Role of fine-needle aspiration cytology in diagnosis of disseminated histoplasmosis in an immunocompetent patient: A case report

ABSTRACT
Histoplasmosis is a mycotic infection caused by dimorphic fungus, *Histoplasma capsulatum*. The organisms are usually found within the cells (macrophages). This organism mostly affects lungs in immunocompetent individuals and disseminated forms are seen in immunocompromised cases. Here, we describe a case of disseminated histoplasmosis in an immunocompetent, 35-year-old female with lymphadenopathy diagnosed by fine-needle aspiration cytology and cell block.

Key words: Disseminated histoplasmosis, fine-needle aspiration cytology, FNAC, immunocompetent

Introduction
Histoplasmosis is a systemic mycosis caused by the dimorphic fungus, *Histoplasma capsulatum*, a small uninucleated dimorphic fungus measuring 2–4 μm in diameter. It is found predominantly intracellularly and is usually present in clusters inside the cytoplasm of macrophages, with a light area surrounding the organism (pseudo capsule).[1] Although worldwide in distribution, it is endemic in a broad area of the central and eastern United States, concentrated along the Mississippi and Ohio river valleys.[2]

Clinical manifestation ranges from an acute pulmonary to a chronic pulmonary infection or a progressive disseminated disease. Disseminated histoplasmosis (DH) usually occurs in immunocompromised individuals such as those with AIDS, but there are a few case reports of this disease in immunocompetent hosts.[1]

Here, we present a case of DH in an immunocompetent Indian female initially presented with generalized lymphadenopathy. Diagnosis was done by fine-needle aspiration cytology (FNAC) and confirmed by cell block.

Case Report
A 35-year-old Indian female from state of Odisha in eastern India presented with generalized lymphadenopathy of four months duration. On physical examination lymph nodes were multiple, discrete, and were measuring 3–4 cm in size [Figure 1a]. There was no hepatosplenomegaly. The patient did not complain of fever or cough. There was no other cutaneous lesion observed.

Biochemical parameters were also within normal limits. The serology for hepatitis B surface antigen (HbsAg), Hepatitis...
C virus (HCV), and HIV were negative. Chest X-ray and ultrasonography of whole abdomen were normal.

She had no history of diabetes mellitus, hypertension, pulmonary tuberculosis, intravenous drug abuse, blood transfusion, or of abroad travel. Clinically, she was diagnosed as lymphoma and advised for FNAC.

FNAC was done from all the nodes. While the remaining aspirate was allowed to clot, the cell block was made from formalin-fixed sediment. Cytosmear showed large number of histiocytes with cytoplasm packed with small organisms surrounded by a clear zone or pseudo capsule [Figure 1b]. Thus, cytological diagnosis was suggestive of histoplasmosis. Subsequently, section from cell block showed similar picture like FNAC [Figure 1c].

As it was clinically diagnosed as non-Hodgkin lymphoma (NHL), so surgeon did excisional biopsy of a lymph node. Histopathological sections showed capsule of node with underlying tissue packed with enlarged histiocytes, cytoplasm packed with *H. capsulatum*. Mixed inflammatory cells also present.

Grocott or Gomori methenamine silver (GMS) and periodic acid-Schiff (PAS) staining was done and it showed *H. capsulatum* with inflammatory cells [Figure 1d and e].

**Discussion**

*H. capsulatum* is a dimorphic fungus predominantly found in soils enriched with bird and bat excreta. Infection occurs when aerosolized micro conidia of the mold are inhaled from the environment during day-to-day activities in areas where *H. capsulatum* is highly endemic. Once *in vivo*; the micro conidia transform to the yeast phase and are found within histiocytes and tissues of the reticuloendothelial system.

The infection is self-limiting and restricted to lungs in 99% of the individuals with no preexisting immunological defects. The remaining 1%, however, progress to either disseminated or chronic disease involving the lungs, liver, spleen, lymph nodes, bone marrow and sometimes the skin and mucous membranes.

The disseminated form of the disease usually occurs in immunocompromised individuals such as those with HIV/AIDS, hematological malignancy, solid organ transplant, high-dose corticosteroid administration, advent of biological drugs, especially tumor necrosis factor α (TNF-α) antagonists, extremes of age and defective cell-mediated immunity.

Worldwide, it is very rare in immunocompetent patients. Among all forms of histoplasmosis reported in India, disseminated is the rarest in immunocompetent patients. Panja and Sen reported the first case of DH from Calcutta in 1954.

The symptoms include fever, malaise, anorexia, and weight loss. Physical examination often shows hepatosplenomegaly, lymphadenopathy, pallor, and petechiae if pancytopenia is present and in some patients we also see mucous membrane ulcerations, skin ulcers, nodules or molluscum-like papules.

Majority of infected immunocompetent patients are either asymptomatic or have mild symptoms that are never fully recognized as a fungal infection and are usually considered as differential diagnosis of either tuberculosis or malignancies.

In our case, the patient did not complain anything other than generalized lymphadenopathy. Clinically our patient was diagnosed as lymphoma.

Sometimes wrong diagnosis can lead to unnecessary amputations or radical surgeries with the attendant sequelae instead of a simple administration of amphotericin B with usually quick clinical response.

FNAC is cost-effective, rapid, and readily repeatable with minimal physical and psychological discomfort for initial diagnosis in superficial tissues. Although several cases of histoplasmosis have been reported but cytological diagnosis was made in a few cases in world literature as well as in India.
Histoplasmosis has a textbook cytological description with numerous intracellular organisms that are readily apparent on routine stains but very limited numbers of studies have highlighted the cytomorphological findings of histoplasmosis. A recent study demonstrated that FNAC allows for direct, presumptive diagnosis. In this study, specimen much more commonly consisted of macroscopically necrotic and granular material and smears revealed bland acellular necrosis with scattered epitheliod granulomas. In the vast majority of immunocompetent cases, study could not identify yeast without the aid of GMS staining and only identified rare intracellular yeast. Gupta et al demonstrated a variable load of uniform to oval, about 2–4 μm in diameter, budding yeasts were seen intracellularly (within histiocytes) as well as extracellularly.

In tissue sections, *H. capsulatum* is often found in clusters within the cytoplasm of macrophages and appears as uniform ovoid-spherical 2–4 μm uninucleated yeast with narrow base buds.

In our case, cytosmear from all nodes showed large number of histiocytes with cytoplasm packed with small organism surrounded by a clear zone or pseudo capsule. So, the diagnosis of *H. capsulatum* was given, and the same picture came in cell block sections also. Subsequently, fungal stain GMS and PAS on cell block sections showed *H. capsulatum* with inflammatory cells.

**Conclusion**

FNAC is rapid, cost effective, presumptive, and less invasive initial diagnostic method for diagnosis of DH in an immunocompetent patient. Cell block preparations from remaining aspirates provide better diagnosis and further useful for special stain.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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