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CASE REPORT

GASTROINTESTINAL HISTOPLASMOSIS: A CASE REPORT AND LITERATURE REVIEW

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Abstract:

A 33-year-old female with a history of renal transplant 18 months prior was transferred to our hospital with acute kidney injury after presenting with acute gastrointestinal symptoms. Computed tomography (CT) imaging suggested diffuse colitis. Her symptoms persisted on empiric antibiotics, and she developed hematochezia. Colonoscopy revealed discontinuous ulcers, and Histoplasma urine antigen was positive. Grocott's methenamine silver (GMS) staining of a large intestine biopsy revealed narrow-based budding yeast compatible with Histoplasma capsulatum. Itraconazole was initiated, and her symptoms improved within two days. This case demonstrates the importance of suspecting histoplasmosis in immunocompromised patients presenting with gastrointestinal symptoms.

Keywords: *Gastrointestinal histoplasmosis, histoplasmosis*

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Introduction:

Histoplasmosis is an infection caused by the dimorphic fungi Histoplasma capsulatum, which primarily occurs in endemic areas worldwide, including the Ohio and Mississippi river basins.[1,2] Inhaled spores from soil containing bat and bird droppings are phagocytosed by macrophages within the respiratory tract, where they can divide and disseminate to other tissues.[1,3] Individuals living in endemic areas have high estimated exposure rates; however, illness severity depends on the host's immunological status and exposure level.t Immunosuppressed populations are at higher risk for severe infections, including disseminated disease.[4] Gastrointestinal histoplasmosis (GIH) is an uncommon manifestation of disseminated histoplasmosis (DH), occurring along any part of the gastrointestinal tract.u GIH occurs in only 3-12% of DH cases.[6] Patients commonly present with diarrhea, abdominal pain, weight loss, and fever.[5]

Objective We present this rare case of histoplasmosis with isolated gastrointestinal symptoms to emphasize the importance of evaluating for Histoplasma infection using antigen tests or special stains, such as GMS, particularly in immunocompromised patients residing in endemic regions.

Case Report:

A 33-year-old female with a history of renal transplant 18 months prior was transferred to our hospital with acute kidney injury after presenting with acute onset abdominal pain, non-bloody diarrhea, nausea, and vomiting. The patient denied recent travel or known sick contacts. Upon arrival, she was tachycardic (101 beats/minute), afebrile (99.8°F), with blood pressure of 136/82 mmHg. Initial laboratory findings are summarized in Table I.

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Table I
A summary of blood test results upon arrival to our hospital

White blood cell count	2.5 x 10^9/L
Neutrophils	2.13 x 10^9/L
Lymphocytes	0.13 x 10^9/L
Hemoglobin	7.5 g/dL
Hematocrit	22.9 %
Platelets	221 x 10^9/L
Sodium	132 mmol/L
Potassium	5.2 mmol/L
Blood urea nitrogen	47
Creatinine	2.62
eGFR	24 mL/min
Lactic acid	1.2 mmol/L
Creatinine kinase	29 U/L

Empiric antibiotics with ciprofloxacin and metronidazole were initiated. Transplant nephrology managed immunosuppression; mycophenolate was held, while tacrolimus and prednisone continued. One year earlier, the biopsy of the transplanted kidney revealed budding yeast compatible with Histoplasma capsulatum, though urine and serum antigens were negative at that time. Itraconazole was discontinued previously due to gastrointestinal side effects. Initial infectious investigations, including COVID-19, influenza, blood cultures, stool ova and parasites, cytomegalovirus (CMV), Clostridium difficile, and gastrointestinal pathogen panel, were negative except for mildly elevated quantitative plasma CMV PCR (33 IU/mL). Elevated inflammatory markers included erythrocyte sedimentation rate (49 mm/hr), C-reactive protein (11.9 mg/dL), and fecal calprotectin (925 µg/g). CT imaging showed diffuse colonic wall thickening suggestive of colitis. Symptoms persisted, and hematochezia developed on day six, accompanied by nightly fevers up to 101.9°F. Colonoscopy revealed discontinuous ulcerations in the sigmoid and descending colon (Figure 1).

Initial colon biopsy indicated active colitis without CMV infection, granulomas, or inflammatory bowel disease. Further infectious investigations revealed negative HIV testing, but urine Histoplasma antigen was significantly elevated (13.23 ng/mL). GMS staining confirmed Histoplasma capsulatum infection (Figure 2).

