Disseminated Histoplasmosis in a Patient with Aplastic Anemia

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Dear Editor,

Histoplasmosis is a systemic mycosis which has a world-wide distribution. In India disseminated histoplasmosis has been reported from various parts of the country [1, 2]. Humans are infected by inhalation of microconidia and mycelial fragments of *H. capsulatum* [3]. Disease manifestation can vary from completely asymptomatic, self limited infection in immunocompetent individuals to highly fatal progressive disseminated histoplasmosis in patients receiving immunosuppressive agents, infected with HIV, or in extremes of age [4, 5]. Cell mediated immunity is critical for the control of proliferation and dissemination of histoplasma. Though common in immunocompromised patients, disseminated histoplasmosis has rarely been reported in patients with aplastic anemia. We report here a case of very severe aplastic anemia who developed disseminated histoplasmosis in the form of hepatic involvement, which proved fatal due to lack of cell mediated immunity.

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A 4-years-old boy, who had been diagnosed as a case of very severe aplastic anemia 2 months ago, was admitted with febrile neutropenia. He had pulse rate 130/min, respiratory rate 24/min and temperature of 38.5 °C. Chest examination revealed bilateral crepitations, and abdominal examination revealed tender liver palpable 3 cm below right costal margin. Hemogram showed hemoglobin 8.2 g/dl, total leukocyte count $0.18 \times 10^9/l$, absolute neutrophil count $0.03 \times 10^9/l$, platelet count $25 \times 10^9/l$ and prothrombin time 14 s (control 13 s). His total bilirubin was 1.1 mg/dl and alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were 62/58/840 IU/l, respectively. Lactate dehydrogenase was 640 U/l (normal value: 100–240 U/l). He was started on empirical antibiotics for febrile neutropenia. Blood and urine cultures were sterile. Chest X-ray showed bilateral pneumonitis. Thoraco-abdominal computed tomography (CT) revealed bilateral lower lobe consolidations and two well circumscribed large focal lesions in the liver (measuring 4×4 cm and 4×5 cm, respectively) (Fig. 1). Ultrasound guided liver biopsy showed Histoplasma capsulatum (Fig. 2). Considering disseminated histoplasmosis, the patient was started on liposomal amphotericin B 3 mg/kg/day alongwith injection Granulocyte-Colony Stimulating Factor (G-CSF, 5 mg/kg/day) and supportive treatment with blood and platelet transfusions. Voriconazole (6 mg/kg/day for 1 day followed by 4 mg/kg/day) was added on day 7 of liposomal amphotericin B as he continued to have high grade fever. G-CSF was stopped as there was no response after 7 days. Follow-up CT scan of chest and abdomen after 30 days showed partial resolution of pneumonitis and 60 % reduction in liver lesions (Fig. 3). In spite of radiological regression in lesions, the patient continued to have high grade fever and succumbed to febrile neutropenia on day 40.

Fig. 1 Computed tomograph scan showing two large well circumscribed focal intrahepatic target like lesions

Fig. 2 Gomori's methanamine silver stain showing oval bodies consistent with histoplasma

Lungs are the most common primary site of involvement from where infection can spread to involve other organs. Gastrointestinal involvement is common in disseminated histoplasmosis [6], but gross hepatic lesions are infrequently reported [7].

The differential diagnosis of disseminated histoplasmosis includes pneumocystis pneumonia, invasive fungal infections, and mycobacterial and other opportunistic pathogens [8]. The gold standard for diagnosis is culture of *H. capsulatum* from clinical specimens. Microscopic examination of specimens stained with periodic acid-Schiff or methenamine silver may show the characteristic morphologic features of yeasts with budding and provide the rapid diagnosis [9, 10]. Our diagnosis of histoplasmosis was based on the characteristic morphologic features of the fungus, and repeat biopsy for fungal culture could not be done because of refractory thrombocytopenia and poor general condition of the patient. The most effective treatment is amphotericin B, though azoles particularly itraconazole and sometimes voriconazole have also been

Fig. 3 Follow-up CT scan after 1 month of treatment showed partial resolution of lesions

successfully used [5, 11]. Since our patient was immunocompromised and recovery of neutrophils was unlikely without definite treatment for aplastic anemia, we used both amphotericin and voriconazole for the treatment of disseminated histoplasmosis. Lack of recovery of specific cell mediated immunity in our patient with aplastic anemia led to dissemination of the disease, which inspite of partial response with antifungals, proved fatal, before any definitive management of aplastic anemia could be considered.

References

1. Randhawa HS, Khan ZU (1994) Histoplasmosis in India: current status. *Indian J Chest Dis Allied Sci* 36:193–213
2. Subramanian S, Abraham OC, Ruplai P, Zachariah A, Mathews MS (2005) Disseminated histoplasmosis. *J Assoc Physicians Indian* 53:185–189
3. Kauffman CA (2009) Histoplasmosis. *Clin Chest Med* 30:217–225
4. Wheat LJ (2009) Approach to the diagnosis of the endemic mycoses. *Clin Chest Med* 30:379–389
5. Wheat LJ, Freifeld AG, Kleiman MB (2007) Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. *Clin Infect Dis* 45:807–825
6. Goodwin RA, Shapiro JL, Thurman GH (1980) Disseminated histoplasmosis: clinical and pathologic correlations. *Medicine* 59:1–33
7. Lamps LW, Haggitt RC, Claudia P (2000) The pathologic spectrum of gastrointestinal and hepatic histoplasmosis. *Am J Clin Pathol* 113:64–72
8. Knox KS, Hage CA (2010) Histoplasmosis. *Proc Am Thorac Soc* 7:169–172
9. Kauffman CA (2008) Diagnosis of histoplasmosis in immunosuppressed patients. *Curr Opin Infect Dis* 21:421–425
10. Guimarães AJ, Nosanchuk JD, Zancopé-Oliveira RM (2006) Diagnosis of histoplasmosis. *Braz J Microbiol* 37:1–13
11. Freifeld A, Proia L, Andes D, Baddour LM, Blair J (2009) Voriconazole use for endemic fungal infections. *Antimicrob Agents Chemother* 53:1648–1651