1731. Immune Dysregulation in Mucormycosis

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Background. Mucormycosis is a fatal fungal infection with unique predisposition to affect diabetics. Disregulated adaptive immunity contributes to the pathogenesis in all fungal diseases, but activated Th17 cells have laid a new dimension to chronic inflammatory response which was previously attributed to uncontrolled Th1 response. We attempted to study the Th17 and T regulatory (Treg) immune response in diabetic patients with mucormycosis and compared the data with a healthy control and a T2DM case without fungal infection. In addition we could follow-up one patient post 6-month treatment and performed immunological studies.

Methods. 2 ml of blood samples were collected in EDTA vial from two patients who were suffering from diabetes with mucormycosis for immunological investigations. Samples were also taken from age-matched T2DM patient without fungal infection and a healthy volunteer as controls for T-cell parameters. Repeat blood sample was taken to study immune parameters in one patient who was followed up after 6 months. The expression of various T-cell markers was analyzed by immunostaining with the antibodies against CD3, CD4, CD25, CD161, IL-23R [Becton Dickinson (BD) Pharmingen]. Fluorescence profiles were analyzed using Flow Jo software (BD Biosciences). The results are expressed as a percentage of positive cells.

Results. The percentages of CD4+ cells were low in both patients when compared with healthy control but it is much higher in diabetes case when compared with others. CD161+ cell population was higher in both patients when compared with healthy control and diabetic patient without fungal infection. The percentage of CD25+ cells was significantly high in patient before treatment when compared with healthy control and diabetics, and both the patients post treatment. The percentage of CD25+ cells was highest in healthy control when compared with others. The profile of CD25+ cells was comparatively similar in patient before treatment and diabetics but we found a higher percentage, in patients after treatment.

Conclusion. The findings in this study imminently indicate the mechanism of immune dysregulation involving Th17 and Treg pathways in mucormycosis and provide evidence that restoration of Th17/Treg may be considered as a therapeutic option for long-term benefit in diabetics.

Disclosures. All authors: No reported disclosures.

1732. A Canine Target Species Challenge Model to Evaluate Efficacy of a Coccidioidomycosis Vaccine

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Background. The preferred efficacy design for licensing a vaccine for animal use by the Animal and Plant Health Inspection Services (USDA) is a prospective, placebo-controlled, randomized, and double-blinded vaccination-challenge trial. In such studies, each subject receives the same exposure to the virulent pathogen by active challenge. To test a cps1, live avirulent canine coccidioidomycosis vaccine, an infection disease model was developed in beagle dogs.

Methods. 6-month old male beagle dogs were housed according to PHS standards. All procedures, approved by the Institutional Animal Care and Use Committee for Colorado State University, were performed at ARSL3. Dogs were infected by nebulization with low, medium or high counts of arthroconidia of Coccioides posadasii, strain Silveira, delivered via endotracheal tube under injectable anesthesia. Thoracic radiographs, CBC, and serum chemistries and body weights were obtained at 2- or 3-week intervals and dogs were euthanized 8 weeks p.i., or earlier if necessary. Approximately 1 gram lung specimens from each lobe were cultured for fungal burden. Fixed tissues were examined histologically. Specific markers were used for antigen detection.

Results. Ten of 11 dogs were successfully infected; 5 required early removal at 33 to 48-days p.i. Elevated globulin, decreased albumin, decreased A/G ratio, monocytosis and weight loss were present in all infected dogs. Radiographic and histopathological findings were very extensive in those dogs with the most consistent scoring and clinical findings, including some early removal, without overwhelming disease, while the low dose produced the least consistent quantifiable features. All dogs developed antibodies.

Conclusion. Nebulized aerosol delivery of spores reproducibly produced significant coccidioidomycosis in 10 of 11 dogs. Overall, the challenge model demonstrated consistent characteristic findings sufficient to assess vaccine efficacy in dogs during an 8-week period post challenge without producing a potentially overwhelming infection. The aerosol nebulization of arthroconidia in beagle dogs should provide a vaccination-challenge experimental design in line with Chapter 9 Code of Federal Regulations, parts 102.5 and 104.5.

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