391 Biologic Interventions in Silent Allergic Bronchopulmonary Aspergillosis Relapse: A case report on asymptomatic management

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RATIONALE: Allergic bronchopulmonary aspergillosis (ABPA) is an immune-mediated pulmonary condition caused by hypersensitivity to Aspergillus fumigatus, resulting in worsening respiratory symptoms and reduced lung function. Current treatments aim to decrease inflammation and prevent long-term lung injury utilizing systemic corticosteroids and antifungals. The role of monoclonal antibodies in ABPA, particularly asymptomatic patients, is not well studied. This case report describes the role of benralizumab and omalizumab in managing relapsing ABPA in an asymptomatic asthmatic patient.

METHODS: We conducted a comprehensive chart review of patient's history, diagnostics, and pharmacologic interventions. Biologic selection was based on literature review. Outcomes and therapeutic success were measured by clinical course, serologies, CT imaging and spirometry.

RESULTS: Our ABPA patient presented with hemoptysis, eosinophilia, elevated IgE level, IgE and IgG to Aspergillus fumigatus and migratory pulmonary infiltrates on CT. She received systemic steroids and antifungals. Although asymptomatic with well-controlled asthma and normal spirometry, benralizumab was added to reduce exacerbations and respiratory decline. Initially responsive with decreased eosinophilia, lower IgE level and ABPA markers, but repeat CT revealed new pulmonary cavitary lesions with elevated IgE level, IgE and IgG to Aspergillus fumigatus without eosinophilia. Systematic reviews of omalizumab use in symptomatic ABPA cases showed reduction of symptoms, exacerbations, steroid use and serum markers, prompting transition to omalizumab.

CONCLUSIONS: In setting of relapsing ABPA, benralizumab showed benefit and current use of omalizumab is proving effective in mitigating risk of exacerbations and preserving respiratory function. Future large-scale studies are needed to evaluate efficacy and safety of monoclonal antibody in ABPA, especially in asymptomatic cases.

392 Identifying Immunodominant Major Urinary Proteins (MUPs) in Mouse Urine

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RATIONALE: Mouse allergens trigger respiratory allergies in urban households and laboratory workers. Mouse allergen Mus m 1, consists of several major urinary proteins (MUPs) present in urine and pelt. The purpose of this study is to identify and quantify the immunodominant MUPs. Previously, we expressed two central (MUP7 and MUP10) and 3 peripheral (MUP4, MUP11 and MUP20) MUPs. To determine IgE reactivity to these rMUPs, we employed ImmunoCAP assays using clinical human sera.

METHODS: Fourteen IgE anti-MUP (sIgE) positive sera were diluted to 25 kUA/L and preincubated individually with rMUP 4, 7, 10, 11 and 20 allergen or mouse IgG and albumin that was pre-diluted serially from $3.0x10^{-3}$ to $1.28x10^{-5}$ g/L. Each sIgE-MUP preparation was analyzed by ImmunoCAP using E72 (urine) and E88 (epithelium, serum, and urine) allergosorbents. The IgE concentration measured at 50% inhibition (IC50) for each sIgE:MUP combination was used to compute the degree of competitive inhibition to determine which MUP induced the highest sIgE response.

RESULTS: No inhibition was observed with mouse albumin or IgG. All 5 rMUPs inhibited sIgE binding to both mouse allergosorbents to different degrees. As an illustration, serum V9533 preincubated with allergosorbent E72 produced IC50 at 127.6 g/L-(MUP4), 1.67 g/L-(MUP7) and 54.5 g/L-(MUP20) while E88 IC50s were achieved at 14.9 g/L-(MUP4), 0.0426 g/L-(MUP7) and 7.19 g/L-(MUP20). Results with other sIgE positive sera were consistent with these results.

CONCLUSIONS: rMUP7 inhibited sIgE at 1-2 logs lower concentration than the peripheral MUPs, indicating that the central MUPs are immunodominant for these MUP sensitized patients.

393 Investigating sex differences and the role of IL-5 in Aspergillus versicolor and Stachybotrys chartarum-induced pulmonary responses

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RATIONALE: Climate change increases occurrence of natural disasters, rising temperatures, and precipitation promoting expansion of fungal niches. Humans spend over 90% of their time indoors, leaving them highly susceptible to inhalation of fungal contaminants *Aspergillus versicolor* and *Stachybotrys chartarum*. Inflammation and cell infiltration in response to fungal exposure can cause allergic disease and are often mitigated by targeting IL-5 due to its role in eosinophil differentiation. To improve the assessment/treatment of fungal exposure, it's crucial to understand the role of IL-5 and the impact of biological sex.

METHODS: Mice (C57BL/6J or IL-5 genetic knockout) were exposed to HEPA-filtered air, *S. chartarum* ($1x10^4$), or *A. versicolor* ($3x10^5$) spores twice weekly for 13 weeks using an acoustical aerosol generator inhalation system. Twenty-four hours following final exposure, functional assessments and immunological responses were measured by whole body plethysmography, histology, antibody quantification, flow cytometry, and quantitative polymerase chain reaction.

RESULTS: Preliminary data suggests fungal exposure led to decreased respiratory function, and significantly increased cell infiltration and adaptive immune responses in wild-type mice. Responses to *S. chartarum* and *A. versicolor* exhibited differences in the lymphocyte and T helper response. Sex differences were observed between wild-type and IL-5-/- mice.

CONCLUSIONS: Elucidating the role of IL-5 in the immune response to fungal exposure is imperative given the use of anti-IL-5 therapies against allergic disease. Understanding how the immune response is modulated 1) by species-specific differences in fungal contaminants, and 2) by sex as a biological variable is of paramount importance in development of strategies to assess and treat fungal-related respiratory diseases.

THE JOURNAL OF
Allergy AND Clinical Immunology

VOLUME 155 • NUMBER 2

American Academy of Allergy Asthma & Immunology

AMERICAN ACADEMY OF ALLERGY, ASTHMA & IMMUNOLOGY

2025 AAAAI/WAO Joint Congress, San Diego, CA
February 28-March 3, 2025

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