Disseminated histoplasmosis causing splenic rupture in a patient receiving infliximab

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To the Editor,

Infection with the soil fungus *Histoplasma capsulatum* accounts for the most prevalent endemic mycosis in the United States but it rarely results in serious and fatal disease (1). The usual manifestation of histoplasmosis is in the form of pulmonary disease, but in immunocompromised individuals it may present as a disseminated infection (2). Hepatomegaly and splenomegaly with variable degrees of severity are known clinical manifestations in disseminated disease, but these are usually uncomplicated. We present the first reported case of disseminated histoplasmosis complicated by splenic rupture.

A 23-year-old white male, presented to the hospital with a one week history of fever, dyspnea, and vomiting. Patient had rheumatoid arthritis and was being treated with methotrexate and infliximab. He was febrile at 39.4° C, and had crackles at the base of right lung. Chest x-ray confirmed right lower lobe pneumonia and levofloxacin was started. Two days later, patient clinically deteriorated and developed abdominal pain along with drop in hemoglobin from 12 to 8.7 g/dL. Emergent CT scan of abdomen showed a large subcapsular splenic hematoma with moderate ascites (Fig. 1A). Exploratory laparotomy confirmed hemoperitoneum and splenic rupture needing splenectomy. Splenic and liver biopsies showed fungal organisms in background of necrotizing granulomas with acute inflammation. Pathology report was consistent with histoplasmosis (Fig. 1B). The patient was started on amphotericin B and gradually improved. He was transitioned to itraconazole and discharged home. On a 6-month follow-up the patient was doing well.

H. capsulatum is endemic to the Mississippi and Ohio River valleys. Each year, thousands of individuals are infected with *H. capsulatum,* but less than 1% of exposed persons develop appreciable clinical disease (3,4). T cell immunity is essential to recovery from Histoplasmosis and usually takes about 2 weeks to develop. Interleukin 12 and tumor necrosis factor α (TNF-α) facilitate macrophages in halting progression of the disease. In immune competent individuals, macrophages, lymphocytes, and epithelial cells organize to form granulomas that contain the organism. The granulomas usually fibrose and calcify ; and are frequently found in healthy persons as calcified mediastinal lymph nodes and hepatosplenic calcifications, in endemic areas. In immunocompromised patients, failure to activate macrophage fungicidal capacity may result in Progressive Disseminated Histoplasmosis (PDH). The severe infections occurring in the patients receiving TNF antagonists highlight the importance of cell-mediated immunity in protection against histoplasmosis (4).

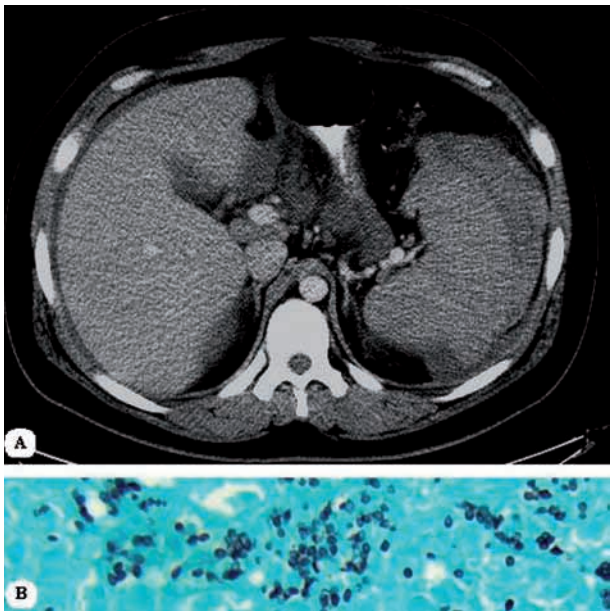

Fig. 1. — A : CT scan of abdomen showed a large subcapsular splenic hematoma. B : Splenic tissue with *Gomori methenamine silver* stain : numerous yeasts with narrow budding consistent with histoplasma (100×).

Marked enlargement of the involved organs can be seen with heavy infections and at times, normal parenchyma may be displaced resulting in organ dysfunction (1). In one of the case studies of patients with

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PDH, splenomegaly was noted in 38% and hepatomegaly in 63% of the patients and 12% had one or more splenic infarcts (5).

In conclusion, our patient suffered from PDH with multi-organ involvement resulting in splenic rupture likely due to splenic enlargement or infarct. Patients receiving TNF-α antagonists are at a risk for developing PDH, and complication of significant organ damage should be entertained in these individuals, in appropriate clinical situation. To the best of our knowledge, this is the first reported case of disseminated histoplasmosis resulting in splenic rupture in a patient receiving TNF-α antagonist therapy.

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