

# Gastrointestinal histoplasmosis with regional lymphadenopathy masquerading as malignancy

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## Citation

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## Abstract

Gastrointestinal involvement with histoplasmosis is rarely diagnosed during life, and very few patients present with clinical symptoms. It can be misdiagnosed as inflammatory bowel disease, malignancy or other diseases causing intestinal stricture and perforation. Herein we report a case of colonic histoplasmosis presenting with abdominal pain, anorexia and weight loss, and was clinically suspected to be a carcinoma. This suspicion was further supported by endoscopic findings, which revealed an ulcero-nodular colonic mucosa with luminal compromise. Histological examination of the resected specimen and enlarged regional lymph nodes revealed dense lymphohistiocytic infiltrate, granulomas and many budding yeast forms of histoplasma both extracellularly and within the macrophages. The patient was later found to be positive for human immunodeficiency virus. Histoplasmosis should be considered in the differential diagnosis in patients with intestinal stricture simulating malignancy. This is particularly true for immunocompromised patients, as timely intervention can avoid further dissemination and disastrous consequences.

## INTRODUCTION

Although gastrointestinal histoplasmosis (GIH) has been detected in autopsy, it is uncommonly diagnosed during the life of the patient. It can affect both immunocompetent and immunocompromised patients, particularly individuals with acquired immunodeficiency syndrome (AIDS). As it causes clinical symptoms in as few as 3-12% of cases<sup>1</sup>, it may remain undiagnosed and is often misdiagnosed as inflammatory bowel disease or malignancy.

We report a case of GIH with colonic ulcer, stricture and perforation with strong clinical suspicion of malignancy. This is one of the very few reports of colonic disease with regional lymph node involvement in AIDS, which may contribute in understanding the clinical, endoscopic, radiological and pathological spectrum of histoplasmosis.

## CASE PRESENTATION

A 45 year old male patient presented with complaints of fever off and on and continuous dull aching pain in the left iliac fossa for last 5 months. There was anorexia and significant weight loss, but no complaints of malena or altered bowel habits. There was no history of diabetes, tuberculosis or operative intervention. Neither was there any hepato-splenomegaly or palpable lump.

Barium enema revealed a circumferential asymmetric thickening of the wall of distal descending colon causing irregular narrowing of lumen, producing an apple core appearance. Colonoscopy showed a stretch of 10-15 cm ulcero-nodular mucosa with luminal compromise in the descending colon. Wall thickening in the sigmoid and descending colon was also appreciated in Contrast Enhanced Computed Tomography (CECT) scan.

The patient was operated with a suspicion of malignant stricture. Left colectomy and anorectal anastomosis was performed. Intraoperatively a 5-6 cm long circumferential stricture, with perforation at the anti-mesenteric aspect was identified. Enlarged lymph nodes were also seen in the mesocolon. The resected segment of colon was 11 cm in length. Surface of lesion was irregular, shaggy, with areas of blackish discoloration and firm to hard base (Figure 1).

**Figure 1**

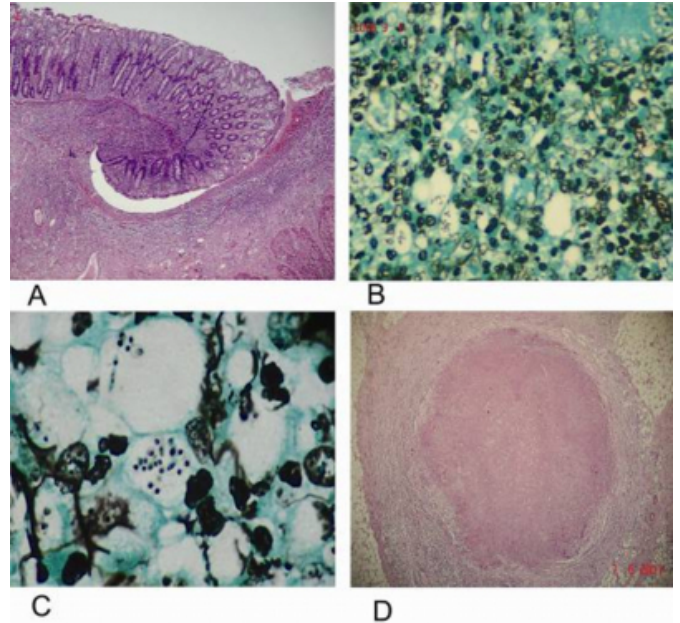
Figure 1: Resected specimen of colon showing stricture with mucosal ulceration.