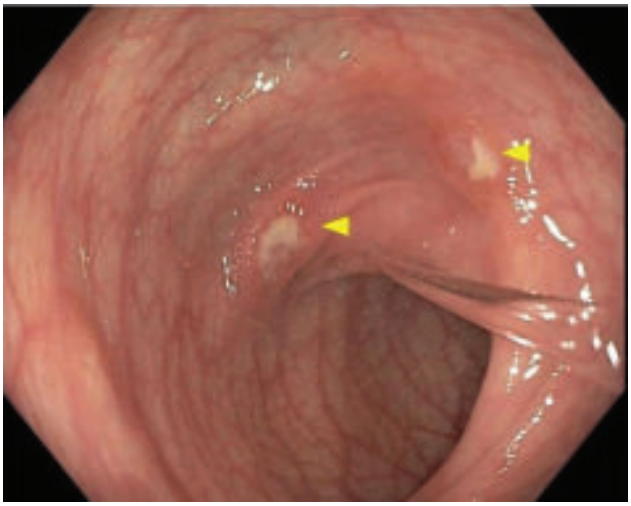

Figure 1: *Endoscopic imaging of the sigmoid colon showing multiple ulcerated lesions (arrows).*

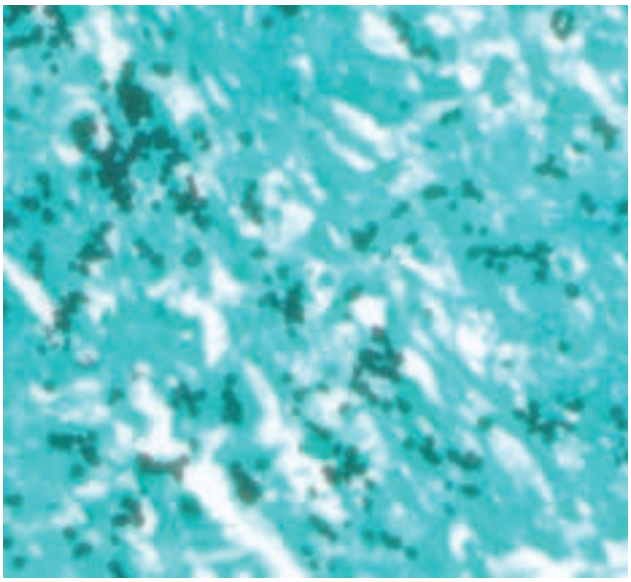

Figure 2: *Colon biopsy showed narrow based budding yeast consistent with Histoplasma capsulatum (GMS stain, 40x).*

Subsequent fungal blood cultures, serum Histoplasma antigen (0.97 ng/mL), brain MRI, and chest CT were negative for additional dissemination sites. Infectious disease consultation recommended itraconazole therapy despite previous intolerance, initiated at 200 mg orally three times daily for three days, then twice daily. Tacrolimus dosage was reduced. The patient tolerated itraconazole well, with significant symptom improvement within two days, normalization of creatinine, and discharge on treatment day four. Lifelong itraconazole therapy was planned due to the high risk of reinfection or reactivation, with close follow-up arranged.

Discussion:

Histoplasmosis is the most common endemic mycotic infection among solid organ transplant (SOT) recipients, although rare, with a one-year incidence of 0.1%.[7,8,9] Disseminated disease frequently presents as moderate to severe. [7,8,9] Symptomatic gastrointestinal histoplasmosis, as observed in this case, occurs in only 3-12% of DH cases.[6,9] Overlapping symptoms with more common gastrointestinal diseases can delay diagnosis. This patient's clinical presentation was typical of GIH yet also aligned with common gastrointestinal diseases.[5] Given her immunosuppressed state, a broad differential diagnosis was essential. Her previous history of histoplasmosis and poor initial treatment response guided further investigation, ultimately leading to the diagnosis. While tissue biopsy and fungal cultures are gold standards for diagnosis, antigen testing provides less invasive and timely alternatives. Serum and urine antigen testing should be included early in the workup when histoplasmosis is suspected.[11] Histological confirmation via PAS or GMS staining offers better visualization compared to hematoxylin and eosin staining.[10] Proper communication with pathology to ensure appropriate staining is vital. Recommended GIH treatment includes itraconazole for at least 12 months, with or without initial Amphotericin B, based on symptom severity.[9] Immunosuppressive regimen adjustments should be collaboratively decided through shared decision-making.[11,12] Regular monitoring of antigen levels at baseline, two weeks after therapy initiation, and every three months thereafter for 6-12 months is recommended.[10] Antigen levels may persist at low levels but discontinuation after completing therapy is considered safe in SOT patients.[13,14]

This case highlights a rare presentation of GIH in SOT recipients, underscoring the necessity of broad differential diagnoses and the consideration of histoplasmosis in immunocompromised patients with gastrointestinal symptoms, particularly with prior histoplasmosis exposure. Prompt antigen testing and appropriate tissue staining facilitate timely diagnosis and effective treatment.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research received no external funding.

Consent:

For the purpose of publishing this case report and any related photos, the parents are written informed consent was acquired.

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