Disseminated histoplasmosis in an immunocompetent haweli dweller: A diagnosis and follow-up by endoscopic ultrasound-guided fine-needle aspiration

ABSTRACT
Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is nowadays widespread minimally invasive procedure for diagnosing a large number of benign as well as malignant lesions. We report a case of a 62-year-old immunocompetent elderly male, who presented with high-grade fever, hepatosplenomegaly and mediastinal and intra-abdominal lymph nodes. He was residing in an old haweli with bats infestation. EUS-FNA of the subcarinal and the preaortic lymph node clinched the diagnosis. A rapid on-site evaluation of the cytology material revealed organisms conforming to the morphology of *Histoplasma capsulatum*. The patient was immediately started on amphotericin B and itraconazole and responded well. In this case, we found the role of EUS-FNA not only in diagnosis, but also in the follow-up of the patient.

Key words: Disseminated histoplasmosis; endoscopic ultrasound-guided fine needle aspiration; haweli resident, immunocompetent lymph node

Introduction
Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is nowadays widespread minimally invasive procedure for sampling organs in proximity to the gastro-intestinal tract and to obtain samples for cytology as well as core biopsies. It serves many functions, that is, from diagnosing benign conditions to malignant conditions. Benign conditions include a range of noninfective to infective pathology with most common being tuberculosis in India. Histoplasmosis is a disease of worldwide occurrence caused by dimorphic fungus *Histoplasma capsulatum*. In India, till now only sporadic cases are reported. Disseminated histoplasmosis is defined as a clinical condition where fungus is present in more than one location[1] and is a less common manifestation of the disease, mainly infecting immunodeficient (transplanted or AIDS) patients, as well as the very young or very old. The clinical presentation varies from the acute disseminated form, which is uncommon in immunocompetent individuals to chronic progressive course typically seen in nonimmunocompromised middle-aged to older adults[3,4] We report the case of an immunocompetent patient who presented with the disease, probably as a result of prolonged exposure and delayed diagnosis.

Case Report
A 62-year-old male patient presented with complaints of fever and dry cough since 1½ months duration. Fever was
of high grade with chills, rigor, and sweating episodes. On general examination, the positive findings were fever, pallor, and mild hepatosplenomegaly. Peripheral lymph nodes were not enlarged. He had a history of pulmonary tuberculosis 20 years back and had completed 9 months of antituberculous treatment. He was diagnosed with diabetes 2 years back and was put on insulin. However, he was irregular with the treatment. In last 2 years, the patient had recurrent episodes of upper respiratory tract infection and had taken antibiotics and bronchodilators for the same. The patient denied any history of parenteral drug abuse, homosexual behavior, or blood transfusion. In view of clinical presentation and radiological findings, a diagnosis of tuberculosis was highly suspected. Laboratory investigations revealed normocytic normochromic anemia with neutrophilia. The platelet count was normal. AST-74 U/L, (normal 5-50 U/L), ALT-56 U/L (normal 0-50), serum alkaline phosphatase 248 U/L (normal 25-125 U/L), serum bilirubin 1.1 mg/dl (normal 0.2-1.1), blood sugar random 312 mg, Mantoux test and antiretroviral antibody were negative. Malarial antigen and rapid test for typhoid were negative. A chest radiograph showed bilateral nodular opacities. Abdominal ultrasound revealed mild hepatosplenomegaly with few lymph nodes in the preaortic region. A computed tomography scan of the chest and abdomen revealed a single lymph node of 3 cm diameter in the subcarinal area and two lymph nodes of 1.5 cm diameter in the preaortic region near the celiac artery. EUS examination also revealed lymph nodes in preaortic and subcarinal area [Figure 1]. A 22 G Wilson cook Echotip needle was used for EUS-FNA. The cytology smears prepared were stained with Diff-Quick stain and examined. An immediate on-site examination of the aspirated material from both the sites, that is, subcarinal and preaortic lymph node showed high cellularity with a predominant reactive lymphoid cell population. An increase in histiocytes was noted with small necrotic fragments. Many intracellular round to oval organisms with peripheral halo conforming to the morphology of \textit{H. capsulatum} were found [Figure 2]. No kinetoplast was seen, thereby excluding \textit{Leishmania donovani}, morphologically. These organisms were positive for periodic acid-Schiff’s stain. No granulomas were seen. Further history taken later revealed that he had been residing in an old haweli, which had bat infestation.

He was started immediately on amphotericin B for 7 days, followed by itraconazole for 2 weeks and responded well to the treatment. After a follow-up for 12 months, the patient is doing well and is negative for histoplasma serology. A repeat EUS showed a regression in the size of the lymph nodes with EUS-FNA showing normal morphology.

