

Cryptococcus neoformans causing meningitis in AIDS patients

Meningite causada pelo *Cryptococcus neoformans* em pacientes com AIDS

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Abstract *Cryptococcus neoformans* causes meningitis in AIDS patients. In the São José Hospital, reference center for patients with AIDS in Fortaleza - Ceará State - Brazil, 54 samples of the cerebrospinal fluid were analyzed from January 1st through December 31st 2000. Direct examination with India ink and culture in Sabouraud's agar at 37°C were done. Of the specimens studied 5(9.25%) were positive.

Key-words: *Cryptococcus neoformans*. Meningitis. Cerebrospinal fluid. AIDS.

Resumo *Cryptococcus neoformans* causa meningite em pacientes com AIDS. Foram analisadas 54 amostras de líquido cefalorraquidiano no período de 1 de janeiro a 31 de dezembro de 2000, no Hospital São José, centro de referência para pacientes com AIDS em Fortaleza - Ceará - Brasil. Foram realizados exame direto com tinta da Índia e cultura em ágar Sabouraud a 37°C. Entre as amostras estudadas, 5 (9,25%) foram positivas.

Palavras-chaves: *Cryptococcus neoformans*. Meningite. Líquido cefalorraquidiano. AIDS.

Cryptococcosis is an infectious mycosis that begins as a pulmonary infection and spreads in a hematogenous manner to involve the meninges, skin, kidneys, and other organs¹. *Cryptococcus neoformans*, the etiologic agent of the disease, is a saprobe in nature, with a worldwide distribution and is especially common in pigeon droppings. While birds are not affected, they apparently harbor the organism in a commensal form. Human infection occurs when dust from soil contaminated with the organism is inhaled. *Cryptococcus* is rare in persons with an unimpaired immune system. Cryptococcosis is a leading mycological cause of morbidity and mortality among AIDS patients. In many patients, cryptococcosis is the first indication of AIDS. In Brazil *Cryptococcus neoformans* is the sixth most common opportunistic agent of infection in patients with AIDS, surpassed by *Candida* species, *P. carinii*, *Mycobacterium* species, *Toxoplasma gondii*, and herpes simplex virus. In northeast region of Brazil there have

been few studies regarding cryptococcosis realized until this moment, which explains the lack of knowledge about this disease². Signs and symptoms are referable to meningeal involvement or to increased intracranial pressure: headache at first, then vertigo, dizziness, neck rigidity, amblyopia, and clouding of the sensorium. Central nervous system symptoms are usually the presenting features, while pulmonary involvement may go unnoticed⁵. Untreated cryptococcosis meningitidis is fatal, with very rare exceptions¹⁰. The association of cryptococcosis with AIDS has a new dimension to descriptive diagnosis. In this setting therapy can achieve suppression of active cryptococcosis disease, but cure is essentially unknown.

The purpose of the research was to verify the occurrence of cryptococcal meningitis in patients with AIDS at São José Hospital, reference center for patients with infectious diseases in Ceará State, Brazil.

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Patients. Cerebrospinal fluid (CSF) was studied from HIV infected patients with signs and symptoms of meningitis at São José Hospital - Ceará, Brazil.

Samples. A total of 54 samples of cerebrospinal fluid were analyzed from 1st January 2000 through 31st December 2000. They were collected from HIV patients with signs and symptoms of meningitis at São José Hospital - Ceará, Brazil.

Direct examination. Laboratory investigation of cerebrospinal fluid (CSF) is traditionally based on microscopic examination of India ink preparations. The direct examination was first made through India ink diluted at 1:5⁶.

Culture. The cerebrospinal fluid was cultured on Sabouraud's glucose agar and incubated at 37°C for five or eight days⁵.

Identification. Two biochemical tests that define *C. neoformans*, assimilation of inositol and production of urease were performed⁶.

The India ink examination showed capsulated yeast cells in five (9.25%) samples of cerebrospinal fluid from HIV patients. The centrifuged cerebrospinal fluid contains thick-walled oval or spherical cells, 10 to 15µm in diameter. A thick capsule surrounds these cells. Culture confirmation is required to establish a diagnosis.

Five (9.25%) samples of the cerebrospinal fluid presented growth in Sabouraud's glucose agar. The isolated colonies were whitish to brownish, slimy and mucoid.

The confirmation of the *Cryptococcus neoformans* was done by assimilation of inositol and production of urease. The two tests were positive in five yeasts grown in Sabouraud's glucose agar. It was concluded that five (9.25%) of the samples of cerebrospinal fluid contained *Cryptococcus neoformans*.

Cryptococcal meningitis characteristically occurs in a setting of depressed cell-mediated immunity and is usually associated with AIDS patients⁴. Cryptococcosis is rare in individuals with an unimpaired immune system. Human infection occurs when dust from soil and the environment contaminated with *Cryptococcus neoformans* is inhaled. Clinical types include infections of the pulmonary system, central nervous system, and other organs³. Laboratory investigation of cerebrospinal

fluid (CSF) is traditionally based on microscopic examination of India ink preparations, but direct microscopic examination is a rapid but relatively insensitive test that strongly depends on the operator's skills. Moreover, the simple culture of CSF samples on Sabouraud's agar is time-consuming; in fact, at least four days are necessary to detect positive cultures of *C. neoformans*⁹. In our study, although the fungi were isolated from five AIDS patients with cryptococcal meningitis, we could not determine whether these sites were the real source of the fungal infection, thus in AIDS patients *C. neoformans* usually tends to disseminate, the most common local for extrapulmonary infection being the meninges. The frequency and intensity of human exposure to environmental sources of *Cryptococcus neoformans* might account for the observed differences in the incidence of cryptococcal meningitis among AIDS patients according to geographical area, since clinical and environmental isolates from different areas have shown similar pathogenicity⁷. Investigations carried out in Central Africa by Passony et al⁸ showed that AIDS patients with cryptococcosis are frequently exposed to *C. neoformans* in their immediate daily, domestic environment. In New York, the fungus was isolated in 35% of the AIDS-associated cryptococcosis patients¹¹. Divergences in the literature make conclusions difficult, however the prevalence of *C. neoformans* in domestic environments probably depends on housing conditions, people's habits, and climatic aspects occurring in distinct geographical areas.

C. neoformans is cosmopolitan, which means that the area selected for sampling is not necessarily the area where the patient acquired the infection. Moreover, the time interval between the inhalation of the organism and expression of the disease is not known and some cases might arise from reactivation of a latent focus rather than from exposure to a saprophytic source⁴. Varma et al¹² suggest that presence of *C. neoformans* in the domestic environment of HIV-infected individuals might favor their infection or reinfection by the fungus. Consequently, if we consider the possible participation of environmental factors in opportunistic cryptococcosis, it seems prudent to advise HIV-infected individuals of situations that carry a potential risk of acquiring cryptococcosis.

This short study is important to provide physicians with initial information about cryptococcal meningitis in Fortaleza, Ceará, Brazil, which will increase the possibilities of understanding this disease.

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