Commentary

Central Nervous System and *Cryptococcus neoformans*

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Cryptococcus neoformans continues to be an important cause of morbidity and mortality, and is the most common central nervous system (CNS) mycosis in immunocompromised patients, in particular those with AIDS. *C. neoformans* has also increased in immunocompromised transplant patients,[1-4] and is a systemic mycosis. The incidence of infection due to *C. neoformans* varies among continents.

C. neoformans is a form of yeast with biochemical, antigenic, and epidemiological differences. There are two known varieties. Most infections are due to *C. neoformans* var. *grubii* and a lesser number due to *C. gattii* (Africa, Australia, Canada, Latin America). Clinical presentations also depend on the characteristics of the immunological competency of the patients. In general, it is a systemic fungal infection with its origin as the inhalation of *C. neoformans*, initially affecting the lungs. Therefore, CNS manifestations are as a result of the dissemination of this fungus from the lung.[5]

The polysaccharide capsule of *C. neoformans* is the most potent virulence factor, which also allows it to evade the immune system. Laboratory diagnosis is accomplished either by ELISA or latex agglutination test, or visualization of the capsule upon direct examination of fresh cerebrospinal fluid (CSF), in particular with China ink (India ink staining or nigrosine allows for the identification of the yeast from 4-20 mm in diameter). With this negative stain, identification of the image of the capsule and yeast in the center will be possible. When the fungal burden is high, the pseudomycelium may be observed most of the time. On other occasions it is practical to centrifuge the CSF at 3,000 rpm × 10 min. The sediment is useful for microscopic study and cultures. Another accessible study is latex agglutination, which identifies the A, B, C, and D serotypes that constitute the *C. neoformans/C. gattii* complex.

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Clinical correlation and suspicion of the infection are important. As in all laboratory tests, there are false negatives and false positives, thereby the importance of obtaining the CSF culture, which allows identification of the yeasts of *C. neoformans*. Genotypic identification proposed by the genotyping working group of *C. neoformans* and *C. gattii* selected multilocus sequence typing (MLST), which identifies structural genes.[6]

Treatment has been established,[7] however, we must pay close attention not only to the diagnosis and treatment, but also to the cryptococcal immune reconstitution inflammatory syndrome (IRIS) that may present itself as clinical deterioration or as a new or recurrent presentation of cryptococcal disease after initiation of antiretroviral therapy (ART), despite microbiological evidence of effective antifungal treatment.[8,9]

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