Clues to hepatic histoplasmosis in an immunocompromised patient

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Abstract

Disseminated histoplasmosis can be the initial clue to the presence of AIDS. In HIV infected patients, histoplasmosis can present with unusual manifestations, without a positive exposure history or outside the typical endemic area. Untreated histoplasmosis can be potentially life-threatening and clues to diagnose it effectively and efficiently are essential.

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We describe an HIV infected patient who presented with unintentional weight loss and hepatomegaly. The patient gradually gained weight with complete resolution of his hepatomegaly after a four week course of systemic antifungal therapy directed against *Histoplasma*.

Case Report

A 35-year-old white male teacher, previously healthy, presented at our casualty department in 2004 with a three month history of unintentional weight loss, almost fourteen kilograms, generalised fatigue and malaise accompanied by a disseminated itchy skin rash. He was admitted to the hospital for further investigations. On systemic enquiry he denied fever, night sweats or rigors, and dyspnoea. In addition, he had no history of travel, normal bowel habits and owned no domestic pets.

On physical examination, the patient was afebrile. He was moderately cachetic with no pallor, jaundice or lymphadenopathy. The rest of his vital signs were normal. Multiple hyperpigmented skin lesions were evident. Abdominal examination revealed a sixteen centimetre firm non-tender hepatomegaly. The rest of the physical examination was normal.

Laboratory findings on admission included an Hb 14.7 g/dL, WBC of 2.03 x 10^9/L, ESR 64 mm/hr. The liver function parameters were all grossly elevated as indicated, serum alkaline phosphatase (ALP) 357 U/L, serum gamma-glutamyl transpeptidase (GGT) 673 U/L, serum aspartate transferase (AST) 471 U/L, serum alanine transferase (ALT) 160 U/L and lactate dehydrogenase (LDH) 4 044 U/L and a ferritin of 117 475 µg/L.

An abdominal ultrasound demonstrated a sixteen centimetre hepatomegaly with normal parenchyma and a normal biliary system with two small haemangiomas. The computerised tomography scan of the abdomen showed lesions characteristic of haemangiomas as shown in Figure 1. The serology for the following viral studies viz., EBV, CMV and HTLV were all negative. The patient consented to an HIV test which turned out to be positive with a CD4 count of 7 x 10^6/L.

Testing for serum *Histoplasma* antigen was not performed. The patient however, underwent a liver biopsy which was reported microscopically to show mild, acute on chronic infection in the portal tracts with a few suspiciously small, weakly formed granulomas. A few yeast cells, typical of possible histoplasmosis were observed in the portal tracts.

Treatment with oral fluconazole was begun at a dose of 200 mg b.i.d. for one week followed by 200 mg daily for three weeks. Follow-up liver function parameters dramatically decreased / normalized as indicated, ALP 117 U/L, GGT 45 U/L, AST 26 U/L, ALT 22 U/L and LDH 161 U/L

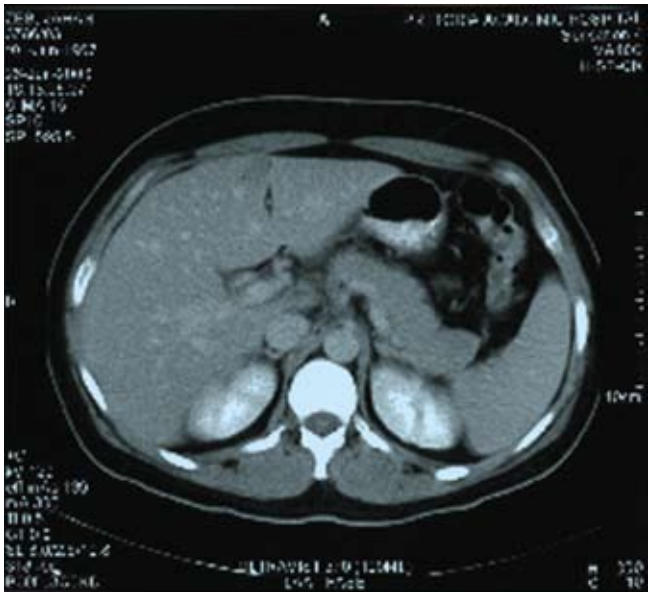

Figure 1. A CT scan (with contrast of the abdomen) of a 35 year old man with progressively worsening of generalized fatigue, weight loss and a rash but no fever. The scan obtained at the time of presentation in 2004, demonstrates 2 x 1 cm lesion at falciform ligament which fills with contrast, fits in with a haemangiomas.

and a ferritin of 234 µg/L by that time. The disseminated skin rash was ascribed to seborrheic dermatitis of HIV. Finally the CD4 had increased to 156 post anti-fungal treatment. Patient was not on any form of anti-retroviral therapy.

Discussion

Histoplasmosis encapsulatum is a dimorphic organism whose hyphae can be inhaled.[1] In immunocompromised patients *Histoplasma* may spread throughout the body via the reticulo-endothelial system and cause disseminated histoplasmosis infecting nearly all organs.[2] Serum ferritin is produced by the monocytes and macrophages of the reticulo-endothelial system.[3] HIV induces dysregulation of the synthesis and secretion of ferritin from reticuloendothelial cells. [4]

Most patients will experience hepatobiliary manifestations at some point during the course of their HIV disease, with hepatomegaly and or jaundice in 50% and abnormal liver function tests in over 80%.[5] HIV can involve the liver directly, as demonstrated by the presence of HIV p24 within the Kupffer cells and hepatic endothelial cells and HIV messenger RNA within hepatocytes.[5] Fungi usually involve the liver only with disseminated disease. These infections share a nonspecific clinical presentation, including unexplained fever, hepatomegaly and elevated alkaline phosphatase levels, although large fungal abscesses are occasionally seen on imaging studies. [5]

Histology is crucial to confirm the diagnosis. In tissue samples, typical intracellular budding yeast can be observed within the macrophages with a periodic acid Schiff or Grocott stain. The liver is almost always infected, making it a good target organ for biopsy.[1]

Conclusion

A high index of suspicion needs to be considered when confronted with patients with low CD4 counts, high serum ferritin, elevated LDH and skin lesions in the presence/absence of fever. Disseminated histoplasmosis, if left untreated can be both lethal and fatal.

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