

EDITORIAL

Eosinophilic oesophagitis and pollen

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Eosinophils are observed in allergic and parasitic disorders as well as the site of injury. They also can be present in small numbers in normal gastrointestinal tract; however, eosinophils are not typically found in the oesophagus except in active disease states. Eosinophils have been reported in the oesophagus in two disorders: gastroesophageal reflux disease (GERD) and eosinophilic esophagitis. Eosinophil counts from biopsies of patients with GERD have eosinophil counts less than 10 per high-power field, while patients with eosinophilic oesophagitis have eosinophils counts of greater than 15 eosinophils per $\times 40$ high-power field [1].

Eosinophilic oesophagitis is also an increasingly reported disorder. The Children's Hospital of Cincinnati examined their pathology database and identified 315 cases of eosinophilic oesophagitis from 1991 to 2003. They found only 2.8% of the cases were identified before the 2000 with the majority identified in the last 3 years of the study [2]. The Children's Hospital of Philadelphia has reported a similar dramatic increase from two cases in 1994 to 72 cases reported in 2003. Not surprising, a similar increase in the number of publication from a total of two publications in the 1970s to nine in 1980s to 27 in 1990s and 34 only in 2004 and already more than 25 in 2005. The aetiology of the rise of eosinophilic oesophagitis is unclear. It is possible that the rise is because of the increased number of endoscopies and biopsies being done or increased recognition of the symptoms and the disorder. However, the study from Children's Hospital of Cincinnati and The Children's Hospital of Philadelphia have still seen this large increase in the last couple of years even with the number of biopsies being relatively constant [2].

The symptoms of eosinophilic oesophagitis are similar to symptoms of gastroesophageal reflux, but do not respond to standard or even aggressive GERD medications. Other symptoms of eosinophilic oesophagitis include dysphagia in older children and failure to thrive in infants. The leading aetiology for the cause of eosinophilic oesophagitis is because of food. The early papers by Kelly [3] showed that elimination of food with an elemental diet lead to resolution of symptoms and reintroduction of foods caused reoccurrence of the symptoms. More definitive work was done by Markowitz et al. [4] that showed normalization of eosinophil counts in 51 children, starting an elemental diet for 1 month. Foods that trigger or cause eosinophilic oesophagitis do not react only via an IgE-mediated mechanism, but also by a non-IgE-mediated mechanism. This explains some of the lack of efficacy when only IgE-mediated food reactions are identified. When both IgE-mediated and non-IgE-positive foods are eliminated, the patients show significant improvement of eosinophils to near-normal levels [5].

However, aeroallergen sensitization is also proposed for the proposed aetiology for eosinophilic oesophagitis. The original

evidence comes from a murine model of eosinophilic oesophagitis from Rothenberg's laboratory. Mishra et al. [6] found intranasal exposure to *Aspergillus fumigatus* or dust mite allergen caused a localized eosinophilia in the oesophagus, while oral or intragastric exposure to the allergen did not cause oesophageal eosinophilia. Recent work from the same laboratory confirmed that this sensitization is a TH2 process dependent on IL-5 [7]. The first clinical evidence in humans came from a case report by Fogg et al. We found one patient without any food allergy on testing or diet evaluation. Her eosinophilia count in her biopsy spiked 20–40 eosinophils per high-power field during the pollen season and returned to normal out of pollen season indicating the role of pollen in eosinophilic oesophagitis.

In the work by Onbasi et al. [8] in this issue of *Clinical and Experimental Allergy*, they performed a more extensive analysis of the role of pollen-associated eosinophilia in the oesophagus. They examined three groups: patients with asthma or allergic rhinitis (AR), patients with GERD or normal controls (no atopy or GERD with negative skin tests). The GERD patients had a low level of oesophageal eosinophilia ranging from 1.7 to ± 1.5 eosinophils per high-power field. The atopic population had increased levels of eosinophils in their oesophagus compared with the normal patients for biopsies taken during the pollen season. Their biopsies showed 5.5 ± 7.3 eosinophils per high-power field, but these levels were not at the levels observed in eosinophilic oesophagitis patients with a minimal of 15–24 eosinophils per high-power field for diagnosis. Similar percentages (21–26%) of patients with atopy or GERD were found to have eosinophils on biopsy. These results indicate that pollen plays a role in eosinophilic oesophagitis, but is probably not a main causative factor.

These data and other studies indicate that allergen sensitization is not just a local event, but also a systemic event. Wood et al. [9] found that allergen exposure in the asthmatic airway induced eosinophilia not only in the local airway, but also distally in bone marrow with increased IL-5 expression. Similarly, we found that allergen sensitization on the skin induced localized allergic dermatitis and airway eosinophilia in a murine model of atopic dermatitis consistent with the concept of the atopic march [10]. Akei et al. [7] found the airway sensitization in the murine model not only caused eosinophilic oesophagitis but also significant skin eosinophilia, accelerated bone marrow eosinophilopoiesis and blood eosinophilia. The current work by Onbasi suggests that allergen sensitization of the airway can cause eosinophilia in the gastrointestinal tract in humans. Therefore, the treatment of atopic individuals should involve treatment of all of their atopic diseases for optimal control. For example, to get optimal control of asthma, you need to treat the patients'

asthma, AR and atopic dermatitis. For the patients with eosinophilic oesophagitis, you will need to treat the allergic airway disease as well as the food allergies.

References

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