Histoplasmosis presenting as isolated cervical lymphadenopathy: A rare presentation

ABSTRACT

Histoplasmosis is an opportunistic fungal infection caused by inhaling the spores of a fungus called *Histoplasma capsulatum*. Disseminated histoplasmosis is the most common form associated with acquired immune deficiency syndrome (AIDS). Here, we report a case of histoplasmosis presenting as isolated cervical lymphadenopathy in a human immunodeficiency virus (HIV)-infected patient diagnosed by a less invasive method (fine-needle aspiration cytology) and confirmed by fungal culture of fine-needle aspiration material. Due to varied and nonspecific clinical manifestations of histoplasmosis, most of the infections are misdiagnosed or underreported. It has to be considered in differential diagnosis of cervical lymphadenopathy, particularly in immunocompromised patients so that patients can be treated medically at an early stage before dissemination occurs and unnecessary surgery can be avoided. Here, we present this case because of its rare presentation as isolated cervical lymphadenopathy and classical cytological picture.

Key words: Acquired immune deficiency syndrome (AIDS); histoplasmosis; isolated cervical lymphadenopathy

Introduction

Histoplasmosis is an opportunistic fungal infection caused by inhaling the spores of a fungus called *Histoplasma capsulatum*. It is frequently associated with acquired immune deficiency syndrome (AIDS) and other immunocompromised states. Histoplasmosis usually presents in two forms; pulmonary and extrapulmonary, which is also known as disseminated histoplasmosis (DH). Disseminated histoplasmosis is the most common form associated with AIDS. Here, we report a case of histoplasmosis presenting as isolated cervical lymphadenopathy without pulmonary involvement or dissemination in a human immunodeficiency virus (HIV)-infected patient, which was diagnosed by a less invasive method (fine-needle aspiration cytology) and confirmed by the fungal culture of fine needle-aspiration material.

Case Report

A 25-year-old male presented with left cervical lymphadenopathy since 1 month. The patient was diagnosed as HIV seropositive 6 months earlier and was on treatment. He was clinically asymptomatic. Routine laboratory investigations were performed, which showed hemoglobin of 8 g%, a total leukocyte count of 6,000/mm³, with a differential count of neutrophils 65%, lymphocytes 33%, and monocytes and eosinophils 1% each. The CD4 counts were 47 per milliliter. Erythrocyte sedimentation rate (ESR) was 80 mm in 1 h. Chest radiograph was normal. Fine-needle aspiration was...
performed from enlarged left side cervical node. The aspirate was necrotic. Smears were prepared and stained with Giemsa and hematoxylin and eosin (H and E) stains.

The aspirate smear showed macrophages containing intracellular spherical to ovoid bodies each surrounded by a small light halo. Some of the macrophages were ruptured and yeast-like organisms released outside were also seen [Figure 1]. So, a diagnosis suggestive of histoplasmosis was made and the remaining material was sent for culture for confirmation. Culture was done in Sabouraud dextrose agar at 25°C; after 2 weeks, it showed colony of the mold which was white-brown with a cottony appearance. Lactophenol cotton blue stain of the isolated mold was done and viewed under microscopy. It showed a knobby appearance of thick-walled and tuberculate macroconidia and microconidia with long septate hyphae. Hence, the diagnosis of histoplasmosis of lymph node was confirmed.

Discussion

Histoplasmosis, also called as Darling’s disease, is caused by the dimorphic fungus *H. capsulatum* var. *capsulatum* found in America and the tropics or *H. capsulatum* var. *duboisii* found in Africa.[2] Panja and Sen[3] first reported histoplasmosis from India in 1959. The disease is not very frequently reported from India except for the eastern Indian states such as West Bengal, which is considered as the endemic region for histoplasmosis.[4] The organism exists as a saprophyte in nature and is isolated from the soil, particularly when contaminated with chicken feathers or droppings. The infection to humans is acquired by the inhalation of mycelia fragments and microconidia. It is the most common opportunistic fungal infection in HIV-affected individuals in areas where it is endemic and hence, has been included in the definition of diagnostic criteria of AIDS by the Center of Disease Control and Prevention (CDC).[4] In immunocompetent individuals, it is usually self-limiting or localized, whereas in patients with AIDS it occurs in the disseminated form in 95% of the cases.[3] Histoplasmosis as a cause of isolated lymphadenopathy is uncommon, particularly in India where tuberculosis is the leading cause in most cases. The most common organ affected by histoplasmosis is the lung followed by other organs such as the skin, oral cavity, adrenal, liver, and central nervous system (CNS).[6] The patient usually presents with nonspecific symptoms such as fever, malaise, cough, and chest pain.

