Case Report

HIV infection presenting as bone marrow cryptococcosis

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Abstract

Disseminated cryptococcal infection is an uncommon initial manifestation in immunocompromised patients. We report a rare case of a 40-year-old female presenting with fever and burning epigastrium. Peripheral blood film revealed a leukoerythroblastic picture with thrombocytopenia. Bone marrow aspiration showed granulomas along with cryptococcal yeast forms. The ELISA test for detection of human immunodeficiency virus (HIV) antigen was positive. Disseminated cryptococcosis can develop as the first manifestation of HIV infection in previously healthy individuals and granulomas in such bone marrow aspiration smears are a valuable clue to an underlying opportunistic infection.

Key Words: Bone marrow, cryptococcus, granuloma, immunosuppression

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INTRODUCTION

Granulomas are an infrequent finding in bone marrow aspirations.[1] Several diseases like tuberculosis, sarcoidosis, fungal and viral infections, connective tissue disorders, lymphomas and metastatic carcinomas are associated with the formation of granulomas in the marrow.[1,2] Cryptococcal infection occurs commonly in patients with immunosuppression. It frequently involves either the lung or the central nervous system.[3-5] We report a rare case of disseminated cryptococcosis with granulomatous reaction in bone marrow. It was the initial manifestation in a patient who subsequently tested positive for human immunodeficiency virus (HIV).

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CASE REPORT

A 40-year-old female presented with fever, loss of appetite, burning epigastrium and non-productive cough since seven days. On examination there was mild hepatosplenomegaly. She was provisionally diagnosed as a case of acid peptic disease. Routine hematological investigations showed hemoglobin of 7 gm/dl and ESR-58 mm at the end of one hour. On peripheral smear the red cells were microcytic, hypochromic and white cells were within normal limits with total leucocyte count of 3600/cu.mm. However, few late normoblasts and 6% myelocytes and meta-myelocytes were noticed. Platelets were reduced. No hemoparasites or immature cells were noted in the smear. Hence a bone marrow aspiration was advised.

On evaluating the marrow, it was hypercellular with erythroid hyperplasia. Myelopoiesis was normal. Megakaryocytes were normal. Granulomas containing epithelioid cells were noted [Figure 1]. Encapsulated round organisms suggestive of Cryptococcus were also seen around the granulomas [Figure 2]. Acid fast bacilli were not demonstrable. Special stains

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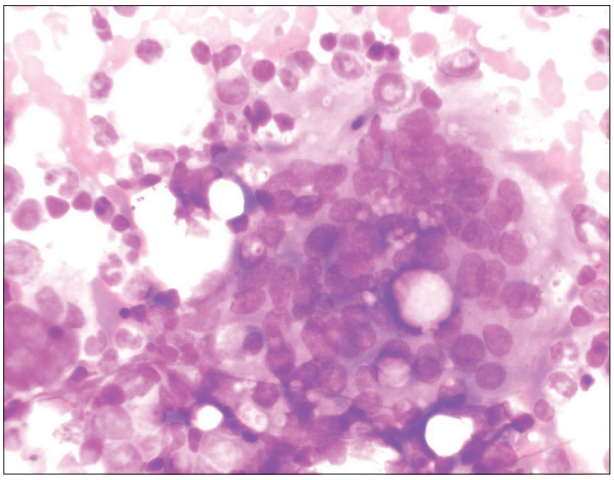

Figure 1: Bone marrow aspirate showing a granuloma with epithelioid cells and encapsulated yeast forms. [Leishman's stain, x40]

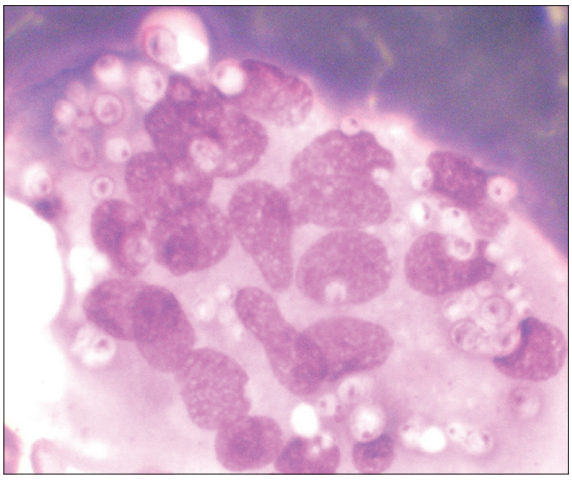

Figure 2: Higher magnification of the encapsulated yeast forms. [Leishman's stain, x40]

like mucicarmine and PAS were done to demonstrate the yeast forms. It was reported as a case of chronic granulomatous infection with cryptococcosis and test for HIV was advised.

