC), characterized by a thick subepithelial collagen band (>10  $\mu\text{m}$ ). The cause of MC is unknown. Medications found to have a high likelihood of causing MC include acarbose, aspirin, lansoprazole, nonsteroidal anti-inflammatory drugs, ranitidine, sertraline, ticlopidine, cyclo3fort, and cirkan.<sup>1</sup>

The first cases of lansoprazole-induced MC were published in 2001 after a national formulary change from omeprazole to lansoprazole in the VA hospital system. A recently published case series and systematic review of cases of lansoprazole-induced MC found a median time of symptom onset after lansoprazole initiation of 28 days in LC and 60 days in CC.<sup>2</sup> Macroscopic findings such as linear ulcers and submucosal hemorrhages were more common in lansoprazole-induced CC (72.2%) than in lansoprazole-induced LC (6.6%). Other reports of macroscopic findings in MC describe associations with nonsteroidal anti-inflammatory drugs, aspirin, lansoprazole, recent antibiotics, or infection.<sup>3</sup>

One retrospective, case-control study found an adjusted odds ratio of 4.5 (95% confidence interval, 2–9.5) for the association between MC and PPI use in the preceding 180 days of MC diagnosis.<sup>2</sup> The prevalence of use of individual PPIs in this cohort was omeprazole (40%), esomeprazole (22.8%), pantoprazole (28.6%), rabeprazole (5.7%), and lansoprazole (2.8%).

Management of drug-induced colitis includes removal of the offending agent. In the case of lansoprazole-induced MC, the median time for symptom resolution after drug removal was 7 days for LC and 14 for CC.<sup>2</sup> If symptoms do not resolve, treatment can include antidiarrheals, cholestyramine, budesonide, or systemic corticosteroids, depending on the severity of disease.

We suspect our patient had lansoprazole-induced MC. It is conceivable that his symptom resolution was owing to the corticosteroid course rather than discontinuation of the lansoprazole. However, in >11 months he has not had symptom relapse, his time course is consistent with other published cases of lansoprazole-induced MC, and other potential etiologies of diarrhea were ruled out. Furthermore, he has remained on aspirin, which is also known to be associated with MC, without relapse.

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## Answer to the Clinical Challenges and Images in GI Question: Image 4 (page 697): Gastrointestinal Infection by *Histoplasma capsulatum* Infection Identified With Internal Transcribed Spacer Primer Sets

Because the patient's symptoms did not improve with fluconazole treatment, colonoscopy was repeated 1 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 in immunosuppressed or immunocompromised patients; in HIV-infected patients, it presents in the disseminated form in 95% of cases.<sup>1</sup> Because 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.<sup>2</sup> It most commonly affects the ileocecum (~30%) or colon (~60%).<sup>2</sup> 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 2 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 Gomori's methenamine silver 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 because an organism could not be identified with standard serologic testing and cultures.<sup>3</sup>

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