PEDIATRIC EOSINOPHILIC ESOPHAGITIS: FROM PATHOGENESIS TO TREATMENT

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Background

Eosinophilic esophagitis (EoE) is a chronic immune/antigen-mediated inflammatory disease associated with esophageal dysfunction and severe eosinophil-predominant inflammation.

Clinical progress in EoE has occurred on the front of the pathophysiology. It is well known that EoE is triggered by food antigens, and the cytokine profile of the esophageal tissue is consistent with an allergic T-helper type 2 disease. A unique esophageal transcriptome with distinct genetic susceptibility elements at 5q22 (TSLP) and 2p23 (CAPN14) has been established. In addition, it is known about the involvement of other immune cells besides eosinophils, such as mast cells, basophils, and T-lymphocytes, in the pathophysiology of EoE, in addition to a disruption of the esophageal epithelial barrier, suggestive of possible food antigen uptake at the esophageal level.

Formal guidelines addressing the diagnosis and management of EoE were first published in 2007. In parallel with the growing body of research, additional updated guidelines have been published, creating practical management algorithms. One of the significant topics which have evolved in the guidelines over the past 2 decades has been the approach to proton pump inhibitor responsive esophageal eosinophilia (PPI-REE). Although PPI responsive disease was initially considered a variant of gastroesophageal reflux, it later became a separate entity, PPI-REE. Most recently, response of esophageal eosinophilia to PPI has been defined as a treatment option for EoE, rather than an exclusionary criterion. Endoscopy with esophageal biopsies

is universally recommended for both diagnosis and for assessment of response to treatment. Treatments for EoE include elimination diets or topical steroids, and more rarely, mechanical dilation or systemic steroids.

Main achievements

The research group has 3 active members (EM, MM and CS) of the Eosinophilic Gastrointestinal Disease Working Group of the ESPGHAN and it is therefore actively involved in several multicenter studies. Recently, as a part of the EGID WG, our research group participated to the largest pediatric European EoE cohort study. This retrospective investigation allowed to describe the natural history of the disease, define the most frequent allegens and differences in therapeutic management among Europe.
In an italian multicenter, we partially clarified some of the molecular EoE mechanisms, showing that IL-5, IL-13 and eotaxin-3/CCL26 are significantly over-expressed in the oesophageal epithelium of children with eosinophilic esophagitis.
In a pilot-study, our group has first described the possible association between celiac disease (CD) and eosinophilic esophagitis. The high proportion of patients affected by both diseases, EoE and CD, the lack of IgE sensitization for food allergens in these children as well as the significant clinical and histological remission on gluten-free diet compared to the group of subjects with EoE only, suggested that CD itself could cause esophageal eosinophilic infiltration and dyspeptic symptoms.

Future perspectives

We are currently leading an European multicenter trial with the aim of clarifying some of the molecuar mechanisms underlying EoE. We propose to perform genome wide DNA methylation profiling on oesophageal mucosal biopsies obtained from a prospectively recruited patient cohort of children diagnosed with EoE. Given the highly cell type specific nature of epigenetic signatures, we expect to detect distinct differences in the biopsies containing increased numbers of eosinophils. As a result we will aim to correlate DNA methylation profiles with disease phenotype as well as clinical outcome ultimely leading to the development of a diagnostic as well as prognostic biomarker.

Publications

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External collaborations

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