Histopathological examination from the area of stricture showed an ulcer with dense inflammatory granulation tissue in the ulcer bed (Figure 2A). The inflammation was extending transmurally, destroying the muscularis propria and reaching up to the serosa. The inflammatory infiltrate comprised of sheets of lymphohistiocytic cells, admixed with neutrophils. Few granulomas and multinucleated giant cells were also seen. Many fungal profiles, scattered as well as in groups, conforming to the morphology of yeast forms of histoplasma were noted (Figure 2B and Figure 3). The fungal profiles were seen within the macrophages as well as extracellularly, and were better appreciated on tissue sections stained by periodic acid Schiff (PAS) and silver methenamine stains (Figure 2C). Regional lymph nodes showed large areas of necrosis (Figure 2D) with nuclear debris, sinus histiocytosis, few granulomas and multinucleated giant cells. Similar yeast forms were also identified in the lymph nodes (Figure 4). Stain for acid-fast bacilli (AFB) was negative in the sections from the stricture as well as from lymph nodes.

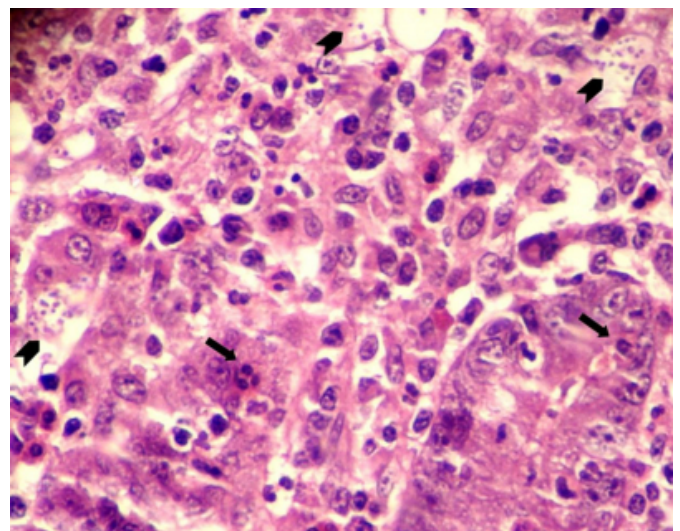
**Figure 2**

Figure 2A: Microscopy showing colonic ulceration with fissure of the mucosa (H&E, 20x) Figure 2B: Colonies of yeast forms of histoplasma; a colonic crypt seen in the upper right corner (Methenamine silver stain, 400x) Figure 2C: Intracellular organisms within a macrophage (Methenamine silver stain, 1000x) Figure 2D: Necrosis in regional lymph node; similar yeast forms were also identified in the lymph nodes (H&E, 20x).



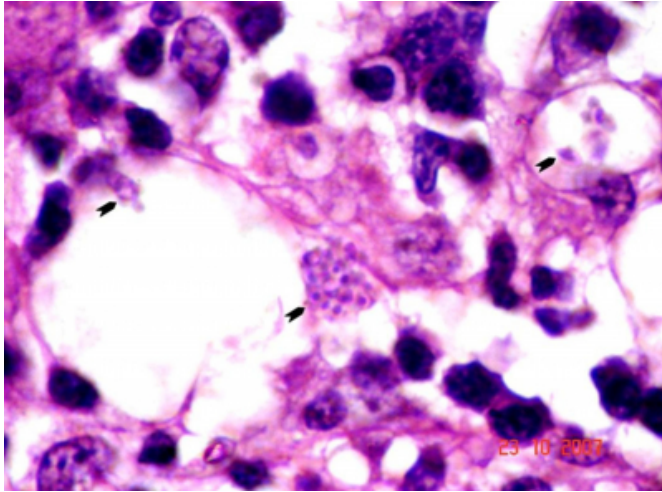
**Figure 3**

Figure 3: High power view of the colonic lesion showing lymphohistiocytic cell infiltrate admixed with neutrophils; colonic crypts with cryptitis shown with black arrows, the organisms are shown with black arrow heads (H&E stain, 400x magnification)



**Figure 4**

Figure 4: High power view of the histoplasmosis of a regional lymph node; the organisms are shown with black arrow heads. Note the cluster of organisms within a histiocyte at the centre. (H&E stain, 1000x magnification)



Post operatively patient had breathlessness, and X-ray chest revealed bilateral upper lobe infiltrate and hilar lymphadenopathy. The sputum was positive for AFB. *Klebsiella* and *Pseudomonas aeruginosa* were also isolated from the sputum culture. The patient's blood sample at this time was positive for HIV serology. The patient survived for 15 days post operative, and in spite of receiving broad spectrum antibiotics and anti-fungal drugs, later succumbed to the immuno-compromised state and secondary infections.

