Fall 2014

Does Your Child Have Reflux or Could There be More to it Than That

Cody Elam
Otterbein University, cody.elam@otterbein.edu

Does your child have reflux or could there be more to it than that

Cody R. Elam, RN

Otterbein University, Westerville, Ohio

Underlying Pathophysiology.

Eosinophilic esophagitis (EE) is differentiated from Gastroesophageal Reflux Disease (GERD) by endoscopic and histopathologic examination. The hallmark of EE is eosinophilic infiltration of the esophagus. EE has been defined as "a clinicopathologic entity, combining clinical data on (1) relevant symptoms (distinct in the pediatric or adult populations with mostly food impaction and dysphagia in adults and feeding intolerance, failure to thrive, and GERD symptoms in children); (2) esophageal biopsies with adequate histologic findings in the esophageal biopsies (>15 eosinophils/high power field [HPF]); and (3) exclusion of other diseases with overlapping features, especially GERD" (Genevay, Rubbia-Brandt, & Rougemont, 2010, p.816).

Under normal circumstances, the esophageal mucosa is devoid of resident eosinophils, however there are certain disease states in which eosinophils infiltrate into and accumulate within the esophageal mucosa. EE and GERD are two of these disease states, with lower numbers of infiltrating eosinophils in GERD, and more numerous eosinophils in EE.

Although the etiology of EE is not fully established, for whatever reason there is an infiltration/migration of eosinophils into the esophageal mucosa. There is strong evidence that points towards an IgE-mediated allergic reaction, with the offending agent being either a food allergen or an aeroallergen (inhaled). There also seems to be a correlation between asthma and EE, as evidenced by the high numbers of EE patients who also suffer from asthma.

The effects that eosinophils play on the esophageal mucosa are multiple. In general, the effects are proinflammatory and include the upregulation of adhesion systems, and the mediation of cell trafficking through the release of various cytokines, chemokines, and lipid mediators. The tissue damage and dysfunction that results from the release of cationic proteins results in fibrosis of the esophagus. Toxic granule proteins are released that cause further mast cell degranulation, resulting in a vicious cycle of inflammation and tissue damage (Swoger, et al, 2007, p.1542).

Swoger, et al have proposed a method of eosinophil recruitment to the normally eosinophil-devoid esophagus involving interleukin(IL) 5 and procedes as such: The cytokine IL-5, produced by T-helper type II lymphocytes primes eosinophils to react to chemoattracts such as eotaxin. IL-5 also promotes the eosinophil's development, as well as activation, migration, and effector functions. Furthermore, IL-5 is overexpressed, and this systemic overexpression may directly promote migration of the eosinophils to the esophagus. The presence of an increased number of mast cells and T cells in the esophagus of EE patients has also been documented (Swoger, et al, 2007, p.1543). Eotaxin promotes eosinophil accumulation and adhesion to the esophageal endothelium by way of vascular cell adhesion molecule (CAM) 1, present on the surface of endothelial tissues and has also been found to be overexpressed in patients with EE (Swoger, et al, 2007, p.1543)

Another cytokine, cytokine IL-13, which upregulates IgE, is important for eosinophil survival, and activates adhesion systems also plays a role. Studies have proven a dysregulation of IL-13 in several allergic disorders such as asthma, atopic dermatitis, and allergic rhinitis (Swoger, et al, 2007, p.1543). This lends credibility to the proposed link between EE and an allergic (IgE-mediated) provocation.

To lend further evidence to the allergy-associated theory, it has been reported that "approximately 80% of pediatric patients with EE had a positive skin test result to a panel of food allergens and aeroallergens" (Swoger, et al, 2007, p.1543).

It is important to note, however, that a direct correlation does not always exist between a positive food allergy test result and the development of EE. Some patients continue to have symptoms even after foods that were positive on traditional allergy testing are eliminated (Swoger, et al, 2007, p.1543).

Several foods have been identified as being most-problematic for patients with EE. These foods are rich in protein and the classic examples include: milk, eggs, soy-beans, corn, wheat, chicken, and nuts (Swoger, et al, 2007, p.1543). Recall the patient in the case study who failed to show a positive response to a soy-based formula.

