Eosinophilic (Allergic) Esophagitis

Intraepithelial eosinophils are part of the inflammatory response in many types of esophageal injury, including gastroesophageal reflux disease (GERD), drug-related damage, chemo- and radiation therapy, and Crohn’s disease. In recent years, a distinctive clinicopathologic entity termed “Eosinophilic Esophagitis (EoE)” has been defined, in which eosinophils constitute the predominant morphologic finding. Although probably first reported in 1978 by Landres et al. It was not until the published series of 12 patients by Attwood et al in 1993 that the parameters of the condition became more completely defined. Since then the disorder has gained considerable recognition and has shown an increasing prevalence.

Clinical Features

EoE is currently defined as a “chronic immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.” It occurs in all age groups from early childhood to late middle age, with the current incidence estimated at 1.7-3/10,000, and is significantly more common in males than females (ratio 2-4:1). Infants and toddlers often present with feeding difficulties and failure to thrive, whereas school-aged children typically have vomiting and pain. Young and older adults generally have solid-food dysphagia, chest pain and often experience food impaction.

While there is significant symptomatic overlap with GERD, by definition, patients with EoE have normal or near-normal pH monitoring levels and fail to respond to antireflux therapy, although a subgroup of patients do respond to proton pump inhibitors. In addition, EoE patients have a high prevalence (42-92% of pediatrics and 28-86% of adults) of other concurrent allergic disorders, such as asthma, atopic dermatitis and chronic rhinitis.
Peripheral blood eosinophilia has been documented in adults and pediatric patients in several studies.

**Endoscopic Features**

In over 90% of patients with EoE, the esophagus exhibits at least one of the following gross findings: fixed esophageal rings (aka trachealization or ringed esophagus), transient esophageal rings (aka feline folds), white mucosal plaques or exudates, longitudinal furrows, edema, strictures, and mucosal friability. These features, however, have been described in other conditions and are not pathognomonic of EoE.

**Microscopic Features**

Histologically, most of the features of EoE overlap with those of GERD, particularly in distal esophageal biopsies. Major microscopic features that are considered characteristic and necessary to establish a diagnosis, but are not pathognomonic, include:

1. Increased intraepithelial eosinophils (≥15/HPF) obtained from the most densely populated areas (peak density),
2. Eosinophilic microabssceses (cluster of ≥ 4 eosinophils),
3. Surface layering of eosinophils,
4. Surface sloughing of squamous cells mixed with eosinophils, and
5. Degranulation of eosinophils

"EoE is best evaluated in biopsy specimens obtained after 2 months of anti GERD therapy."

Other reactive-type epithelial changes are also present (e.g. basal zone hyperplasia and intercellular edema). There is no evidence of significant eosinophilia in other parts of the gastrointestinal tract to warrant a diagnosis of gastrointestinal gastroenteritis.

EoE often involves long segments of the esophagus, may be patchy, and typically involves the proximal, middle and distal esophagus equally. In contrast, patients with GERD typically have higher eosinophil counts in the distal esophagus than in the proximal esophagus, due to the area in which the reflux affects the esophagus more severely. EoE is best evaluated in biopsy specimens obtained after 2 months of anti-GERD therapy.

**Pathogenesis**

Although the pathogenesis is poorly understood, the prevailing belief is that EoE represents a disease of type 2 (Th2) helper T cells in which an allergic background (from food or inhaled), environmental exposures, genetic predisposition, and probably other factors may act as triggers. Eosinophil recruitment and activation are carried out by these lymphocytes and involve eotaxin-3 (now called CCL26, a gene that encodes a component of the immunologic cascade) and interleukin secretion (IL13 and IL15).

**Treatment**

Currently, therapy is based on antigen elimination trials (especially in children, but often not well tolerated in adults), anti-inflammatory medications, and physical dilatation if strictures are present. Of the anti-inflammatory medications, topical glucocorticoids (oral budesonide, and fluticasone prior to 2007) have been shown to have a significant positive effect. Systemic steroids are used for
acute exacerbations, such as severe dysphagia, hospitalization and weight loss. Clinical trials with humanized antibody therapy directed to block interleukin secretion are currently underway.

Natural History
The natural history of EoE is still being defined. Dysphagia tends to be persistent if left untreated. Relapse occurs in 25–40% of successfully treated patients. To date, no malignant potential has been associated with this disorder, nor have systemic hypereosinophilic syndromes developed.

References:

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SEROUS CARCINOMA: A SERIOUS CARCINOMA

HGSC is one of the most deadly gynecologic malignancies. In the vast majority of patients (90% in some studies) present with stage III or IV disease, with spread beyond the pelvis and regional lymph node metastases common. Although surgical debulking to remove all visible tumor (“cytoreduction”) followed by cytotoxic chemotherapy frequently results in a progression-free interval, the rule for advanced stage disease is eventual recurrence and death from disease.

As HGSC often presents at a relatively advanced stage with widespread peritoneal involvement, it can be difficult to determine the exact site of origin. Traditionally, the site of origin of HGSC has been assigned to the organ most affected, and it was long thought that the majority of these cases arose within the ovary. Primary fallopian tube tumors were classified as such when the tumor was either restricted to the tube, or when the fallopian tube was most affected, with other sites showing only minimal involvement or a different histology entirely.

There has been a recent shift in thinking about the putative site of origin of HGSC, resulting from increased scrutiny of the changes occurring within the fallopian tube in women undergoing risk-reducing salpingo-oophorectomy (RRSO).