The ELISA test for detection of HIV was positive. A chest X-ray and CT-scan done later also showed multiple nodular lesions in the lung base [Figure 3]. The patient was put on antifungal regime and referred to an anti-retroviral therapy (ART) center at a nearby government hospital for further management.

DISCUSSION

Fungal and mycobacterial infections are among the most common opportunistic infections in patients infected with human immunodeficiency virus (HIV). Cryptococcus infections affect few HIV positive patients in the initial clinical course but involve 10-30% with AIDS.[6]

Cryptococcus neoformans is an encapsulated yeast-like fungus. It usually grows as yeast (unicellular) and replicates by budding.[7] The major environmental sources of cryptococcus neoformans have been shown to be either soil contaminated with pigeon droppings or eucalyptus trees and decaying wood forming hollows in trees.[8]

The principal sites of cryptococcal infection are the lung, central nervous system and disseminated disease. Disseminated cryptococcosis is defined as the recovery of C. neoformans from blood, sterile body fluids, or tissues other than pulmonary tissue. Cutaneous manifestations occur in 10-15% of cases. Unusual forms of this disease like granulomas of the brain or spinal cord are occasionally seen.[9]

Disseminated cryptococcal infection is an uncommon initial manifestation with acquired immunodeficiency

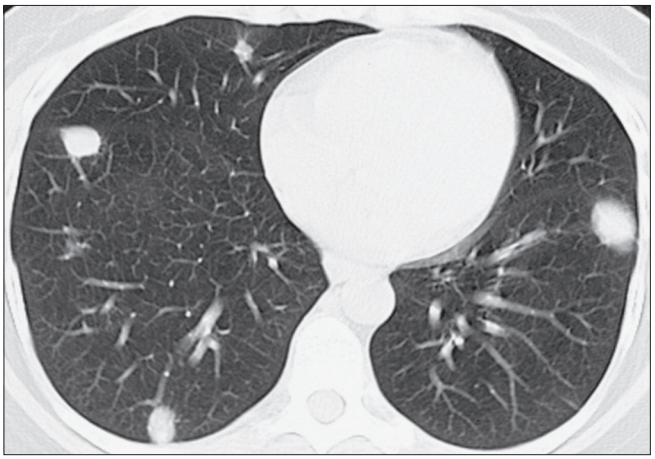

Figure 3: CT scan showing several nodules in the lung base

syndrome. Involvement of bone marrow is rare. The yeast forms of Cryptococcus stimulate a granulomatous response in all cases despite immunosuppression. The number of cryptococcal organisms appears to be inversely proportional to the adequacy of the granulomatous response. Typical epithelioid-cell granuloma may not be present in the marrow of immunocompromised patients with disseminated mycobacterial or fungal infection. Infection of bone marrow with cryptococci may act in synergy with the HIV to cause cytopenia[10] as seen in our case.

Pulmonary nodules, either solitary or multiple, are the most common CT finding, other findings include masses, CT halo sign, and consolidation.[11] Associated adenopathy, pleural effusions, and cavitation are uncommon; when present, these are more common in immunocompromised patients. Establishing the diagnosis can be difficult, but pulmonary Cryptococcosis should be considered in the differential

diagnosis of patients in the proper clinical setting and with compatible radiographic findings.[12]

Bone marrow examination can be a useful method of diagnosing opportunistic fungal and mycobacterial infections in patients with fever, anemia or thrombocytopenia and underlying HIV infection. The detection of an unusual fungal infection in bone marrow smears leads us to suspect and confirm HIV infection in this case.

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