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Case Report

Disseminated Blastomycosis Dermatitidis Causing Hepatitis in an Immunocompromised Patient

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Abstract

We present a rare case of disseminated blastomycosis dermatitis causing hepatitis in an immunocompromised patient. A 46-year-old woman with history of crohn's disease presents with one week of fever and right upper quadrant pain. She is found to have elevated liver function tests and normal liver and bile duct imaging. In humans, there is no other published case study in the literature of liver involvement on presentation.

INTRODUCTION

Most extrapulmonary sites of blastomyces in humans are skin, skeleton, male genitourinary system, and central nervous system in decreasing order [1,2]. Extrapulmonary manifestations are only seen in 30% of women [1]. Reticuloendothelial system involvement (lymph nodes and/or liver) is exceedingly rare and has been reported only a few times [2].

CASE PRESENTATION

A 46 year-old female with a history of Crohn's disease on adalimumab and methotrexate for 10 years was hospitalized with complaints of chest pain, shortness of breath and fevers for one week. Physical examination revealed stable vital signs, anicteric sclera, mild right upper quadrant tenderness, and no skin nodules. Her labs on admission were a total serum bilirubin of 1.2 mg/dl, serum lipase at 439 U/l, alkaline phosphatase (AlkP) of 304 U/l, and a serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) of 716 and 1044, respectively. Computer tomography (CT) scan of the chest, abdomen and pelvis confirmed mild fatty liver and diffuse gallbladder wall thickening, but also a right lower lobe infiltrate and mild effusion. Ultrasound of the gallbladder revealed a thick wall with some mild pericholecystic fluid. No stones were identified. A hepatobiliary iminodiacetic acid (HIDA) scan revealed normal uptake in the liver and no uptake in the hepatic ducts, common bile duct and the gallbladder. A Magnetic Resonance Cholangiopancreatography (MRCP) revealed a normal liver, intrahepatic and common bile ducts and no stones (Figure 1). All other organs on imaging were unremarkable. Autoimmune liver and viral hepatitis panels as well as EBV, HSV, CMV, VZV, and HIV were all negative. The patient had a bronchoscopy with lavage with cultures pending, but the urine antigen was positive for histoplasma, so the patient was started on liposomal amphotericin B. Adalimumab and methotrexate were held during her hospital stay.

Her AlkP, AST, ALT and bilirubin continued to increase during the admission to 804, 1361, 914 and 8.5 respectively. Conjugated

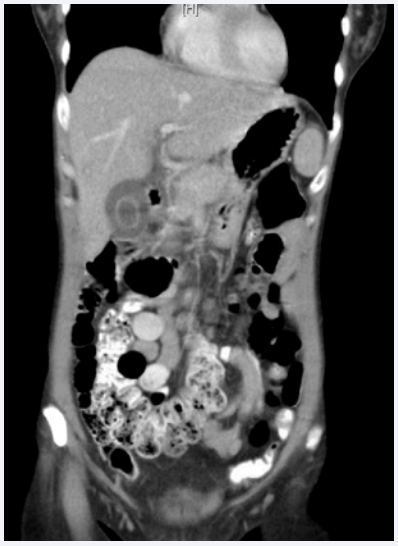

Figure 1 MRCP illustrating a normal liver, intrahepatic and common bile ducts and no stones.

bilirubin reached a maximum value of 7.5 mg/dl. She clinically improved despite the increasing LFTs. The amphotericin B was changed after 3 days to oral itraconazole, and by then, her lavage cultures grew blastomyces dermatitidis. Serum was also positive for blastomyces dermatitidis antigen. She was discharged home with improved LFTs and completed her itracanozole course. She resumed adalimumab and methotrexate without any further lab abnormalities including LFTs. She remains clear of blastomyces at 1.5 years of follow up with her Crohn's disease also controlled.

DISCUSSION

To our knowledge, there are no reported cases in the literature of disseminated blastomyces dermatitidis causing hepatitis in a patient. Our patient presented with right upper quadrant pain that was likely due to both pulmonary involvement as well as acute hepatitis. Initial imaging of the liver and biliary tree suggested gallbladder irritation and cholestasis, but were otherwise anatomically normal despite elevated liver function tests (LFTs). Our patient clinically improved on amphotericin B although her already elevated LFTs transient increased as well, until switched to itraconazole.

There are only 2 other cases of patients presenting with acute blastomycosis pneumonia have been reported where elevated LFTs have been mentioned as part of the hospital course. In one case, a 44 year-old white female presented with fever, cough and alcoholic hepatitis in June 1982. She was diagnosed by sputum culture. She was non-compliant with her anti-fungal medications and she ultimately died of delirium tremens. Liver involvement was not pathologically confirmed [3]. In the second case reported in 2013, a seventeen-year-old male presented with cough, hemoptysis, lethargy, twenty-pound weight loss, and skin lesions. He was diagnosed by skin biopsy and was found to have bone but no brain involvement. He was started on amphotericin B and suffered complications of hypokalemia, hypomagnesemia, high creatinine, and elevated LFTs thought to be due to the medication. He was changed to itraconazole. Liver involvement was also not confirmed and LFTs were not elevated prior to medication initiation [4]. In the first patient, the likely cause of elevated LFTs at diagnosis was alcohol-induced, and for the second patient, it was a complication of medication rather than the initial disease. Thus, our case is different in that it is the first reported case of a patient presenting with hepatitis from infectious causes. Our imaging, which included CT, HIDA, and MRCP, confirmed that there were no gallstones or bile duct blockage as a source of the hepatitis. Our case is similar to the second case only in that the LFTs worsened with amphotericin.

In non-humans, there is a reported case of disseminated blastomycosis in a Rhesus monkey. The animal had gross necropsy that revealed miliary granulomatous pneumonia, multifocal cerebral abscess, granulomatous splenitis, and minimal focal hepatitis. Involvement of the spleen, liver and/or lymph nodes has been reported as more common in other animals like dogs (Rhesus paper). In humans, there is no other published case study in the literature.

A far more likely infectious source of both lung and liver is histoplasmosis [1,4]. Both histoplasmosis and blastomycosis are dimorphic fungi that exist in soil in the mycelial phase, are introduced by inhalation, and convert to the yeast phase at body temperature [1]. The positive histoplasma urine antigen seen in our patient was likely secondary to cross reactivity with blastomyces. The treatment for disseminated cases of histoplasmosis and blastomyces is similar, starting with amphotericin B. Her clinical improvement but worsening LFTs (over her initial elevation at presentation) was likely due to cholestasis from amphotericin-B on top of the underlying liver involvement. Crohn's disease does not involve the liver, and her disease and medications have been stable for over 10 years. During her admission, her Crohn's medications had been held, and so did not contribute to the hepatitis either. Again, our imaging ruled out stones as possible cause of the initial elevated LFTs.

CONFLICT OF INTEREST

There is no financial support of the manuscript, and any potential financial or other conflicts of interest.

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