Disseminated Cryptococcosis

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Background: Fungal infections, especially in immunocompetent children are uncommon causes of fever of unknown origin. **Case characteristics**: A 5-year-old boy with prolonged fever and no evidence of immunosuppression. **Observation**: Ultrasound-guided retroperitoneal lymph node biopsy showed granulomas and intracytoplamic fungal yeasts; staining charactristics were suggestive of cryptococci. Clinical and radiological improvement was seen after treatment with amphoterecin-B. **Outcome**: Disseminated fungal infection should be suspected as a cause of pyrexia of unknown origin after ruling out the commoner causes. Biopsy from enlarged lymph node or organomegaly may yield the diagnosis when non-invasive tests fail.

Keywords: *Cryptococcal infection, Fever of unknown origin, Immunocompetent.*

Pyrexia of unknown origin (PUO) is mostly due to an infection, especially in developing countries [1]. We report disseminated cryptococcosis in a 5-year-old immunocompetent child.

CASE REPORT

A 5-year-old boy was admitted with complaints of continuous high grade fever for one month along with abdominal distension, fast breathing and constipation. There was history of occasional blood in stools and recurrent oral ulcers. There was no significant past history. On examination, child was conscious and oriented, febrile with pulse rate of 108/min and respiratory rate of 35/min. There was no pallor, icterus, cyanosis, clubbing, edema, wasting, stunting or any evidence of micronutrient deficiency. The abdomen was soft on palpation with a firm, non-tender hepatomegaly (liver span 13 cm) but no splenomegaly. The examination of chest, cardiovascular system and central nervous system was normal.

Peripheral smear examination revealed leukocytosis (Total leukocyte count, 50.2×10^3/L) with eosinophilia (66% eosinophils, 18% neutrophils, 15% lymphocytes and 1% monocytes) without anemia or thrombocytopenia. Mantoux test, *X*-ray chest and gastric aspirates for Acid-fast bacilli were negative. Bone marrow examination revealed increase in eosinophils and its precursors but no abnormal cells. Serum RK-39 antibody detection test and aldehyde test were negative. Blood culture was sterile. Contrast enhanced computed tomography (CT) of chest and abdomen showed small focal areas of consolidation and patchy ground glass opacities in posterior basal segments of lower lobes, along with multiple centrilobular and peribronchial tiny nodules in both lungs suggestive of infective etiology. Enlarged, homogenous, hypodense lymphnodes in pretracheal, subcarinal, hilar and axillary regions, largest measuring 1.5 cm and periportal, peripancreatic and retroperitoneal region, largest measuring 3 cm were also reported. In view of lymphadenopathy, hepatomegaly and pulmonary nodules on CT, differential diagnoses of disseminated fungal or mycobacterial infections, metastasis, lymphoma, and sarcoidosis were considered. Work up for the cell mediated, humoral and phagocytic immunity did not show any evidence of an underlying immunodeficiency. Ultrasound guided retroperitoneal lymph node biopsy showed granulomatous inflammation with multinucleated giant cells and intracytoplasmic yeast forms with narrow based budding (***Fig.* 1**). Alcian blue-periodic acid schiff (PAS) and mucicarmine stained the capsule of the organisms, morphologically consistent with *Cryptococcus*. A definite species categorization

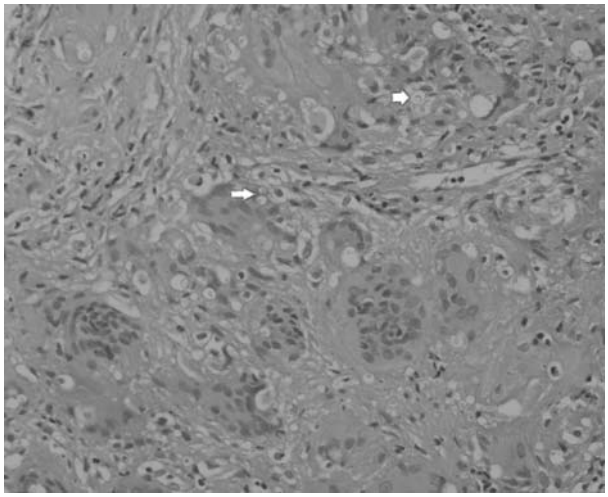

Fig. 1 *Hematoxylin and eosin stained tissue showing multinucleated giant cells with intracytoplasmic yeast forms with narrow based budding.*

could not be done in absence of culture. Serum and CSF cryptococcal titers were negative.

The child was initially started on broad spectrum intravenous antibiotics and was given albendazole in view of eosinophilia. After lymph node biopsy report, he was started on intravenous amphotericin B (1 mg/kg/d) which was continued for 6 weeks. The child passed multiple round worms in stool and gradually, the leukocytosis and eosinophilia also settled. Ultrasono-graphy of abdomen done at the end of 6 weeks showed some reduction in the size of retroperitoneal lymph nodes. Child was discharged on 6 mg/kg/d of oral fluconazole with a plan to continue it for 8 weeks, and then to reassess the size of lymph nodes on CT abdomen [2]. On follow up, the size of retroperitoneal lymph nodes decreased further and the child remained afebrile and asymptomatic.

DISCUSSION

Disseminated cryptococcosis is a systemic fungal infection generally seen in immunocompromised individuals. Recently, there have been reports of cryptococcosis in immunocompetent patients [3]. It usually presents with respiratory tract, central nervous system and skin involvement. Hepatic, lymph node and bone marrow involvement in immunocompetent people has been occasionally reported [4,5]. Cryptococcal infection is difficult to diagnose because of the non-specific signs and symptoms, the insidiousness of the course and the coexistence with other diseases [3]. The report of retroperitoneal lymph node biopsy helped us clinch the diagnosis of disseminated cryptococcosis, after commoner causes like disseminated tuberculosis and lymphoreticular malignancy were ruled out. Diagnosis of cryptococcal infection depends upon demonstration of growth of organisms on Saboraud's media with characteristic biochemical reactions (urease, phenyloxidase) or demonstration of encapsulated yeast like organisms on India ink or PAS staining followed by positive mucicarmine or Masson Fontana staining. Demonstration of cryptococcal capsular polysaccharide antigen in titers more than 1:8 in serum or CSF is also diagnostic [4].

Amphotericin B (0.7 to 1.0 mg/kg/d, intravenously) plus flucytosine (100 mg/kg/d, orally, in four divided doses) is recommended for at least four weeks for initial therapy [6]. Consolidation therapy should then be initiated with fluconazole (6 mg/kg/d) for eight weeks, and 3 mg/kg/d for six to twelve months [2].

We conclude that systemic fungal infections including disseminated Cryptococcosis is possible even in immunocompetent children and should be considered as cause of PUO after commoner causes have been ruled out.

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