Systemic Humicolus Cryptococcosis

S.M. Shinde
K.S. Vanarse
A.N. Pandit

We report a 7½-year-boy with disseminated systemic cryptococcosis. Although other species have been incriminated, this appears to be the first report of Cryptococcus humicolus. The child was HIV negative. He was treated with amphotericin B and fluconazole with intensive supportive care. The child responded after 6 weeks and is now on maintenance fluconazole therapy.

Keywords: *Amphotericin B, Fluconazole, Cryptococcus humicolus, Systemic cryptococcosis.*

Systemic cryptococcosis is a rare infection in pediatric patients(1). Most of the reports described are in adults with immunodeficiency disorders, or malignant condition on chemotherapeutic agents(2). However, pediatric cases are equally distributed(3). Of the various strains incriminated, *Cryptococcus neoformans* serotype A appears to affect immunodeficient hosts such as children with HIV or on steroid therapy, whereas *Cryptococcus neoformans* var gattii affects normal immunocompetent children(2), We report for the first time, a systemic infection with *cryptococcus humicolus* species affecting a young child.

From the Department of Pediatrics, KEM Hospital, Sardar Mudliar Road, Rastapeth, Pune 411 001, India.

Correspondence to: Dr. S.M. Shinde, Department of Pediatrics, KEM Hospital, Sardar Mudliar Road, Rastapeth, Pune 411 001, India.
E-mail: shinde_sandeep@hotmail.com

Manuscript received: December 10, 2003;
Initial review completed: January 29, 2004;
Revision accepted: June 1, 2004.

Case Report

A 7½-year-boy was referred with history of low grade fever, cough and weight loss for a duration of 2 months. He was dyspneic for one week. Chest *X*-ray prior to the admission was suggestive of bilateral miliary shadows (*Fig.1*). Erythrocytic sedimentation rate was normal and tuberculin test was negative. The pediatrician had started 4 drug antitubercular therapy (SHRZ) with oral betamethasone. However, the condition had deteriorated even after 2 months of antitubercular therapy. The patient had five attacks of oral thrush during two years prior to admission. The thrush responded each time to clotrimoxazole mouth paint and oral fluconazole therapy. There was no history of contact with tuberculosis. On

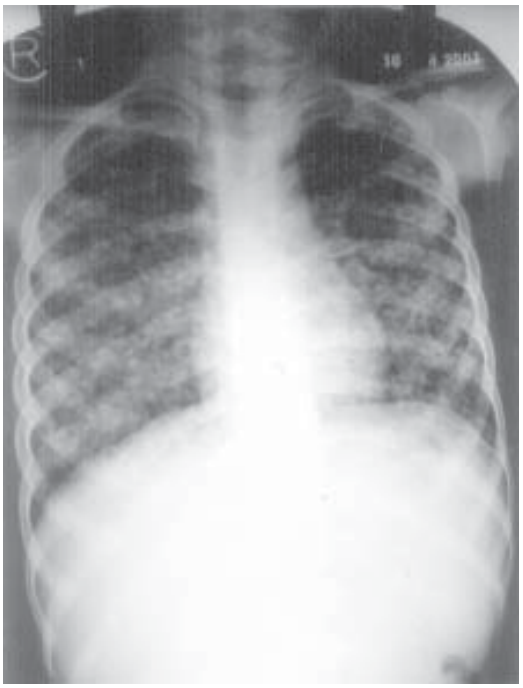

Fig. 1. X-ray chest on admission suggestive of bilateral miliary shadows.

admission the child was dyspneic with respiratory rate of 70/min. The patient had tachycardia, generalized significant lymph-adenopathy and bilateral pedal edema. There were rales and rhonchi on auscultation of chest. Liver was enlarged 6.5 cm, firm, and spleen was 3.5 cm below costal margin.

