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Effect of corticosteroids on the host immune response and in vitro growth characteristics during dermatophyte infection

Anarima Sharma, Shreya Singh, Sunil Dogra, Tanan Nanang, Biram Sisakia, Uma Nahar Sisakia, Arunaloke Chakrabarti, Harshad Chatterjee, Anuj Srivastava, Shivaprasad Dogra,
Post Graduate Institute of Medical Education and Research, Chandigarh, India

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Objective: During the current epidemic of dermatophytes, dermatologists in India are noticing atypical-clinical presentations of dermatophyte infections. Though direct fungal cultures of topical application containing cortisone-antifungal antibacterial drugs are attributed to this phenomenon, it is still unclear about its exact role. Corticosteroids alluring due to its non-toxic effects till now, but can clump off dermatophyte infections from the skin surfaces, which may lead to a collapse of dermatophytes. Therefore, we analyzed the effect of corticosteroids on host immune response and pathogens in vitro during dermatophyte infection.

Methodology: Patients (n = 15) were recruited in three groups; group one patients of dermatophyte cases with a history of corticosteroids for > 30 days (Group A), dermatophytes without any history of corticosteroids for > 30 days (Group B) and without dermatophytes and patients expected to have normal skin (Group C). Skin biopsies were collected and subjected to testing for immuno-cytokine (SEM) and cytokine expression analysis. All in vitro experiments were performed with Trichophyton mentagrophytes cells co-cultured with TSL-pcy expressing complex fungal isolates from classical and atypical cases (n = 3) as well as standard strains (n = 5, ATCC 18478). Biosamples were fixed in 2.5% glutaraldehyde and dehydrated through 50%-100% ethanol gradients. RT-PCR expression of pro-inflammatory cytokines (IL-1, TNF-a, IL-6, IL-1a, IFN-gamma 1b, IL-2R, and TNF-a) from skin biopsies and HAT cells were conducted using beta-actin as the reference gene. The viability and cell-cycle analysis of HAT cells in the presence and absence of dibutyl phosphate (0.5%) were performed by flow cytometry and established by optical microscope.

Conclusion: Increased atrophy caused by corticosteroids allows dermatophytes to thrive on the intact keratin atrophy when normal epidermis are removed. Reduced inflammatory cytokine synthesis, and SphK activity in keratinocytes with delayed clearance of dermatophyte infection from skin. Reduced growth of dermatophytes in the presence of corticosteroids and upgrowth of sail dermatophyte when co-cultured with keratinocytes and corticosteroids correlates with recurrence infection. In addition, increased production of sulfite ions that degrade keratin may lead to the initiation of widespread lesions.

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Myeloid-derived suppressor cells as a potential biomarker and therapeutic target in rhino-orbital mucormycosis patients

Preenix Singh1, Shikha Das2, Gargi Rafi1, Mohmad Ahmad Ansa1, Neelima Gupta3, Sonal Sharma1,3
1Department of Microbiology, University College of Medical Sciences (University of Delhi) and Guru Teg Bahadur Hospital, Delhi, India
2Department of Otolaryngology, University College of Medical Sciences (University of Delhi) and Guru Teg Bahadur Hospital, Delhi, India
3Department of Pathology, University College of Medical Sciences (University of Delhi) and Guru Teg Bahadur Hospital, Delhi, India

Poster session 1, September 21, 2022, 12:30 PM - 1:30 PM

Background: Mucormycosis is a deadly fungal infection that emerges in patients afflicted with COVID-19. All fungal illnesses are caused by deranged adaptive immunity, but Myeloid-derived suppressor cells (MDSC) have added a new dimension to the chronic inflammatory response.

Objective: We attempted to measure the MDSC immune response in rhino-orbital mucormycosis patients before and after treatment and compared the data with healthy controls.

Methods: A total of 3 ml of blood samples were taken in an EDTA tube from 21 patients with mucormycosis and 20 age-matched healthy control. A second blood sample was collected to examine the immune system post three months of treatment. Flow cytometry analysis was performed on whole blood using BD FACSCanto™ II and analyzed by FlowJo software (BD Biosciences). The percentage of positive cells in isotype controls was used to express the results. The GraphPad Prism 8, GraphPad software, LaJolla, CA, USA was used to analyze the results. All the results were considered significant when P < 0.05.

Results: All of the patients tested for RHOTF antibodies, which was confirmed by the culture. The percentages of Monocytes-MDCs (mMDSC; CD14+CD16-), Granulocyte-MDSCs (gMDSC; CD16+CD11b+) were significantly high in patients compared to healthy control.

Conclusion: MDSCs regulates T cells and other immune cells with a different mode of action. This finding in this study implies that the mechanism of immune-dysregulation involving MDSC pathways in mucormycosis and provides evidence that the therapeutic role of immunosuppressant drugs in MDSCs may be considered a therapeutic option for long-term benefit.