CRYPTOCOCCOSIS AND HIV-INFECTION/AIDS

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Dear Editor

Cryptococcal infection affects the lungs and central nervous system (CNS) of people with HIV infection/AIDS; relapses are related to high mortality, and immune reconstitution inflammatory syndrome (IRIS) should be a concern [1-5]. This syndrome may appear as unmasking IRIS after the beginning of highly active antiretroviral therapy (HAART), or paradoxical IRIS during the treatment of cryptococcosis from one to six months after the initiation of this treatment [2-4]. The IRIS occurs due to the recovery of cryptococcus-specific immune responses, manifested by fever, headache, seizures, hemiplegia, paraplegia, dysarthria, lymphadenopathy, lung nodules and infiltrates, cerebral edema and abscess [2]. Following the HAART, up to 45% of HIV/AIDS patients with cryptococcal meningoencephalitis may have a risk of lethal IRIS, similar to the post-infectious inflammatory response syndrome (PIIRS) in non-HIV transplant recipients with cryptococcal meningoencephalitis, after the immune conditioning reduction [4,5]. Either IRIS or PIIRS can cause deaths of up to one-third of affected people [4,5]. Their management includes restarting amphotericin B therapy (or increasing the fluconazole dose to 1200 mg daily) and associated higher doses of dexamethasone for severe CNS inflammation, besides reduction of intracranial hypertension [2].

We read with interest the article published in this Journal by Volos LI and Stoliar HL focusing on findings of cryptococcal lesions in the lungs and central nervous system of autopsied patients diagnosed with HIV infection and AIDS [5]. Pathological data of three women and one man between 32 and 55 years of age with antecedent of under- or misdiagnosed secondary diseases and/or inadequate treatment; two presented associated pulmonary lesions, and two had disseminated lesions to liver, spleen, mesenteric lymph nodes, and ovaries. Meningitis and meningoencephalitis were found in all patients with disseminated cryptococcosis as the major ominous prognostic factor of the course of disease; in the lungs, there were interstitial infiltrates of round-cells, granulomas containing cryptococci, besides lympho-macrophage reaction with multinucleated cells [5].

The authors emphasized the fatal outcomes of pulmonary infections, with the presence of fungi within the capillaries, and the giant cells of type Langhans; they also cited the mortality from pulmonary cryptococcosis by the year 2000 (up to 74%) in the HIV-infected, and these fatalities were associated with disseminated disease [5].

In this scenery, some comments on additional literature data may be useful [1-4]. A male patient in his 40s presented with weight loss, fever, headache, vomiting, disorientation, diplopia, neck rigidity, Kernig's and Brudzinski's signs, and had the diagnosis of HIV infection and CD4 cell count of 22 cells/mm3; the chest X-ray and imaging studies of the brain were normal, but cryptococcal antigen was detected in the CSF and serum, and C. neoformans was isolated in the CSF [3]. He underwent two weeks of liposomal amphotericin B and flucytosine, and 8 weeks of fluconazole with clinical and laboratory improvement; 4 weeks later used HAART (tenofovir disoproxil fumarate, emtricitabine, and dolutegravir) [3].

There was no neurological sequel after this episode of cryptococcal meningitis, but one year later, there was a relapse of meningoencephalitis by *C. neoformans* non-resistant to fluconazole, which was successfully controlled; the authors stressed the needed studies to establish the duration of secondary prophylaxis, besides effective options to optimized induction and consolidation treatment [3]. Worthy of note was the Brazilian autopsy study of a 33-year-old male with HIV/AIDS who died due to generalized infection caused by *Mycobacterium avium-intracellulare* complex that affected both lungs, kidneys, adrenals, spleen, and liver, besides lymph nodes, without infectious involvement of the CNS [1]. The prostate evaluation revealed an unexpected (2.0 x 2.0 cm) cryptococcoma containing abundant yeast forms either unviable or in single twinning by the Mucicarmin staining, as well as a total absence of local inflammatory reaction [1]. The cryptococcosis was restricted to the prostate, in an HIV-AIDS patient who died because of immunosuppression and widespread mycobacterial infection [1]. The authors emphasized that this patient never utilized medicines against cryptococcal infection, and the prostate of AIDS patients may be a focus of persistent and recurrent infection by these fungi, even after a specific therapy [1].

The case studies of potentially severe conditions can enhance the suspicion index among non-specialist healthy care workers, contributing to stablish early diagnosis and prompt adequate management, which result in better outcomes.

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