**DISCUSSION**

GIH is an uncommon but documented manifestation of histoplasma infection. However, cases simulating carcinoma in HIV positive patients have been rarely discussed in literature from the clinicopathological standpoint<sup>2, 3</sup>. Our case is an uncommon and interesting presentation of GIH in which there was localized ulceronodular lesion involving colon and regional lymphadenopathy with clinical suspicion of malignancy.

Predisposing factors for development of disseminated histoplasmosis include immunocompromised states like AIDS, immunosuppressive medications, extremes of age, various other causes of CD4 lymphocytopenia and other immune deficiency disorders like Job's syndrome, common variable immunodeficiency<sup>1</sup>. Dissemination and extrapulmonary histoplasmosis is now included in the case definition of AIDS<sup>4</sup>. Disseminated disease often leads to gastrointestinal histoplasmosis, but with gastrointestinal involvement, pulmonary symptoms are uncommon and

gastrointestinal symptoms predominate<sup>5, 6</sup>. Our case also presented primarily with complaints related to colonic involvement for 5 months. Breathlessness was elicited after the histopathological diagnosis of GIH. Subsequently, sputum culture was done which showed presence of acid fast bacilli, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. HIV sero-positive profile was also detected at this time, simultaneously with the sputum culture reports.

Irrespective of the immune status, most patients with GIH present in fifth decade of life with non-specific symptoms of abdominal pain, fever, weight loss, or diarrhea<sup>7, 8</sup>, and 68-76% are males<sup>1</sup>. In our case also the patient was a 45 year old male, presenting with non-specific complaints of pain abdomen, weight loss and anorexia.

The most common lesions are ulcers or mass, which often mimic inflammatory bowel disease, sarcoidosis or carcinoma<sup>2, 3, 6, 9</sup>, thus creating diagnostic dilemma and difficulty in management. Small bowel obstruction due to stricture has been reported<sup>4, 5</sup>. The patient may also present with hemorrhage, perforation or peritonitis<sup>7</sup>. Lee et al<sup>10</sup> reported a case of colonic perforation requiring emergency surgery. In our case colonoscopy revealed an ulceronodular lesion in colon with stricture and perforation. Colonoscopy, intraoperative findings and gross examination of the resected specimen were highly suspicious of malignancy.

Hepatomegaly and/or splenomegaly are reported in 30-100% of the cases. Intraabdominal lymphadenopathy can be seen in two-third of patients on CT scan<sup>1</sup>. In our case, there was no hepato-splenomegaly; however regional lymphadenopathy with nodal histoplasmosis had been documented.

In histologic sections of fixed tissue specimens, diffuse lymphohistiocytic infiltrates and nodules involving the mucosa and submucosa are commonly seen. Histoplasma capsulatum are usually small, 2-4µ in diameter, uniform, ovoid to spherical, uninucleate budding yeast with narrow-based buds. The organisms are often present in clusters within the cytoplasm of the macrophages. In hematoxylin and eosin (H&E) stained sections, the basophilic cytoplasm of H capsulatum retracts from the relatively thin cytoplasm thus leaving a clear area or halo-like zone around the organism. Periodic acid Schiff (PAS) and Gomori (Grocott) methenamine silver stains are useful for demonstrating H capsulatum in tissue<sup>1</sup>.

In our case, both colonic wall and adjacent pericolonic

lymph nodes showed epithelioid cell granulomas, lymphohistiocytic infiltrate and large areas of necrosis. Fungal profiles were seen within the macrophages and also lying extraellularly, in both these sites in H&E stain. The organisms were better appreciated in special stains like PAS and methenamine silver.

The diagnosis of GIH can be challenging as in the present case where the presentation was with localized colonic involvement and no immunocompromised state was documented at the time of presentation. GIH should be considered in the differential diagnosis of inflammatory bowel disease and suspected carcinoma even if the history of immunocompromised state is lacking initially. Conversely, in a known immunosuppressed patient, GIH should be considered in patients presenting with ulcer, stricture or perforation. Diagnosis of GIH is important as if left untreated can lead to lethal complications. On the other hand, timely and appropriate treatment can result in long term survival.

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