Hepatic Histoplasmosis Masquerading as Cirrhosis and Portal Hypertension: A Case Report

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Abstract

Histoplasmosis is an uncommon cause of pyrexia of unknown origin in India. We present a case of hepatic histoplasmosis presenting as pyrexia of unknown origin. The patient had splenomegaly, thrombocytopenia, high serum-ascites albumin gradient, and imaging suggestive of cirrhosis. The patient had received 2 months of antitubercular treatment and came to us because of a lack of improvement. A liver biopsy was done because of cholestatic liver function tests and normal biliary system on imaging, thus raising the possibility of infiltrative liver disease. A transjugular liver biopsy revealed histoplasmosis. The patients improved after treatment. It is a common practice to start antitubercular treatment in patients with pyrexia of unknown origin, which should not be practiced in the current era. Every effort should be made for a correct diagnosis. The case highlights the importance of liver biopsy in cases with no definite diagnosis and also that hepatic histoplasmosis could mimic cirrhosis.

Keywords
- histoplasma
- ascites
- fever
- hepatic

Case

A 42-year-old female presented with complaints of intermittent fever associated with weight loss for 5 months. An ultrasound abdomen showed coarse echotexture of the liver and splenomegaly. FibroScan (vibration-controlled transient elastography) showed a liver stiffness value of 23 kPa. The patient developed ascites and pedal edema in the later course. Routine investigations for the cause of the fever were negative. Computed tomography showed caudate lobe prominence, irregular liver margins (►**Fig. 1A**), and splenomegaly. Ascitic fluid investigations revealed transudative nature with a high serum ascitic albumin gradient of 1.5. The adenosine deaminase value of ascitic fluid was 6 U/L. She was suspected of having an underlying chronic liver disease with portal hypertension because of imaging, high gradient ascites, low albumin, low platelet count, splenomegaly, and high liver stiffness value. She had received empirical antitubercular therapy for pyrexia of unknown origin (PUO) for 2 months. However, there was no improvement. At this point, she came to our hospital. Investigations

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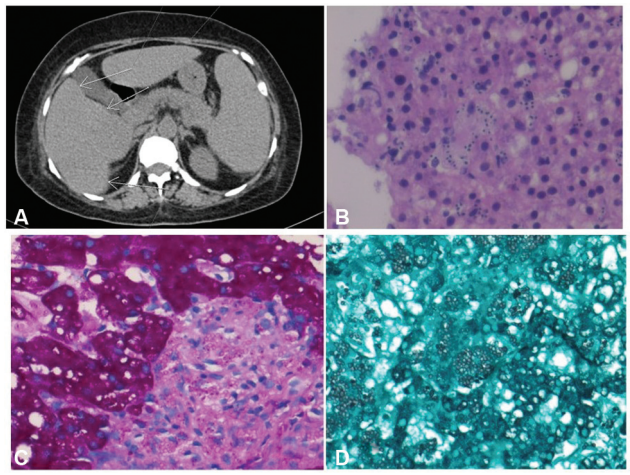

Fig. 1 (**A**) Irregularity of inferior margins of the liver (marked by arrows) and splenomegaly. (**B**) Hematoxylin and eosin stain showing small round organisms within hepatocytes and in sinusoids. (**C**) Periodic acid–Schiff staining showing small, round to ovoid fungal organisms. (**D**) Grocott's methenamine silver stain showing round to ovoid 2 to 4 µm narrow-based budding fungal organisms suggestive of histoplasmosis.

at our hospital revealed hemoglobin 8.8 g/dL, total leucocyte count 7.73×10^3/µL, platelets 38×10^3/µL, bilirubin 1.0 mg/dL, alanine transaminase 29 U/L, aspartate transaminase 17 U/L, alkaline phosphatase 394 U/L, gamma-glutamyl transpeptidase 185 U/L, and albumin 1.9 g/dL. Viral markers (hepatitis B surface antigen, hepatitis C antibody, and anti-human immunodeficiency virus 1 and 2) were nonreactive. A gastroscopy was negative for varices. There was no history of immunosuppressive medications. In view of the cholestatic liver function test and normal biliary system on imaging, a transjugular liver biopsy was performed to exclude infiltrative liver disease The liver biopsy showed small round fungal organisms within hepatocytes and within sinusoids as shown in ►**Fig. 1B** (hematoxylin and eosin stain). ►**Fig. 1C** (Periodic acid–Schiff staining) and ►**Fig. 1D** (Grocott's methenamine silver stain) show round to ovoid 2 to 4 µm narrow-based budding fungal organisms, the morphology was suggestive of histoplasmosis. The liver biopsy showed 3/6 fibrosis and was negative for granulomas, necrosis, or Kupffer cell hyperplasia. The patient improved with itraconazole treatment for 1 year, ascites disappeared at 3 months of follow-up, and she was asymptomatic at 1 year.

Discussion

Histoplasma capsulatum is an intracellular dimorphic fungus that exists in mycelial and budding yeast forms. India is a nonendemic area for histoplasmosis, with few reports only.[1] The spores of Histoplasma are found in soils contaminated with bird droppings. The fungal spores have been shown to present in Gangetic delta soil.[2] The disease remains underreported due to an asymptomatic self-limiting course in the majority, tuberculosis masquerading the disease, and lack of diagnostic facilities. Histoplasma infection develops when microconidia are inhaled into the lungs and ingested by macrophages. Macrophages assist in spreading the organism via lymphatics and the blood to adjacent lymph nodes and the reticuloendothelial system (liver, spleen, lymph nodes, and bone marrow). Most of the infections are acute and self-limited.[3] Histologically, the involved liver may show portal lymphohistiocytic infiltrates, Kupffer cell hyperplasia, discrete granulomas, and Histoplasma within macrophages with minimal inflammatory reaction.[3,4] Although we did not expect a diagnosis of hepatic histoplasmosis initially, a liver biopsy was done due to the possibility of infiltrative liver disease, and the biopsy provided the correct diagnosis.

Histoplasmosis is increasingly diagnosed nowadays as a cause of PUO due to efforts to make a definitive diagnosis, and is not so uncommon in India.[5–8] In a series of 52 cases with PUO and adrenal enlargement from North India, 13 had histoplasmosis.[5] The disease generally presents with lymph nodes or adrenal involvement.[5–7] The index case highlights that the practice of empirical antitubercular therapy should be discouraged as it delays the correct diagnosis in anticipation of a response to antitubercular therapy. Ascites has been reported in some cases of histoplasmosis. However, the cause of ascites should be portal hypertension in the current case, which can occur in the noncirrhotic liver due to systemic diseases including infections.[9] The index case highlights the importance of liver biopsy in cases with no definite diagnosis.

Ethical Statement
Informed consent was obtained from the patient. Institutional ethical approval obtained to publish the report.

Data Availability Statement
There is no data associated with this work.

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Conflict of Interest
None declared.

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