\section*{Discussion}

Immunocompromised patients who reside in \textit{H. capsulatum}-endemic regions were more prone to suffer from disseminated histoplasmosis. The usual patient profile includes small children (especially infants), aged persons, and patients with AIDS, cancer, solid organ or bone marrow transplant\cite{2}. \textit{H. capsulatum} is a dimorphic fungus that remains in a mycelial form at ambient temperatures and grows as yeast at body temperature in mammals. In endemic areas, soil provides an acidic damp environment with high organic content good for mycelial growth. Highly infectious soil is found near areas inhabited by bats and birds. Birds cannot be infected neither can transmit the disease; however, bird excretions contaminate the soil, thereby enriching the growth medium for the mycelium. In contrast, bats can become infected, and they transmit the fungus through droppings. Contaminated soil remains potentially infectious for years\cite{3,4}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Endoscopic ultrasound shows a large triangular hypoechoic lymph node in the subcarinal region}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Intracellular round to oval organisms with peripheral halo confirming to the morphology of \textit{Histoplasma capsulatum} (Diff-Quick, ×400)}
\end{figure}
In India, it is an uncommon disease.\cite{5-7} Since the first report of disseminated histoplasmosis in 1954, sporadic cases have been reported from different parts of India. Most of the cases reported are from West Bengal followed by Maharashtra.

Our index case is a resident in a part of Meerut, Uttar Pradesh and had been residing in an old haweli which was infested by bats and had been in close contact with bats guano. In this case, they might have served as the potential source of infection with uncontrolled diabetes and old age serving as additional predisposing factors. We perform nearly 450 EUS-FNA per year. This is the first case of disseminated histoplasmosis diagnosed by EUS-FNA of lymph node observed in our institute and probably in this region. An immediate on-site examination of the cytology material, in this case, obviated the need for unnecessary tests in this patient, and the treatment was started early.

Presenting clinical features of histoplasmosis can range from skin and mucous involvement, lymphadenopathy, fever, hepatosplenomegaly, pulmonary, and ocular involvement. Chest radiograph may show focal infiltrates and hilar or mediastinal lymphadenopathy.\cite{18} Progressive disseminated histoplasmosis is rare in an immunocompetent adult. The chronic progressive disease is slowly progressive and generally fatal infection due to \textit{H. capsulatum} that occurs mostly in older adults who are not overtly immunosuppressed. These patients have no obvious immunosuppression, but their macrophages clearly cannot effectively kill the organism. It is thought that there is a specific defect in the cellular immune response to this organism. This is in contrast to the rapidly fatal acute form of dissemination that occurs in infants and immunosuppressed patients.\cite{8} Awareness and prompt diagnosis of \textit{H. capsulatum} are important because 100% mortality is seen in an untreated group, whereas early treatment is very effective.\cite{9}

The diagnosis can be established by Wright-stained smear of aspirate samples and by cultures. Careful examination of the peripheral blood smears might yield an early diagnosis of systemic histoplasmosis.\cite{10} In this case, EUS-FNAC from both the abdominal and subcarinal lymph nodes revealed \textit{H. capsulatum} and confirmed the diagnosis of a disseminated form of the disease. In addition, EUS was helpful in the follow-up of the patient also.

**Conclusion**

Infective diseases can be diagnosed by EUS-FNA. Though due to overlapping cytological picture diagnosis can be complex in a certain situation. However, identification of specific organism during on-site examination obviates the need of unnecessary test and helps in the prompt initiation of therapy.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Gerke H. If cancer is not the answer: Endoscopic ultrasound-guided biopsies in the diagnosis of infections. Gastroenterol Hepatol (N Y) 2010;6:727-9.
2. Kauffman CA. Histoplasmosis: A clinical and laboratory update. Clin Microbiol Rev 2007;20:115-32.
3. Kauffman CA. Histoplasmosis. Clin Chest Med 2009;30:217-25, v.
4. Wheat LJ, Kauffman CA. Histoplasmosis. Infect Dis Clin North Am 2003;17:1-19, vii.
5. Randhawa HS, Khan ZU. Histoplasmosis in India: Current status. Indian J Chest Dis Allied Sci 1994;36:193-213.
6. Gopalakrishnan R, Nambi PS, Ramasubramanian V, Abdul Ghafur K, Parameswaran A. Histoplasmosis in India: Truly uncommon or uncommonly recognised? J Assoc Physicians India 2012;60:25-8.
7. Subbalaxmi MV, Umabala P, Paul R, Chandra N, Raju YS, Rudrumurthy SM. A rare presentation of progressive disseminated histoplasmosis in an immunocompetent patient from a non-endemic region. Med Mycol Case Rep 2013;2:103-7.
8. Goodwin RA Jr, Shapiro JL, Thurman GH, Thurman SS, Des Prez RM. Disseminated histoplasmosis: Clinical and pathologic correlations. Medicine (Baltimore) 1980;59:1-33.
9. Chakrabarti A, Slavin MA. Endemic fungal infections in the Asia-Pacific region. Med Mycol 2011;49:337-44.
10. Ecka RS, Bhatia P, Varma N, Marwaha RK. Disseminated histoplasmosis with peripheral blood spill over. Indian J Pediatr 2014;81:313-4.