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Liver Transplantation-associated Food Allergy and Eosinophilic Gastrointestinal Inflammation in Children – Clinical and Immunological Aspects

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i föreläsningssal Järneken, Diagnosvägen 15, Östra sjukhuset, Göteborg, den 28 oktober 2022, klockan 9.00

av

Timo Käppi

Fakultetsopponent:
Professor Dominique Debray
Université Paris Cité, Frankrike

Avhandlingen baseras på följande delarbeten

I. Käppi T, Rabe H, Lingblom C, Hesselmar B, Kullberg-Lindh C, Wold AE, Wennerås C, Saalman R. **High Frequency of Concomitant Food Allergy Development and Autoantibody Formation in Children Who Have Undergone Liver Transplantation.** *Transplantation* 2019; 103(11): 2338-2346.

II. Käppi T, Hesselmar B, Lingblom C, Johansson N, Wennerås C, Wold AE, Saalman R, Rabe H. **Elevated cytokine production and T-cell activation in children after liver transplantation – A link to increased susceptibility to food allergy development?** *In manuscript.*

III. Käppi T, Wanders A, Wolving M, Lingblom C, Davidsson Bården B, Arkel R, Hätting J, Anderzén J, Wennerås C, Saalman R. **Collagenous Gastritis in Children: Incidence, Disease Course and Associations with Autoimmunity and Inflammatory Markers.** *Clinical and Translational Gastroenterology* 2020; 11(8): e00219.

IV. Lingblom C, Käppi T, Bergquist H, Bove M, Arkel R, Saalman R, Wennerås C. **Differences in eosinophil molecular profiles between children and adults with eosinophilic esophagitis.** *Allergy* 2017; 72(9): 1406-1414.

SAHLGRENSKA AKADEMIN
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Abstract

This thesis focuses on three recently described childhood-onset gastrointestinal disorders: liver transplantation-associated food allergy (LTFA), collagenous gastritis (CG) and eosinophilic esophagitis (EoE). Its aim was to gain additional understanding of both the clinical disease characteristics and the associated immunological aberrations in these conditions.

Study I investigated the frequencies of allergy, allergic sensitization as well as autoimmune disease and autoantibodies in a cross-sectional cohort of pediatric liver transplant recipients. The co-occurrence of food allergy and autoantibodies was found to be increased, indicating an underlying immune dysregulation that impairs immune tolerance to both food allergens and autoantigens in the affected individuals. Study II analyzed serum cytokine concentrations and circulating lymphocyte subsets of the same patients who were included in Study I. Signs of ongoing immune activation were found to be prevalent despite clinically stable graft function. Additionally, the excessive underlying immune activation appeared to be associated with an increased susceptibility to develop LTFA. Study III investigated the clinical disease course in childhood-onset CG. Further, CG was found to be associated with autoimmune predisposition and serum calprotectin and amyloid A was proposed as novel candidate biomarkers for monitoring the disease activity in CG. Study IV involved analysis of blood eosinophil phenotype in children with active EoE. We found that these patients had a distinct molecular pattern of blood eosinophils compared with both healthy children and adults with active EoE.

The results of this thesis contribute to the improved clinical follow-up of the patients with the studied conditions. They also provide new insights into the associated immune deviations, which may facilitate the development of the future diagnostic and treatment options for these disorders.

Keywords: liver transplantation; food allergy; autoantibody; immune dysregulation; collagenous gastritis; eosinophilic esophagitis; eosinophilic inflammation; eosinophil; children.

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