1730. Invasive Fusarium Species in Mayo Clinic Patients with Hematologic Malignancies

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Background. The epidemiology of fungal infections in hematologic malignancies has changed in the past decade. Triazole prophylaxis has decreased Candida spp infections while infections due to other molds such as Aspergillus and Fusarium have increased. Fusarium has very poor prognosis, and after aspergillosis, is the most common invasive fungal infection in this patient population. We sought to describe fusariosis in patients with hematologic malignancy at the Mayo Clinic.

Methods. We performed a retrospective review of patients with culture-positive Fusarium infection from January 2003 to October 2016 at the Mayo Clinic, Rochester, MN. The records of patients were reviewed for demographics, diagnosis, treatment, and outcomes including mortality. Patients without a diagnosis of hematologic malignancy were excluded. Patients were classified with proven or probable Fusariosis based on the Revised Definitions of Invasive Fungal Disease from the EORTC/MSG Consensus Group.

Results. We identified 14 patients with hematologic malignancies (age range 17–79 yrs, mean age 60 yrs) with a confirmed culture diagnosis of Fusarium infection classified as proven (9 patients) or probable (5 patients). Two cases were isolated pulmonary infections, 3 extra-pulmonary, and 9 disseminated cases. Two patients had previously undergone stem cell transplantation. Eight patients (57%) were receiving antifungal prophylaxis at the time of diagnosis: 2 on voriconazole, 1 on posaconazole, 1 on flucytosine, 3 on echinocandins, and 1 on Amphotericin B. Nine patients (64%) were neutropenic at the time of diagnosis. Amphotericin was the initial treatment in 7 (50%) patients, with voriconazole added for 4 patients for combination therapy the first week. Voriconazole monotherapy was given initially in 5 patients. Seven patients (50%) were deceased at 6 weeks after culture positivity, with an additional 2 patients deceased by 12 weeks.

Conclusion. Fusarium infection outcomes in patients with hematologic malignancies have dramatically changed in whom Fusarium was common in the past, antifungal infections were more likely to be disseminated, with high mortality rates. Amphotericin B is commonly used as initial treatment, with many physicians recommending combination therapy with two agents, commonly voriconazole.

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1731. Immune Dysregulation in Mucormycosis

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Background. Mucormycosis is a fatal fungal infection with unique predisposition to diabetic patients. Dysregulated 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 uncontrollable 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 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 FlowJo 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 T2DM and 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 IL23R+ cells was significantly high in patient before treatment when compared with, healthy control and diabetics. However, no significant changes were observed at 6 months post 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.

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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 is the “probable cause” model. Coccidioides posadasii (C. posadasii) is a notable cause of disease in humans in the southwestern United States. The Fungal Drug Development Program at the NIH developed a suitable vaccine model in the desert and mountain beagle dog model. This model is similar to human infections and is limited to most other species. The purpose of this model was to develop a licensed vaccine for human use. The challenge 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 ARSIL. Dogs were infected by nebulization with low, medium, or high counts of arthroconidia of Coccidioides posadasii, strain Silverio, 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. Serum was tested for antibodies.

Results. Ten of 11 dogs were successfully infected; 5 required early removal at 33–48 days p.i. Elevated globulin, decreased albumin, decreased A/G ratio, monocytosis and weight loss were present in all infected dogs. Radiographic and histopathologic lesions were very extensive at the high challenge dose. The percentages 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.