Blood culture grew *Cryptococcus humicolus* (by using mini API and ID 32 strip biochemical reactions). Bone marrow (*Fig.2*), liver biopsy and lymph node FNAC all showed *Crytococcus* on histology. Urine culture also grew cryptococci. Serum immunoglobulins were on lower side of normal limit (*Table I*). CD4 count was 22%, HIV by ELISA was negative. Tuberculin test (10 TU) was negative. CT Brain was suggestive of atrophic changes with mild hydrocephalus. We stopped antitubercular therapy and steroids and started the patient on amphotericin B, fluconazole, cefotaxime and amikacin (broad spectrum cover) and supportive therapy (oxygen 5 L/min and enteral nutrition with nasogastric tube feeding). Clinical improvement in the form of reduced dyspnea, improved appetite and regression of hepatosplenometaly was seen only after 3 weeks of therapy. Fever subsided initially but relapsed with one episode of neutropenia (absolute neutrophil count was 150/cmm, total leucocyte count was 1500/cmm). It was treated with granulocyte monocyte colony stimulating factor (GM-CSF) for 5 days. At the end of 6th week blood culture and urine culture were sterile for Cryptococci. Child was then taken off oxygen therapy. He received amphotericin B for a total of 5 weeks. (total cumulative dose 700 mg). We were able to discharge him after 7 weeks of hospitalization on fluconazole prophylaxis. On 2 weeks follow up in out patient clinic, the patient reported significant improvement and showed weight gain and regression of hepatosplenomegaly.

TABLE I–*Immunoglobin Level and CD4 & CD8 Values at Admission*

Test	Result	Normal Range
S. IgM level	815 mg/dL	855 - 1255 mg/dL
S. IgM level	74 mg/dL	74-142 mg/dL
S. IgA level	92 mg/dL	96-206 mg/dL
S. IgE level	3.60 IU/mL	Upto 101 IU/mL
Absolute CD4	461 µL	289 - 2600 µL
Per cent CD4	22%	29 -59%
Absolute CD 8	508/µL	190 - 2120 / µL
Per cent CD8	24.2%	19 - 48%

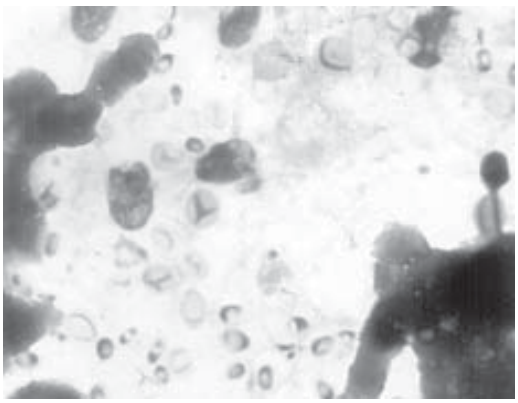

Fig. 2. Bone marrow biopsy stained with leishman stain and seen under 100x oil immersion showing cryptococci.

Discussion

Cryptococcus grows in soil and in bird excreta especially of pigeons(4,5). Infection is acquired in most cases by inhalation of fungal spires(3). *Cryptococcus neoformans* has worldwide distribution and preferentially infects immunosuppressed hosts or patients with HIV infection(1). Prevalence data for India are not available, but in sub Saharan Africa 15-80% of all patients with AIDS develop cryptococcal infection(1). Most of the patients reported are adults, over the age of 40 years(6). As mentioned earlier it is rarely

reported in children(5). However, none of the above reports pertain to the species *Cryptococcus humicolus*.

In view of the miliary shadows on *X*-ray, dyspnea and hepatosplenomegaly our patient was first thought to have disseminated tuberculosis. Fungal culture was attempted because of no response to antitubercular therapy. To our surprise both blood and urine culture grew cryptococci. Liver biopsy, bone marrow biopsy and lymph node biopsy also showed significant number of cryptococci. The boy however, was negative for HIV on ELISA test.

The treatment generally recommended for systemic cryptococcosis is amphotericin B with flucytosine(4,5,7,8). The lipid based amphotericin B is mostly preferred as it is said to be less nephrotoxic(7,8). However in view of financial constraints we used the cheaper non lipid based amphotericin B with fluconazole (flucytosine is not freely available in India)(9). We were worried initially, as response to therapy was poor and child continued to need intensive care support with oxygen and tube feeding for nearly 6 weeks. We were able to discharge him home (after 7 weeks of hospitalization) on fluconazole prophylaxis.

Prior to the use of amphotericin B cryptococcal meningitis and disseminated disease were invariably fatal. However, with the availability of amphotericin B, flucytosine, fluconazole and other azoles, the mortality rate of cryptococcal disease has decreased upto 28% with various regimen(3). However, the cost and non availability of some of the drugs is a particular problem in our country.

Acknowledgement

Authors would like to thank Dr. Avinash Pradhan for interpreting the histology and Dr. Rama Manchanda for the hematological work up of the case. Grateful acknowledgement is also made to Dr. Sheila Bhave for her valuable help in drafting and editing the report.

Contributors: SS drafted the report, carried out literature search and was the resident incharge of the patient. KV looked after the patient on day to day basis. AP decided the patient management and will act as guarantor.

Funding: None.

Competing interests: None stated.

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