Case Report

Disseminated histoplasmosis mimicking metastatic disease of the colon and omentum: Report of a case and literature review

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Introduction

First described in 1906 by an Army physician in Panama, histoplasmosis is caused by the causative agent Histoplasma capsulatum [1]. Usually asymptomatic, histoplasmosis is the most prevalent mycotic infection in the United States [2]. H. capsulatum’s reservoir is soil contaminated with bird or bat droppings. Most infections follow exposure to these droppings in enclosed areas such as caves and attics. In the US, the annual incidence of Histoplasmosis exceeds 500,000 cases, and it is mostly isolated to endemic areas including the Ohio and Mississippi River valleys and smaller areas along the East Coast [3]. Although largely asymptomatic when contracted, inhalation of conidia and mycelial fragments may cause localised, self-limiting acute pulmonary symptoms.

Rarely, in patients that are immunosuppressed due to disease (AIDS) or medication (such as TNF-alpha inhibitors or corticosteroids), the disease can become disseminated and affect multiple organ systems. Involvement of the gastrointestinal (GI) tract by disseminated Histoplasmosis is exceedingly rare, identified in less than 1% of reported cases. We present an unusual case of disseminated Histoplasmosis masquerading as a malignant-appearing colonic mass and peritoneal carcinomatosis.

Case presentation

A 59 year old male presented with initial complaints of progressively worsening abdominal pain and diarrhoea over a period of one month. The abdominal pain was described as epigastric and intermittent that worsened with food intake. He also complained of early satiety, decreased appetite, and a 45 lb weight loss in the previous year. He did not report any fever, chills, or night sweats.

His past medical history included Type 2 diabetes mellitus and rheumatoid arthritis (RA). His RA regimen included non-steroidal anti-inflammatory medications in combination with infliximab and methotrexate. Prior pharmacotherapy also included corticosteroids, though he was not being treated with corticosteroids at the time of presentation.

Social history included a 30 year history of 1 pack per day smoking. He worked as a truck driver, travelling to Nevada and California in the past though his travel was limited to Texas, New Mexico and Oklahoma within the preceding 12 months. He was first evaluated by his rheumatologist who obtained an abdominal CT scan which showed diffuse caking of the omentum with questionable masses in the colon (Fig. 1A).
He was admitted to the hospital for further evaluation of possible omental carcinoma versus metastatic adenocarcinoma of the colon. A gastroenterology consult was obtained. Subsequent colonoscopy showed a fungating, ulcerative, partially obstructing mass in the transverse colon (Fig. 1B). A biopsy of the mass revealed non-specific inflammatory changes. Cancer markers CA 19-9 and CEA were both non suggestive of malignancy. CT scans of the head and chest were negative for metastasis, but the chest CT did reveal multiple pulmonary nodules and patchy peripheral confluent infiltrates. Omental biopsies were then obtained, which were non-revealing, though malignancy could not be ruled out.

The patient then underwent a diagnostic laparoscopy that was converted to a diverting loop ileostomy. Cultures performed on colonic and omental tissue were negative. Biopsies performed on the colon mass and omentum following resection were sent to an outside institution in consultation. During this time, the patient’s condition improved and he was tolerating his ileostomy well. He was discharged home to await the final results. Following discharge, the final pathologic diagnosis was rendered as non-caseating, granulomatous inflammation with fungal organisms, consistent with *H. capsulatum* and confirmed by Gomori Methenamine Silver (GMS) stain (Fig. 1C and D).

He was re-admitted to the hospital, and Infectious Disease was consulted. He was treated with intravenous amphotericin B for 2 weeks, then was transitioned to oral itraconazole, which he continued for an additional 6 weeks while convalescing as an outpatient. Since his last discharge, he has done clinically well with his ileostomy reversed and no further complications observed.

**Discussion**

Disseminated Histoplasmosis is an extremely rare mycotic infection and usually occurs secondary to high inoculum infections, direct invasion due to trauma, or in immunocompromised individuals. Risk factors include extremes of age, AIDS, inherent immune-deficient disorders, and immunosuppressive medications [4–7]. Our patient was taking methotrexate and infliximab for 8 years prior to presentation for rheumatoid arthritis whom most likely allowed for the progression of the disease. Infliximab is a monoclonal antibody that inhibits the activity of tumour necrosis factor-alpha (TNF-α). As with any other fungal infection, phagocytic cells such as neutrophils and macrophages play key roles in the immune defense against Histoplasmosis. In disseminated Histoplasmosis, engorged macrophages are observed. They can be transported to reticuloendothelial tissues such as the spleen, liver, lymph nodes, adrenal glands, and bone marrow which can facilitate the spread of the disease. The cytokine interleukin 12 (IL-12) has been well studied, including its role in increasing the activity of IFN-gamma and TNF-alpha with subsequent destruction of the phagocytised *H. capsulatum* [8,9]. This process outlines the importance of these cellular immune factors, and how immunosuppressive medications such as infliximab can hinder this immune response to fungal infections.

