

Cryptococcal lymphadenitis in a human immunodeficiency virus-infected patient: A diagnostic role of fine needle aspiration cytology and special stains

Sir,

Cryptococcosis is a common opportunistic infection, caused by *Cryptococcus neoformans*, especially in patients with acquired immunodeficiency syndrome where the disease is widely disseminated and life-threatening.^[1-4] *C. neoformans* commonly affects the lung, meninges, and skin. Lymph node is an unusual site of cryptococcal infection.^[1-4] Diagnosis of cryptococcal lymphadenitis remains a potential challenge because the disease may be mild or subclinical with lack of characteristic clinical and radiological features.^[5] Fine needle aspiration cytology (FNAC) is an easy, rapid, and reliable diagnostic method in cryptococcal lymphadenitis, which helps in the prompt initiation of treatment.

A 35-year-old male presented with complaints of fever and generalized weakness for 15 days. The patient was known case of human immunodeficiency virus infection and on treatment. On examination, multiple bilateral very tiny firm, nontender cervical lymph nodes were noted. Kernig's sign and neck rigidity were also present. His white blood cell count is 4200/mm³ with 60% polymorphs, 35% lymphocytes, 1% eosinophils, and 4% monocytes.

The CD4 count was 40/μl. FNAC of the cervical lymph node was requested with a provisional clinical diagnosis of tuberculous infection. Three cytology smears were prepared from scanty whitish particulate aspirate. Hematoxylin and eosin-stained cytology smears showed occasional granulomas and many lymphocytes admixed with, occasional loose aggregates and scatteredly distributed variable-sized, spherical/rounded, budding yeast cells surrounded by clear halo with well-appreciated refractile capsule. Occasional phagocytosed budding yeast cells were also identified within the macrophages [Figure 1]. Caseous necrosis was not seen. Ziehl-Nielsen's stain was negative for acid-fast bacilli. These findings were suggestive of cryptococcal lymphadenitis. Subsequent lymph node biopsy showed occasional budding yeast cells surrounded by optically clear halos that represent capsules on periodic acid-Schiff (PAS) stain [Figure 2]. Cerebrospinal fluid (CSF) examination revealed a total count of 250 cells/mm³, with lymphocytes (85%) and budding yeasts-like encapsulated organisms on India ink preparation. Cryptococcal antigen in CSF and culture confirm *C. neoformans*. Immediately, antifungal treatment was started and the patient showed signs of improvement.

Cervical, axillary, inguinal, supraclavicular, hilar, retroperitoneal, and epitrochlear lymph nodes can be involved by cryptococcosis in either immunocompromised or immunocompetent hosts.^[1-5] The first clinical presentation may be tuberculosis, especially with its high prevalence in India.^[3,4] There are a few cytology case reports of cryptococcal lymphadenitis.^[1-4] The nature of the aspirates include fluidic (more common), whitish particulate (like in the present case), necrotic or thick gelatinous material.^[1,5] Classically, *C. neoformans* on cytology smears appear as intracellular and/or extracellular tear drop-shaped or ovoid to spherical yeast-like cells, some of which show budding daughter yeast cells attached by a narrow base, with a refractile halo-like thick

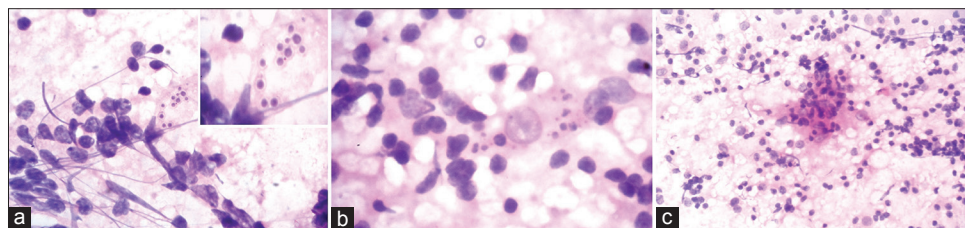


Figure 1: Fine needle aspiration cytology: (a) Cluster of spherical yeast cells with many lymphocytes (H and E, ×400) (inset figure: variable-sized, rounded yeast cells surrounded by halos with well-appreciated refractile capsule [H and E, ×5000]), (b) yeast cells are seen inside the macrophage (H and E, ×5000), (c) granuloma with predominant lymphoid cells (H and E, ×200)

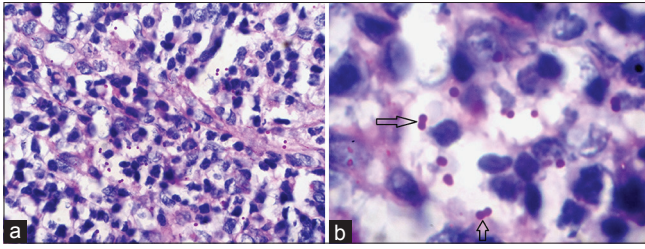


Figure 2: Cervical lymph node biopsy, periodic acid–Schiff stain: (a) few scattered yeast-like organisms are surrounded by optically clear halo ($\times 400$), (b) few yeast-like pinkish fungal bodies exhibit narrow-based budding with surrounding clear halo, represent gelatinous capsules (arrow mark) ($\times 1000$)

mucopolysaccharide capsule.^[1-6] Granulomatous inflammation and giant cell reaction may be slight or absent.^[6] Sometimes, cryptococci can be missed or overlooked because of small size, scanty load of organisms, and necrosis.^[1,4] Unusual cryptococcal morphology (seen in approximately 33% of cases) can give rise to a diagnostic dilemma.^[6] Poorly encapsulated or nonencapsulated yeast-like organisms have the absence of pericellular clear zone.^[6] Germ tube-like structures possess a constriction at their base at the point of attachment to the adjacent yeasts.^[6] Pseudohyphae are seen as a chain of budding yeasts with prominent branching.^[6] The microscopic identification of the cryptococcosis is greatly assisted by special stains. PAS stain demonstrates dark pink yeast cells with halo and magenta-colored capsule. Gomori's silver methenamine stain shows brown to black organisms on a light green background without characteristic capsular halo. Fontana–Masson stain highlights fungal melanin as reddish-brown to black color in the cell wall, whether they are encapsulated or a capsule-deficient form. India ink preparation highlights the capsule of cryptococci in a dark background. On Papanicolaou stain, yeast cells are seen as light pink/cyanophilic with refractile clear halos of capsule on light blue background.^[1-6] The yeast forms of cryptococci need to be differentiated from *Candida* species, *Blastomyces dermatitidis*, *Paracoccidioides brasiliensis*, and *Histoplasma capsulatum*.^[1-6]

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Conflicts of interest

There are no conflicts of interest.

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