It is important to note, however, that the provoking allergen, whether food or aeroallergen may not be a pure IgE mediated reaction and that not all allergens are identifiable by traditional skin-prick testing. For this reason, EE has been described by some as a polygenic allergy disorder. Signs of an IgE-mediated allergic reaction, such as type-I histamine-mediated reactions (in which a reaction occurs within minutes of exposure to the allergen), may coexist with a delayed hypersensitivity reaction that may occur hours to days after the exposure to the offending antingen (Swoger, et al, 2007, p.1543).

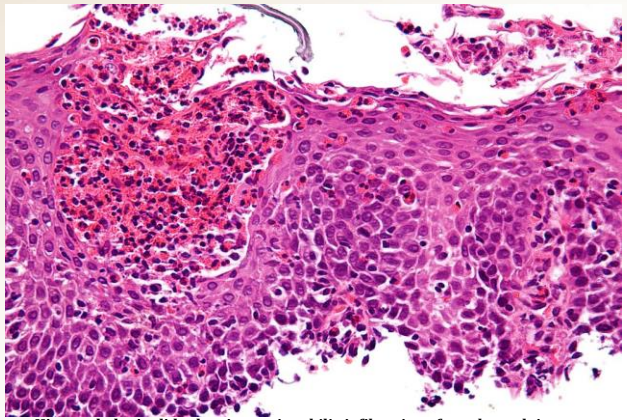
Inhaled (aero) allergens are thought to play a role in the infiltration of the esophageal mucosa as well, as pulmonary exopsure to these inahled antigens may result in esophageal mast cell activation, resulting in the release of cytokines that further activates the inflammatory response. Additionaly, the aeroallergens may be swallowed after being transported from the lung to the oropharynx by a ciliary mechanism where they can then provoke cytokine production in the esophagus.

The combined data on both food and aeroallergens "suggest 2 possible mechanisms of disease in EE. There might be initial sensitization due to a food antigen, with EE occurring on esophageal re-challenge with the same antigen. Alternatively, there might be initial bronchial sensitization followed by esophageal rechallenge" (Swoger, et al, 2007, p. 1454).

A Case Study: Eosinophilic Esophagitis vs GERD in children

A 4 month old girl presents with colic, feeding irritability and copious vomiting that is refractory to H2R antagonists (Zantac), as well as dietary changes from breast milk to a soy-based formula. Medical history at time of presentation includes URI and asthma (wheezing). At age 6 months, she is switched from Zantac to Prevacid, and formula is switched to one with pre-digested milk proteins. During this time, a slow, yet steady improvement in feeding habits and a reduction in the amount of vomiting are noticed, yet symptoms do persist.

Gastroenterology referral is made at the 1 year mark but an appointment cannot be made for another 6 months. During this time, subtle improvements are made through the dietary elimination of all milk products but signs of reflux still persist (i.e. vomiting and slow weight-gain). By two years of age, the toddler undergoes an esophagogastroduodenoscopy to rule out other causes of her GI symptoms. Treatment continues with PPI (Prevacid) until the patient is 4 years of age, at which she is weaned from pharmacologic agents and exhibits resolution of GI symptoms.



Histopathologic slide showing eosinophilic infiltration of esophageal tissue.

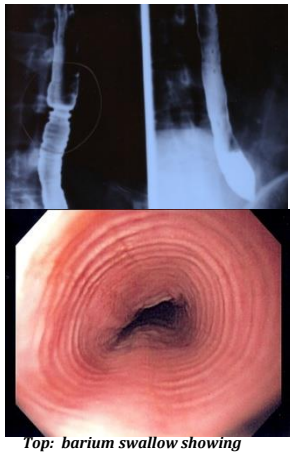
Sign and Symptoms of Eosinophilic Esophagitis in Children

- Nausea
- Recurrent Vomiting
- Weight Loss
- Failure to Thrive
- Anemia
- Choking
- Feeding Disturbances
- Irritability
- Abdominal Pain

*Note the multiple overlaps that correlate with the symptoms of Gastroesophageal Reflux Disease.

Significance of Pathophysiology

As the pathophysiology of EE demonstrates a strong relationship between either food, or aeroallergens, prompt recognition of the offending allergen is crucial. The multi-faceted complications from this disease require a multi-disciplinary approach, which should consist of: gastroenterologist consultation, along with consultation from both a dietician and a specialist in allergy/immunology. Once an individual is diagnosed with EE, every effort must be made to identify the offending allergen. Dietary management then becomes a major focus of treatment. Known as the "six food elimination diet", the removal of the six most common allergenic foods (milk, soy, egg, wheat, peanut/tree nuts, fish/shellfish) has shown a promising effect on the symptomatic relief of patients with EE. According to a study found in Contemporary Pediatrics, 74% of patients with EE showed histopathologic improvements after implementation of the six food elimination diet (Schuval & Gold, 2013, p.17). If diagnosed and properly treated in a timely manner, the long term sequelae caused from EE such as esophageal strictures and small-caliber esophagus may be avoided.