Disseminated Histoplasmosis in the GI tract, which occurs in 1 out of 5000 Histoplasmosis cases, has been documented in the literature within the immunocompromised population. One case has even been reported in the setting of Job’s Syndrome. In our literature search, only one case with severe complications was found where AIDS or immunosuppressant medications were not a precipitating factor [12].

Disseminated Histoplasmosis involving the GI system is commonly mistaken as other infections such as mycobacteria and *Entamoeba histolytica*, inflammatory bowel disease and, as in our case, malignancy [10–12]. Complications including bleeding, perforation, obstruction, and even peritonitis are common in this disease. Uncommon features of this case are the location of the obstruction, omental thickening mimicking metastasis, and the uncertainty of how he acquired the disease. In case reports, GI tract manifestations are usually found in the caecum and ileum, and, therefore, mistaken for Crohn’s Disease or Ulcerative Colitis [11,12]. In our case, the obstructive lesion was found in the transverse colon. Given the abdominal CT scan which showed omental thickening, the clinical picture was easily confused for adenocarcinoma of the colon that had metastasised. This is the first reported case, to our knowledge, describing disseminated histoplasmosis arising in this unique location within the bowel and associated with omental caking mimicking carcinomatosis. Another unique caveat to this case is the unclear contraction of the disease. His immunosuppressant medication does explain his increased susceptibility to contracting the disease, but his exposure history remains uncertain. According to the patient, he did not travel to any endemic areas, enter enclosed spaces, or come in close contact with soil or particulate matter likely to contain significant amounts of bird or bat droppings. His exposure history is purely speculative, and it remains unclear whether the organisms were acquired from the environment or through human to human contact.

Proper and swift diagnosis is critical in the treatment of this disease. With any concern for disseminated Histoplasmosis, urine and blood antigen testing have been the most successful method for diagnosis. Seventy-five percent of non-immunocompromised and 95% of immunocompromised patients with DH were confirmed with urine antigen testing, while 100% of cases were discovered with blood antigen testing [13–15]. Antigen testing was not employed in our case because infection was not in the initial differential diagnosis and biopsies had already been obtained for histologic review. Other means of diagnosis, including polymerase chain reaction (PCR) and antibody testing, have not shown the same success rate. Studies with PCR testing have noted a sensitivity of only 8–11% in urine or bronchoalveolar lavage specimens that were positive for Histoplasma antigen [16]. Antibody testing has shown a low detection rate of only 20% in the setting of patients taking...
immune-modulating medications such as infliximab [14]. Cytology and histopathology as used in this case report looks for 2–4 μm yeast structures of *H. capsulatum* in the biopsies. Although the organism sometimes can be demonstrated by haematoxylin and eosin stain, GMS or periodic acid Schiff (PAS) stains are better choices for visualising the yeast.

Once the diagnosis is made, treatment should be started immediately. Especially in the setting of hospitalisation, IV amphotericin B in its liposomal form is recommended. Itraconazole is another option but only in patients who have mild to moderate symptoms and for step-down therapy in those who have improved with initial amphotericin B administration [17,18]. Itraconazole is not recommended for initial therapy in hospitalised patients because it does not eradicate fungemia as rapidly as amphotericin B [19]. Fluconazole and ketoconazole have not shown the same effectiveness, and ketoconazole is associated with a higher rate of side effects. Our patient received IV amphotericin B for 2 weeks in the hospital followed by oral itraconazole administration for 6 weeks.

This case depicts unique features of disseminated Histoplasmosis involving the GI tract, including development of a mass-forming lesion in the transverse colon and omental caking mimicking carcinomatosis, in an immunocompromised host with no definitive exposure history. These features are previously unreported to our knowledge, and this case highlights the importance of accurate diagnosis and prompt treatment to prevent complications.

**Conflict of interest disclosure**

The corresponding author is the guarantor of submission. Dr. Soape performed background discussions with the patient and created the manuscript. Dr. Romano performed pathological examination of the biopsies and helped revised the manuscript. Dr. Thirumala performed pathological examination of the biopsies and helped revised the manuscript. Dr. Ghandour was the attending physician in the patient’s care, performed the endoscopic procedures, and helped in the revision of the manuscript. No financial support was obtained in the making of this manuscript. There are no other conflicts of interest regarding this manuscript.

**References**


