ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Eosinophilic Esophagitis in Children and Adults

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G&H How do the presenting symptoms of children with eosinophilic esophagitis compare to those in adults with this disease?

GTF The presenting symptoms of patients with eosinophilic esophagitis vary between children and adults. In children, symptoms may be nonspecific such as abdominal pain or those symptoms associated with gastroesophageal reflux disease (GERD), including vomiting, nausea, or heartburn. Less commonly described are nondescript signs and symptoms of feeding difficulties in younger children. Finally, if children's GERD-like symptoms are not improving with antireflux treatments such as proton pump inhibitors or Nissen fundoplication, eosinophilic esophagitis should be strongly considered.

In contrast, most adults with eosinophilic esophagitis present in a typical fashion with either food impaction or dysphagia. Desai and associates showed that eosinophilic esophagitis was the main cause of food impaction seen in a suburban private practice setting. Increasing numbers of studies from various centers across the world have shown that dysphagia is another common symptom associated with eosinophilic esophagitis. A smaller group of patients may present with chest pain likely related to esophageal spasm.

G&H Is eosinophilic esophagitis more prevalent in children than in adults?

GTF Eosinophilic esophagitis has an interesting history in that Straumann and colleagues and Atwell and associates originally described it in adults in the early 1990s. Over the next decade, pediatricians then took the lead in the identification of clinical features and treatment of the disease. Recently, studies in adults have re-emerged, emphasizing the importance of this disease. Thus, we do not yet have long-term studies on the exact incidence, prevalence, or natural history of the disease in either of these patient populations, though data from Rothenberg and colleagues suggest a prevalence of 1–4 per 10,000 children. Similar findings will likely emerge from adults during the next decade.

The American Partnership for Eosinophilic Diseases (APFED.org) recently sponsored successful efforts to adopt an ICD-10 code for eosinophilic esophagitis (new code: 530.13). These codes are important for practitioners to use for tracking both incidence and epidemiology as well as for billing appropriately for this disease.

G&H What is the current understanding of the cause of eosinophilic esophagitis?

GTF As in many diseases, a genetically predisposed host encounters an environmental trigger, leading to symptoms and disease phenotype. This paradigm appears to hold true for many of the patients with eosinophilic esophagitis. One landmark study identified specific gene patterns associated with eosinophilic esophagitis in children, in particular the gene eotaxin-3. Eotaxin 3 is a molecule that is critical for eosinophil migration to tissue spaces. One could speculate that when an exogenous food or aeroallergen encounters the esophageal mucosa, eotaxin 3 production is stimulated, leading to eosinophilic inflammation with large numbers of eosinophils and eosinophil microabscess formation. This inflammatory pattern provides the histologic hallmark of the disease.

G&H Could you explain the difficulties of confirming a diagnosis of eosinophilic esophagitis in patients?

GTF Since eosinophilic esophagitis is a relatively new disease with only recently identified diagnostic guidelines, clinicians must rely on both clinical and histologic data

to make the proper diagnosis of eosinophilic esophagitis. Esophageal eosinophilia is an important finding that must be considered in the clinical context in which it was obtained. Currently, there is a growing tendency to merely read a pathology report and automatically make a diagnosis of eosinophilic esophagitis based upon this single finding. An increasing body of data supports the fact that large numbers of esophageal eosinophils can be found in a variety of diseases, including GERD, eosinophilic esophagitis, inflammatory bowel diseases, and celiac disease. Previous work and clinical experience in children suggests that the majority of children with esophagitis, characterized by increased eosinophils, have reflux, not eosinophilic esophagitis, as the etiology. Thus, prior to making the diagnosis of eosinophilic esophagitis, a thorough examination of the clinical features of the patient must be performed to rule out any other causes. The distinction between reflux and eosinophilic esophagitis is particularly important because the treatments and long-term outcomes of the disease are so divergent.

G&H Are the same diagnostic tests and criteria used when examining children and adults with suspected eosinophilic esophagitis?

