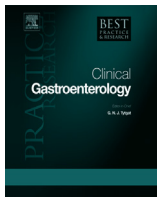
Best Practice & Research Clinical Gastroenterology 29 (2015) 759–769

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology



7

Disease associations in eosinophilic oesophagitis and oesophageal eosinophilia

Alfredo J. Lucendo, MD, PhD, FEBGH, Head of Department *

Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Spain

Keywords:
Eosinophilic oesophagitis
Coeliac disease
Eosinophilic gastroenteritis
Oesophageal atresia
Inflammatory bowel disease
Connective tissue disease
Atopy

A B S T R A C T

Eosinophilic infiltration into oesophageal tissue, typical of eosinophilic oesophagitis (EoE), has been described in several other conditions, including infections, hypersensitivity, and other autoimmune disorders. Since its description, EoE has been associated with an increasing number of diseases also characterized by tissue infiltration, including eosinophilic gastroenteritis and Crohn's disease. While an association between EoE and coeliac disease was previously reported, it is not supported by recent research. In contrast, EoE seems to be common in patients with a history of congenital oesophageal atresia, leading to hypotheses linking both disorders. The prevalence of EoE has also been shown to be eight times higher in patients with connective tissue disorders (CTDs), which has led to the proposal of an EoE-CTD phenotype, although this requires further assessment. This paper reviews the evidence of EoE's associations with several disorders, defining the common bases from an epidemiological, clinical, molecular and genetic perspective whenever possible.

Introduction

EoE has been consensually defined as a chronic, immune/antigen-mediated oesophageal disorder characterised clinically by symptoms related to oesophageal dysfunction, and histologically by an

* Department of Gastroenterology, Hospital General de Tomelloso, Vereda de Socuéllamos, s/n, 13700 Tomelloso, Ciudad Real, Spain. Tel.: +34 926 525 926; fax: +43 926 525 870.
E-mail address: alucendo@vodafone.es.

http://dx.doi.org/10.1016/j.bpg.2015.06.010
1521-6918/

eosinophil-predominant inflammation [1]. In fact, oesophageal eosinophilia, that is, the presence of eosinophils in the squamous epithelium of the oesophagus, has been defined as the histological hallmark of EoE [2]. The persistence of this symptom, even after treatment with proton pump inhibitors (PPI), is required for a definitive diagnosis of EoE according to the most recent guidelines [1,2]. However, the identification and characterisation of PPI-responsive oesophageal eosinophilia (PPI-REE) represents a major breakthrough in the study of this disorder, leading to the description of a potential new phenotype within the spectrum of EoE [3].

The excessive accumulation of eosinophils in tissues is a common finding in numerous gastrointestinal disorders, including IgE-mediated food allergies, eosinophilic gastrointestinal disorders (EGIDs) [4], gastro-oesophageal reflux [5,6], and inflammatory bowel disease (IBD) [7]. In each of these processes, the pro-inflammatory functions of eosinophils may contribute to tissue damage. Because of this, a histological finding of oesophageal eosinophilia should always be interpreted within the clinical context in which it appears, since a finding of eosinophils in oesophageal biopsies alone cannot be taken as a diagnosis of EoE [8,9].

From the first descriptions of the disease, EoE has been associated with an increasing number of other diseases with different characteristics and histological features; many of these have also been associated with oesophageal eosinophilia [1,2] (Table 1). In this paper, we review evidence of EoE's association with several distinct disorders, defining the common bases from an epidemiological, clinical, molecular, and genetic perspective whenever possible.

Eosinophilic oesophagitis and coeliac disease

In recent years, several case reports and cohort studies have suggested an association between EoE and coeliac disease (CD). Whilst this association was initially reported for paediatric patients [10–14], it has since been observed in adult patients as well [13,15,16], although it has not been universally confirmed in large, population-based, epidemiological studies [17]. Even though both diseases are caused by aberrant immune responses to ingested antigens and are potentially responsive to a food elimination diet, differences in the underlying pathophysiological mechanisms leading to each of them [18,19], along with the absence of a genetic connection between EoE and CD, have prevented researchers from establishing a causal relationship [14]. In a recent systematic review assessing the relationship between EoE and CD [20], the authors found a significant publication bias in favour of studies that included small numbers of coeliac patients with an increased prevalence of EoE and vice versa. Such a bias would artificially favour the existence of an association between both disorders. Indeed, most of the studies retrieved presented a high risk of bias due to methodological backwardness, thus lacking sufficient validity to extract solid conclusions. Moreover, a recent retrospective, cross-sectional study conducted with information from a US national pathology database

Table 1
Diseases associated with oesophageal eosinophilia.

Eosinophilic oesophagitis
Gastro-oesophageal reflux disease[a]
Eosinophilic gastrointestinal diseases
Atopy
Coeliac disease
Crohn's disease
Infection
Hypereosinophilic syndrome
Achalasia
Drug hypersensitivity
Vasculitis
Pemphigoid vegetans/penphigo
Connective tissue disease
Oesophageal atresia
Graft-versus-host disease

[a] This topic will be reviewed in a different article in this issue.