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Cryptococcus neoformans and Cryptococcus gattii specific antibodies vary among children and adults with crypto-coccosis and healthy from Colombia

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Presenter session 1, September 21, 2022, 12:10 PM - 1:30 PM

Background: Cryptococcus neoformans and Cryptococcus gattii are two species of fungi that cause cryptococcosis, a global disease affecting mainly immunocompromised adults.

Objective: The study aimed at determining the total and specific antibodies against C. neoformans and C. gattii antigens in sera from patients with cryptococcosis and from healthy individuals from Colombia, which will help to elucidate the epidemiological analysis in the incidence of the disease in the country.

Methods: Sera from children and adult patients with cryptococcosis (n = 109) and sera from healthy children and adults from Colombia (n = 119) were studied. Using ELISA, total and C. neoformans and C. gattii specific levels of immunoglobulins IgG, IgA, and IgM were determined in sera.

Results: Total IgG, IgA, and IgM levels were higher in HIV- compared with HIV+ patients with cryptococcosis. Specific IgG, IgA, and IgM levels were higher in cryp-tococcus patients than in healthy controls and to be higher in adults than in children, with a positive correlation between antibody reactivity and age. All serum immunoglobulins were more reactive against C. gattii than C. neoformans. Including all samples, a positive correlation between total and specific IgG, IgA, and IgM levels was found.

Conclusion: In cryptococcosis patients from Colombia, serum immunoglobulins levels differ depending on HIV status, as reported previously. However, this study shows for the first-time variations in immunoglobulin production among adults and children with cryptococcal disease and between C. neoformans and C. gattii antigens. The observation of differential antibody reactivity with cryptococcal protein encourages further studies of the humoral immunity for host defense against cryptococcosis.

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Histoplasma capsulatum modulates the immune response exerted by macrophage sterol cells

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Background: Macrophage sterol cells (MScs) have become a tool not only for tissue regeneration but also for the treatment of inflammatory diseases. Several studies have demonstrated the therapeutic potential of MScs for the treatment of non-infectious inflammatory diseases; however, they appear to play a dual role in infection diseases. Histoplasma is a systemic mycosis caused by Histoplasma spp., which occurs mainly in immunocompromised individuals; this mycosis can present a severe clinical picture with dissemination to various organs and is associated with an exacerbated inflammatory response and with autotaxin and prostatin if bone marrow is affected. So far, the effect of a possible interaction of Histoplasma with MScs present in the bone marrow is unknown.

Objective: To examine, in vitro, the immunomodulatory effects of MScs in response to Histoplasma infection.

Methods: MScs were obtained from bone marrow of C57BL/6 mice, after isolation and purification, they were induced to modulated baso-line characterized by flow cytometry. Lactate the basal expression of toll-like receptor (TLR)-2, TLR4, and TLR-2 was determined using flow cytometry. MScs were infected with H. capsulatum yeast (induced CB 1980) in a multiplicity of infection (MOI) of 5 and incubated for 24 h. In addition, some of the co-cultures were previously treated with non-specific blocking antibodies for TLR2 and TLR4 or with a blocking peptide specific for TLR 1 (CILECT). Furthermore, another monoclonal antibody and anti-proliferation agents were done, and the expression of the genes encoding the cytokines IL-1β, IL-6, IL-17, TNF-α, and TGF-β, as well as of those for arginase-1 and iNOS were assessed.

Results: We observed that H. capsulatum has the capability to adhere and internalize within these MScs, nonetheless, this process did not affect the survival of the fungus. The interaction of H. capsulatum with MScs induced a slight but significantly increased expression of TLR2 but not TLR4 or TLR-2. In addition, the fungal interaction significantly augmented the expression of IL-6 and a decrease in the expression of IL-1β, IL-17, TNF-α, TGF-β, as well as the immune mediators Ag-1 and iNOS. Interestingly, blocking of these receptors did not affect phagocytosis, but increased IL-1β, IL-17, and TNF-α expression and reduced the expression of Ag-1 and iNOS. Furthermore, H. capsulatum induced apoptosis and ablated the proliferation of these stem cells; furthermore, this fungus significantly reduced the expression of genes related to adipogenic differentiation and increased the expression of genes related to the osteogenic differentiation process.

Conclusion: The above results indicate that H. capsulatum do not exert a variable antifungal effect against H. capsulatum, on the contrary, this fungal pathogen not only modulates the expression of inflammatory mediators in MScs, by a mechanism dependent on TLR2, TLR4, and TLR-2, but also affects their viability and their ability to differentiate into different types of specialized cells. These events could, in principle, affect both homoeostasis and the immune response in the infected host, and in addition, these stem cells may provide a niche for this fungus, allowing it to persist and evade host immunity.