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Case report

Acute Disseminated Histoplasmosis with Atypical Lymphocytosis in an Immunocompetent Host

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ABSTRACT

65 year-old-male presented with a one-week history of high grade fever, fatigue and confusion which began abruptly two days after a cystoscopy procedure. Past medical history included pulmonary sarcoidosis diagnosed by mediastinal lymph biopsy, diabetes and hypertension. On admission he was febrile and confused with stable vital signs. Initial workup included negative Head CT and lumbar puncture. Blood work revealed normal metabolic and liver function tests with progressive anemia, thrombocytopenia and atypical lymphocytosis of 15–20%. Blood, urine and respiratory cultures all were negative for bacteria and. A bone marrow biopsy was done given the abnormal lymphocytes in peripheral smear, revealing budding yeast consistent with *Histoplasma capsulatum*. Histoplasma antigen was positive in urine and eventually blood and bone marrow grew *H. capsulatum*. Patient was started on amphotericin-B for diagnosis of disseminated histoplasmosis. After a 2 week period of amphotericin B, patient was switched to oral Itraconazole to complete 12 months course of treatment.

Introduction

After acute infection, *Histoplasma capsulatum* remains dormant for many years and is typically asymptomatic in immunocompetent patients. Reactivation with dissemination may occur in ~5% of cases and occurs mostly in immunocompromised and patients at extremes of age [1]. Genitourinary involvement with *H. capsulatum* is uncommon with only a few case reports of prostate involvement described in patients with human immunodeficiency virus infection (HIV) [2]. We describe an unusual presentation of acute disseminated histoplasmosis following cystoscopy in an immunocompetent patient.

Case report

A 65 year old male with type 2 diabetes mellitus and hypertension presented with one week of high grade fever, fatigue and confusion. Several days prior to the onset of fever, he underwent elective cystoscopy procedure related to incomplete bladder voiding that didn't show any gross abnormality. The patient carried a diagnosis of sarcoidosis related to asymptomatic enlarged mediastinal lymph nodes which had been biopsied 10 years prior. He never received corticosteroids. He was a nonsmoker and worked as a shoe salesman. On admission, his temperature was 38.9° C, with stable vital signs and room air oxygen saturation was 95%. He was intermittently confused. Lung examination revealed scattered rhonchi. The patient had no palpable lymphadenopathy and rest of the physical examination was unremarkable. Initial workup included head CT and lumbar puncture which were negative for any abnormality. Chest and abdominal CT scans showed modestly enlarged mediastinal and retroperitoneal lymph nodes consistent with sarcoidosis.

His peripheral blood smear showed normocytic anemia (Hgb-12.7 gm/dL), thrombocytopenia ($117 \times 10^3/\mu L$) with a normal total white blood cell count. However, peripheral smear showed 6–19% atypical lymphocytes during the first week of hospitalization. Renal and liver function tests were normal. Bacterial blood, urine and respiratory cultures were negative as was testing for all viruses including: Epstein Barr Virus, Cytomegalovirus, and HIV. A bone

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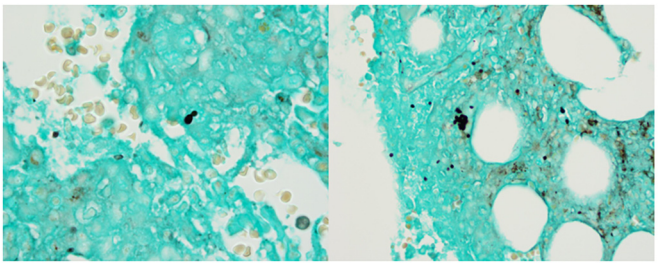

Fig. 1. Methenamine silver stain of bone marrow showing budding yeast consistent with *Histoplasma capsulatum*.

marrow biopsy was done because of the abnormal peripheral blood smear, which revealed budding yeast consistent with *Histoplasma capsulatum* (Fig. 1). Urine histoplasma antigen was positive and eventually blood and bone marrow grew *H. capsulatum*.

The patient was started on intravenous lipid formulation amphotericin B. The patient had a prolonged hospital course complicated by septic shock and respiratory failure requiring mechanical ventilation but eventually recovered and was transitioned to oral itraconazole to complete 12 months treatment course for disseminated histoplasmosis.

Discussion

Histoplasmosis is among the most common endemic mycosis in the United States with the largest burden of disease occurring in Midwestern states around the Ohio and upper Mississippi River valleys. *H. capsulatum* enters the human host by inhalation of spores into the lungs. In immunocompetent patients the lung macrophages ingest the fungi and migrate throughout the body disseminating the organism to various organs. Development of cellular immunity is the prime factor to control infection and generally results in fungal containment within granulomas. Asymptomatic granulomas can be found in a variety of organs and are discovered mainly from autopsy studies [3]. There are case reports of chronic disseminated histoplasmosis especially in the elderly patients with no obvious immunosuppression other than immunosenescence. Specific defects in macrophages and T cells, in the processing of histoplasma antigens have been described in these cases [3]. Sarcoidosis is known to be associated with T cell dysfunction; previous case reports have shown cases of sarcoidosis complicated with disseminated histoplasmosis [4–6]. Although our patient never received corticosteroid treatment, sarcoidosis may have contributed in rapid dissemination of histoplasmosis. Alternatively, he may have been misdiagnosed with sarcoidosis and the enlarged lymph nodes with granulomas were due to histoplasmosis which was missed on biopsy.

Pancytopenia is a common presentation for disseminated histoplasmosis and our patient had progressive anemia and thrombocytopenia. However, significant atypical lymphocytosis has not been described in patients with histoplasmosis. The more common causes of atypical lymphocytosis (viral infection, drug reactions and hematologic malignancies) were ruled out. However, the strikingly abnormal peripheral blood smear did lead to the bone marrow biopsy; through which diagnosis of disseminated histoplasmosis was established. Atypical lymphocytosis disappeared with therapy.

Case reports have shown that histoplasmosis can involve the genitourinary system, and may be asymptomatic. Rarely histoplasmosis may present with testicular and prostatic abscess or epididymitis [2,7]. Given the temporal association with the cystoscopy in our patient, we hypothesize that latent infection in the prostate may have been disrupted by the urologic procedure leading to dissemination of fungi into bloodstream.

Conclusion

This case highlights an unusual presentation for disseminated histoplasmosis with atypical lymphocytosis in relation to a cystoscopy procedure. Disseminated histoplasmosis should be kept in our differentials for fever of unknown origin in elderly immunocompetent patients with hematologic abnormalities.

Conflicts of interest

Authors have no conflicts of interest to declare.

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