GTF To date, that is the case. Due to the diagnostic confusion surrounding this disease, we convened a group of experts in this area approximately 2 years ago to review the literature and provide collective experience as to what diagnostic criteria should be used to make the diagnosis of eosinophilic esophagitis in adults and children. During this review, no features were identified that would help to segregate children and adults into different phenotypes. These results, which were published in October 2007 in *Gastroenterology,* set an initial benchmark for making the diagnosis of eosinophilic esophagitis. Patients with esophageal symptoms who are found to have greater than 15 eosinophils in a high power field from an esophageal mucosal biopsy and in whom other etiologies, in particular, gastroesophageal reflux, have been ruled out, have a diagnosis of eosinophilic esophagitis. The upcoming years will provide revisions to this diagnostic paradigm and perhaps contribute additional information that will aid in differentiating disease phenotypes in adults and children.

G&H Do children and adults with eosinophilic esophagitis share the same standard allergic sensitivities to environmental and food allergens?

GTF We think that they share similar sensitivities, but the data have not yet been fully developed or replicated in multiple centers. Spergel and Liacouras, at the Children's Hospital of Philadelphia, have conducted the most extensive evaluation of pediatric patients for the identification of allergens and have found a variety of different food allergens that are suspect in this disease. In a pediatric study, Kagalwalla and colleagues at Children's Memorial Hospital in Chicago demonstrated that the elimination of the 6 most common food allergens led to remission in 75% of their patients. Gonsalves and associates at Northwestern University are currently conducting a similar study in adults. Preliminary results of this ongoing trial, which were presented at this year's Digestive Disease Week meeting, suggest a similar trend.

G&H How does the age of a patient affect treatment?

GTF There are two different approaches, medical and nutritional, to patients with eosinophilic esophagitis. Both have been shown to impact clinicopathologic features of the disease in children. Overall, nutritional exclusions and elemental diets may be easier to tolerate in younger children than adults and adolescents.

G&H Are there special concerns when treating pediatric patients with eosinophilic esophagitis as opposed to adults?

GTF There are several special concerns for treating pediatric patients that relate to the overall goal of promoting their normal growth and development. First, since nutritional management may include elimination of single, multiple, or all food products, one of the cornerstones of treatment is consultation with a pediatric dietician. The expertise of the dietician is required to ensure that the child's diet includes an appropriate number of calories, protein, fat, carbohydrates, and micronutrients. Second, attempts should be made to limit the exposure to corticosteroids because of their known biochemical impacts on bones, growth, and cataract formation. The third concern relates to initial assessment and attention to the development of feeding skills. Young children enter an important stage of oral development often at the same time that they develop eosinophilic esophagitis. As such, normal oropharyngeal development may be impaired, and milestones may not be reached. Due to inflammation, eating is often associated with pain, which may discourage children from eating. Even if the child's inflammation is brought under control, there may be continued learned avoidance behaviors that may last for months and require special attention. Finally, children may develop psychosocial or behavioral problems associated with the disease or treatment. Eating is clearly an important social and emotional component of daily life. When this component is disrupted, family, school, and social functions are impacted to a significant degree.

G&H Do most children with eosinophilic esophagitis require continued treatment into adulthood?

GTF This is an area that is very important in terms of future research needs. Evidence to date suggests that eosinophilic esophagitis is not a disease that people outgrow and that treatment into and throughout adulthood will be necessary.

G&H What other aspects of this disease constitute research needs?

GTF We need to determine the natural history of eosinophilic esophagitis. We need to better understand the quality of life associated with the disease and treatment. Answers to both of these questions will help determine whether the vigor with which we treat or do not treat patients is appropriate. If a significant number of patients eventually develop complications such as strictures or narrowings, we may need to be more rigorous in our approach and treatment.

Another important area of future study involves the basic pathogenesis of the disease, specifically the molecular mechanisms of how eosinophils impact function and what mechanisms drive eosinophils to the epithelium. It is unknown whether the severity and inflammation of the esophagus increase with age. An interesting question to investigate in the future would be whether the degree of inflammation correlates with the symptomatology of a patient.

Finally, as with all diseases, the identification of novel treatments and biomarkers will be critical for patient care. Currently, the only means of following these patients involves examining their symptoms and histology; the identification of another method of follow-up will be useful.

Suggested Reading

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