NEUROCRYPTOCOCCOSIS IN AIDS PATIENTS

Clóvis Klock, MD
Assistant Professor of Pathology
URI –CAMPUS DE ERECHIM
Brazil

Cryptococcosis is a systemic mycosis caused by an encapsulated and yeast form fungus called Cryptococcus neoformans.
Most of the time, it infects individuals with some immunodeficiency and it is considered an opportunistic mycosis. Cryptococcosis was described for the first time in 1894 by the pathologist Busse and the surgeon Buschke. The first case of neurocryptococcosis was described in 1905 by Van Hanseman in a man with meningitis.
Cryptococcus neoformans has five subtypes (A,B,C,D and AD), and three varieties: grubbi (A serotype), neoformans (D serotype) and gatii (B and C serotypes). The grubbi variety is present worldwide. The gatti variety is found more frequently in tropical and subtropical regions and the neoformans has a major prevalence in Europe and South America. Recently molecular biology PCR-based studies have isolated eight major molecular types classificated as: VNI (grubbi variety, A serotype), VNII (grubii variety, A serotype), VNIII (AD serotype), VNIV (neoformans variety, D serotype), VGI, VGII, VGIII, VGIV (gatti varieties, B and C serotypes). No correlation between the serological and molecular types in the gatti variety was found.
In its anamorphous form, the Cryptococcus neoformans is an encapsulated yeast (with non-encapsulated and capsule-deficient forms), measuring between 5 to 10 um diameter. The capsule is clearly a virulence factor of the fungus. In experimental cryptococcosis, mutant or non - encapsulated fungi are less virulent than the encapsulated species. A number of effects of the capsule can contribute with the virulence and it can inhibit the phagocytosis of macrophages, monocytes and neutrophils. The pathogenesis of cryptococcosis is determined by three factors: the system of defense of the host, the virulence of the type of Cryptococcus neoformans and the size of the entry site. The role of these three factors is not clearly interrelated, but certainly its relation is hugely complex.
The disease is acquired by inhalation of the fungus whose dehydrated spores penetrate throughout the airways, and the initial implantation sites are the lungs. Once in lung parenchyma, the fungus rehydrate and acquire the polysaccharide compositions of the gel capsule, today known as the most important factor of the disease pathogenesis. A primary lesion is established in the lung, with secondary involvement of hilar lymph nodes, constituting a primary complex, similar to tuberculosis and histoplasmosis. The initial lung lesion has a systemic haematogenic spreading potential to several organs, or reactivation potential in immunodepressed patients. In alveolar spaces, the fungic cells are initially taken on by the alveolar macrophages and the infection will depend upon the interaction between the host defense system and the fungus type virulence. The first interaction between the fungus and the alveolar macrophage can determine if the disease is going progress or not.
The Central nervous system is the most important target in cryptococcosis, although the cerebral lesion is always secondary to a lung foci, which is an entry site of this mycosis

and many times can regress or even disappear before the onset of the neurological symptoms.

The neurocryptococcosis infects individuals of all races, predominantly male ones and comprising in 85 % of the cases, immunodepressed patients. The neurological symptoms are mostly sub acute meningitis or a meningoencephalitis, and the patients showing headache, fever, malaise, coma or impairment of the memory. The symptoms last two to four weeks.

The CNS involvement can be classified into meningitis, meninoencephalitis, encephalitis and venticulitis, based upon the distribution of the infection in this site. The inflammatory response is the most common and presents itself in two histological well defined patterns. The lymphocitary type, with small macrophagic role and intensity degree varying between discrete to intense and with focal perivascular pattern, or the diffuse lymphocitary pattern with broadening of subarachnoid space. The granulomatous response, seen in a small portion of cases, presents itself also in variable patterns. Acknowledging that most of cases of exuberant granulomatous response are observed in meningitis.

The alterations observed in selected necropsy cases present themselves as: meningitis with inflammatory infiltrate minimal our absent, meningitis with moderate inflammatory infiltrate, meningitis with granulomatous inflammatory infiltrate, encephalitis with minimal inflammatory infiltrate, encephalitis with gelatinous cysts, encephalitis with necrosis and encephalitis with granulomatous infiltrate.

Some papers show that the inflammatory infiltrate is composed by T cells, showing CD45-RO positively, with minimal role of the B cell lymphocytes. Even in cases with granuloma formation, the response is performed by T cell and macrophages, with absence of B cells. There is some evidence that the B cell lymphocytes can pay a role in neurocryptococcosis in conditions of deficiency of cell immunity.

The most common aspect shown is of a discrete our nearly-absent inflammatory response with great amount of fungi.

The inflammatory cell response seems to be more intense in the cases with big diameter fungi and fungi with more thickened capsule are related to a greater degree of inflammatory response

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