Gastrointestinal Histoplasmosis and CMV Co-Infection in an Immunocompetent Host

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Abstract
A middle aged male with no known comorbidities presented with history of colicky abdominal pain, low grade fever and weight loss. Laboratory parameters were normal except low albumin. Imaging showed multiple areas of mural thickening with enhancement in jejunum & ileum. On Colonoscopy there was a thickened and deformed ileum with multiple ulcers. The biopsy showed co-infection of CMV and histoplasma, urine antigen for histoplasma was positive and CMV DNA detected in blood. He was successfully treated with combination of Valgancyclovir and Amphotericin-B followed by itraconazole.

Introduction
Histoplasmosis is a fungal disease caused by a dimorphic fungus Histoplasma capsulatum. It is endemic in eastern India, certain parts of Africa and America and it most commonly causes pulmonary manifestations. However, around 10-15% patients develop disseminated infection. Most of which occur in setting of immuno compromised state. Gastrointestinal Histoplasmosis is a manifestation of a disseminated disease. CMV infection is also very rare in immunocompetent persons and can involve any part of GI tract from mouth to anus. Here we report an uncommon case of gastrointestinal histoplasmosis with CMV ileitis in an immunocompetent patient. CMV involvement of only ileum and sparing the colon, which is also rare. The merit of this case is that it underlines the importance of considering this diagnosis even in an immunocompetent persons.

Case Report
A middle aged male, farmer, resident of Gorakhpur, U.P, non alcoholic, non smoker, with no known co-morbidities presented to us with a 3 months history of an intermittent colicky abdominal pain around umbilicus increased after meals with abdominal bloating, nausea, occasional vomiting, low grade fever and constipation alternating with intermittent non bloody diarrhoea. He also had weight loss of around 15 kgs in past 3 months. He did not complain of oral ulcers, breathlessness, cough, hemoptysis or headache. He had past history of pulmonary tuberculosis 1.5 years back and was successfully treated with 9 months of ATT. He was not on any immuno-suppressive medication. On examination, he was cachectic with temporal wasting, vitals were stable, there was mild pallor, he had palpable inguinal nodes along with hepatosplenomegaly. There was no icterus, pedal edema, skin changes or clubbing. Routine investigations showed Hb 12.4 gm/dl, TLC 3800, Albumin 2.0 gm/dl, S. IgA, IgG, Cortisol, ANCA, ASCA, TSH, HbA1c were normal, S.HIV was negative. X-ray abdomen showed multiple dilated small bowel loops with air fluid levels. Chest radiograph showed scar of healed TB. CT chest also showed the same & there was no mediastinal lymphadenopathy. CT enterography showed multiple areas of mural thickening in jejunum and distal ileal loops with few mesenteric lymph nodes (Figure 1). Ileocolonoscopy was done which showed deformed ileum with multiple ulcers in ileum and cecum, multiple biopsies were taken (Figure 2). The ileal biopsy showed blunting of villi with ulcerations with granulation tissue containing sheets of macrophages with intracytoplasmic capsulated spores (Figure 3) which were positive on Gomori methenamine silver stain (Figure 4). Lamina propria showed dense chronic inflammation. Immunohistochemistry for CMV was also positive (Figure 5). There was...
no evidence of inflammatory bowel disease. AFB stain was negative. The colonic ulcer biopsy showed features of acute colitis with no evidence of CMV or Histoplasma infection. In view of these findings, blood culture for fungus was sent which came negative, but urine antigen for histoplasma and serum CMV DNA were positive.

Patient was started on lipid formulation of Amphotericin-B, 5 mg/kg dose for 7 days along with valgancyclovir 900mg BD orally for 14 days. After 7 days he was shifted to oral itraconazole 200mg BD for 3 days then 200mg OD. With this treatment his abdominal symptoms improved significantly and he was discharged and advised to follow up after 2 months. Repeat colonoscopy showed almost complete healing of the lesions.

Discussion

Histoplasmosis was first described by Darling in 1906. The natural habitat for this dimorphic fungus is soil. The growth is enhanced by bird and bat droppings. Major route of infection is by droplets. Progressive Disseminated Histoplasmosis (PDH) occurs in individuals deficient in cell-mediated immunity and is fatal if untreated. Progressive disseminated histoplasmosis is defined as a clinical illness that does not improve after at least 3 week of observation and that is associated with physical or radiographic findings and/or laboratory evidence of involvement of extrapulmonary tissues. Risk factors for PDH include AIDS, transplant recipients, use of immunosuppressants like steroids, Anti TNF-alpha, methotrexate etc. However, around 40% of patients do not have any identifiable factors but most of these patients had a disease limited to lung. PDH constitutes only 1% of the disease spectrum and is uncommon in immunocompetent individual. Gastrointestinal involvement in symptomatic patients of PDH is 3-12% however on autopsy studies prevalence is as high as 70%.2 The distal ileum is the most common site involved, followed by colon and stomach. Symptoms include abdominal pain (40-60%), fever (30-50%), diarrhea, weight loss, oral and GI ulcerations. On examination lymphadenopathy in CT scan is seen in 60-70% of cases.4,6 Complications include perforation, peritonitis, bleeding and malabsorption. Small intestinal obstruction has also been rarely reported. Diagnosis is made by histology, urine antigen test or antibody test. Untreated PDH has a very high mortality (85%) however if treated early, its decreases to 25%.5 Cytomegalovirus (CMV) is a β-group herpes virus and usually produces latent infection which becomes active in immune deficient persons. Gastrointestinal tract may be affected anywhere from the mouth to the anus with the esophagus and colon being the most common sites of involvement while small bowel is rarely involved. The clinical manifestations of gastrointestinal CMV infection include gastrointestinal bleeding, abdominal pain, vomiting, fever and diarrhea. On endoscopy, ulcerations (classical - punched out), erosions with mucosal hemorrhage are common. Diagnosis is made by presence of classical intranuclear & intracytoplasmic inclusions on immunohistochemical staining of biopsy specimen. Serology and DNA estimation can also be done. Treatment includes antiviral agents like gancyclovir, valgancyclovir, foscarnet. Treatment is not always indicated in immunocompetent patients. However we treated our patient in view of dual infection and poor nutritional status.

Lokesh et al reported a similar presentation with both CMV and histoplasma infection in an immunosuppressed elderly male. Ju Dong Yang et al reported a case of histoplasmosis with intestinal and adrenal involvement in an immunocompetent patient. Assi MA reported a review of 111 patients with histoplasmosis, 59% patients were immunosuppressed3.

In this case we could see a rare combination of only CMV & Histoplasma co-infection in an immunocompetent host, which underlines the importance of considering Histoplasmosis as a differential in immunocompetent persons as well.

References

8. Sahani L. Disseminated histoplasma and CMV infection presenting as subacute intestinal obstruction in an immunocompromised patient. BMJ Case Reports 2012;10.1136/bcr.08.2011.4732