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Disseminated Histoplasmosis after Vedolizumab Treatment for Ulcerative Colitis

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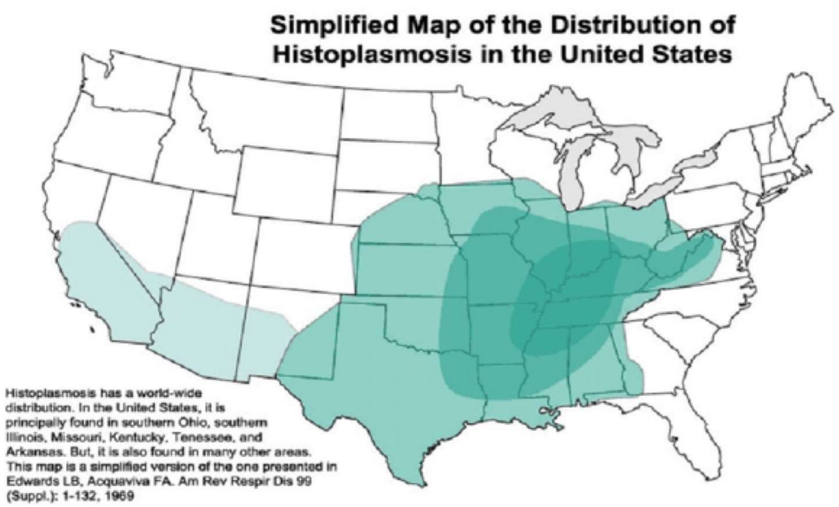
Abstract

We present a case of disseminated histoplasmosis in a non-endemic area in a patient following treatment with vedolizumab, an anti-integrin monoclonal antibody, for ulcerative colitis. The patient was admitted for fevers, elevated liver function tests and liver biopsy showed granulomas with encapsulated yeasts, confirming *Histoplasma capsulatum* infection. Only two cases of histoplasmosis after vedolizumab have been reported.

Background

- Epidemiology: Histoplasmosis is one of the four known systemic mycoses known to be endemic in the Ohio and Mississippi River valleys in the United States and much of Latin America.
- Transmission: Systemic mycotic infections are acquired through inhalation of spores found in the environment. Sources of *Histoplasma capsulatum* spore exposure include farming, cutting down trees, and remodeling or demolition of old buildings.
- Clinical features: It can cause pneumonia and forming granulomas similar to tuberculosis, but it is incapable of being transmitted person-to-person. If immunocompromised, *H. capsulatum* can disseminate and cause a variety of symptoms including fever, fatigue, weight loss, lymphadenopathy, hepatomegaly, splenomegaly with laboratory findings of anemia, leukopenia, thrombocytopenia, elevated hepatic enzymes, bilirubin, lactate dehydrogenase and ferritin.



Case Description

Patient demographics: 41 year old Michigan native with past medical history significant for ulcerative colitis

History of present illness: The patient had recently been started on vedolizumab, and tolerated two transfusions. A few weeks after the patient's last vedolizumab infusion, he presented to urgent care endorsing home temperatures of 102-103°F. A follow up with his primary care physician and subsequent lab work revealed elevated aspartate transaminase (AST) of 266 and alanine transaminase (ALT) of 232 and he was sent to the emergency department for further evaluation.

Social history: He lived his entire life in Michigan and had no recent travel outside the state. At home, the patient was exposed to a rabbit, dog and gecko and he worked as a construction worker. He did endorse frequently chopping wood in the forest and multiple other outdoor activities.

Hospital Course

- Throughout his admission, the patient had cyclic nightly fevers with temperatures reaching 102-103°F. Infectious workup to rule out atypical opportunistic infections was done, including HSV, HIV, Hep B, Hep C, Hep A, C diff. CMV, Giardia, Syphilis and Cryptosporidium.
- MRCP was performed given his transaminitis and was suggestive of possible small duct primary sclerosing cholangitis (PSC). Liver biopsy was done to further characterize and confirm the PSC, but the pathology report showed granulomas, encapsulated yeasts, and no evidence of PSC.
- Test results revealed positive urine histoplasma antigen and positive blood beta-d-glucan. With suspected disseminated histoplasmosis, the patient was started on IV liposome amphotericin B for one week after which he was transitioned to oral itraconazole for 3-6 months. His fevers resolved, and his LFT's returned to normal.

Figure 1. Fever curve before and after initiation of antifungal therapy.

Discussion

- Histoplasma capsulatum is endemic in the Mississippi River valleys, but is rare in Michigan
- There have only been two case reports of *H. capsulatum* infection associated with vedolizumab, only 1 of which progressing to disseminated histoplasmosis
- This patient had a fondness for outdoor activities as well as recent immunomodulator use that increased his risk for disseminated fungal infection
- Maintaining a broad differential in patients on immunomodulator therapy is critical
- Histoplasmosis can present in a variety of ways, and along with other systemic mycoses, should be considered in patients presenting with non-specific systemic symptoms.

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