Top: barium swallow showing esophageal strictures in EE. Bottom: endoscopic image showing trachealization of the esophagus in EE.

Implications for Nursing Care

Eosinophilic esophagitis is a chronic disease with long-term persistence of esophageal inflammation (Schuval & Gold, 2013, p. 20). Timely recognition and diagnosis is key to reducing the impact that long-term irritation by eosinophilic infiltration plays on the esophagus. As nurses are very often on the front-line of history taking and information gathering on a patient, it is important to recognize the signs of reflux-like symptoms that are either refractory to, or slow to respond to traditional reflux therapies (such as the use of PPIs). Many times, nurses for whatever reason are privy to information that is not always divulged from the patient to the primary care giver. Careful analysis of provoking/relieving factors must be made.

Conclusion

Although the symptoms of GERD are shared by those of eosinophilic esophagtitis, for the most part, the resemblances stop here. Treatment of GERD is largely focused on the pharmacologic use of PPIs and H2R antagonists. EE is in large part refractory to these agents. Treatment modalities for EE are labor-intensive and require a multi-disciplinary team of gastreoenterologists, allergists, and dieticians for effective management. Prompt recognition and early treatment of EE vs. GERD leads to an overall improvement in the quality of life of an individual with EE. The saying "time is tissue", although routinely used in terms of a cardiac setting, also very much so applies to eosinophilic esophagitis.

References

Genevay, M., Rubbia-Brandt, L., & Rougemont, A. (2010, June). Do eosinophil numbers differentiate eosinophilic esophagitis from gastroesophageal reflux disease [Electronic version]. *Arch Pathol Lab Med*, *134*, 815-825.

Schuval, S., & Gold, D. (2013, December). Treating eosinophilic esophagitis in children [Electronic version]. *Contemporary Pediatrics*, 14-20.

Swoger, J. M., Weiler, C. R., & Arora, A. S. (20071541, December). Eosinophilic esophagitis: Is it all allergies? [Electronic version]. *Mayo Clinic Proceedings*, *82*(12), 1541-1549.

Additional Sources

Bhatia, J., & Parish, A. (2009). GERD or not GERD: The fussy infant [Electronic version]. *Journal of Perinatology*, *29*, 7-11.

Binkovitz, L. A., Lorenz, E. A., Di Lorenzo, C., & Kahwash, S. (2010). Pediatric eosinophilic esophagitis: Radiologic findings with pathologic correlation [Electronic version]. *Pediatric Radiology*, *40*, 714-719. doi:10.1007/S00247-009-1484-2

Dauer, E. H., Freese, D. K., El-Youssef, M., & Thompson, D. M. (2005, November). Clinical characteristics of eosinophilic esophagitis in children [Electronic version]. *Annals of Otology, Rhinology & Laryngology*, *11*(114), 827-833.

Eroglu, Y., Lu, H., Terry, A., Tendler, J., Knopes, B., Corless, C., & Byrne, W. J., Zhang, Z. (2009). Pediatric eosinophilic esophagitis: Single-center experience in northwestern USA [Electronic version]. *Japan Pediatric Society*, *51*, 612-616. doi:10.1111/j.1442200x.2008.02796.x

Jarocka-Cyrta, E., Wasilewska, J., & Kaczmarski, M. G. (2011, March). Brief report: Eosinophilic esophagitis as a cause of feeding problems in autistic boy. The first reported case [Electronic version]. *Journal of Autism and Developmental Disorders*, *41*(3), 372-374. doi:10.1007/s10803-010-1059-y

Sorser, S. A., Barawi, M., Hagglund, K., Almojaned, M., & Lyons, H. (2013). Eosinophilic esophagitis in children and adolescents: Epidemiology, clinical presentation and seasonal variation [Electronic version]. *J Gastroenterol*, *48*, 81-85. doi:10.1007/s00535-012-0608-x

Topal, E., & Bakirtas, A. (2012). Eosinophilic esophagitis in children [Electronic version]. *Asthma Allergy Immunology*, *10*, 1-9.

OTTERBEIN UNIVERSITY