*H. capsulatum* is a small, uninucleate dimorphic fungus. It is found to be predominantly intracellular and is usually present in clusters inside the cytoplasm of macrophages, with a light area surrounding the organism (pseudocapsule). In tissues, both *H. capsulatum* var. *capsulatum* and *H. capsulatum* var. *duboisii* exist in the yeast phase but a difference in size allows them to be distinguished. The former measures 2-4 μm in diameter, whereas the latter is much larger — about 8-15 μm and with a much thicker wall.[7,8] The other common organisms that cytologically resemble histoplasmosis and have to be differentiated are cryptococcosis and leishmaniasis. Cryptococci are round capsulated organisms with a thick true capsule and show positive capsular staining on Mayer’s mucicarmine but negative staining with India ink preparation. Leishmania forms Leishman-Donovan (LD) bodies, which is distinguished by a nucleus and bar-shaped kinetoplast within each amastigote and it is negative for periodic acid-Schiff (PAS) stain.[9] The laboratory diagnosis of histoplasmosis includes fungal culture, histopathology, serologic tests, antigen detection, and molecular methods, with each test having different sensitivities based on the clinical manifestations and host status.[10] The standard for diagnosis is isolation of *H. capsulatum* from culture. However, it usually requires ≈2 weeks to grow and has a low sensitivity rate (15%) in self-limited histoplasmosis. Identification of *H. capsulatum* by culture is made based on the dimorphic nature of the fungus and the typical morphology of microconidia and macroconidia.

Conclusion

Due to varied and nonspecific clinical manifestations of histoplasmosis and the low index of suspicion, most of the infections are misdiagnosed or underreported. With the continuing pool of AIDS and ever increasing pool of immunocompromised patients, it is important to consider histoplasmosis in differential diagnosis of all cases presenting

---

Figure 1: Photomicrograph showing numerous intracellular and extracellular spores of histoplasmosis each surrounded by a thin halo. (Giemsa, ×1000)
with cervical lymphadenopathy. It is, therefore, suggested that cases presenting with clinicians and pathologists be more aware of the clinical manifestations, laboratory diagnosis, and risk factors of histoplasmosis so that patients can be started with medical therapy at the earliest and unnecessary complications can be avoided.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

**References**

1. Kauffman CA. Histoplasmosis. Clin Chest Med 2009;30:217-25, v.
2. Bhagwat PV, Hanumanthayya K, Tophakhane RS, Rathod RM. Two unusual cases of histoplasmosis in human immunodeficiency virus-infected individuals. Indian J Dermatol Venereol Leprol 2009;75:173-6.
3. Panja G, Sen S. A unique case of histoplasmosis. J Indian Med Assoc 1954;23:257-8.
4. Chande C, Menon S, Gohil A, Lilani S, Bade J, Mohammad S, et al. Cutaneous histoplasmosis in AIDS. Indian J of Med Microbiol 2010;28:404-6.
5. Pervez M, Cobb B, Matin N, Shahrin L, Ford ER, Pietroni M. Disseminated histoplasmosis in a patient with advanced HIV disease — lessons learnt from Bangladesh. J Health Popul Nutr 2010;28:305-7.
6. Guha A, Kulkarni HS. Histoplasmosis fungal disease series. Am J Respir Crit Care Med 2012;185:1-2.
7. Hay RJ, Moore M. Mycology. In: Champion RH, editor. Rook’s Textbook of Dermatology. 6th ed. Oxford: Blackwell Science; 1998. p. 1363-6.
8. Lucas AO. Cutaneous manifestations of African histoplasmosis. Br J Dermatol 1970;82:435-47.
9. Koley S, Mandal RK, Khan K, Choudhary S, Banerjee S. Disseminated cutaneous histoplasmosis, an initial manifestation of HIV, diagnosed with fine needle aspiration cytology. Indian J Dermatol 2014;59:182-5.
10. Wheat LJ. Current diagnosis of histoplasmosis. Trends Microbiol 2003;11:488-94.