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Eosinophilic esophagitis and chronic cough originated beyond the respiratory tree

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Title page

Title: Eosinophilic esophagitis and chronic cough originated beyond the respiratory tree

Brief title : Eosinophilic esophagitis and chronic cough

Conclusion that summarizes the letter:

The frequency of cough as an atypical symptom of eosinophilic esophagitis is low and is characterized by the fact that it is usually daytime and irritative, especially during or after food intake

Eosinophilic esophagitis and chronic cough originated beyond the respiratory tree

CC affects all age groups and is a common complaint in the allergist practice.

Eosinophilic esophagitis (EoE) is a clinicopathologic disease characterized by esophageal dysfunction symptoms (EDS), and [?]15 eosinophils per high-power field (eos / hpf) in the esophagus after exclusion of other disorders with eosinophilia (1). In addition to the typical symptoms, they may have atypical and infrequent symptoms, among which is CC (2).

CC as the main symptom of EoE, associated or not with other EDS has been poorly studied and is not characterized. For this reason, the objective of this study is, research the frequency of CC as an atypical symptom and to investigate epidemiological, demographic, clinical, and endoscopic-histological and allergic characteristics, these co-morbidities, adherence to treatment and evolution.

Results

(Table 1 and 2)

Discussion

Atypical symptoms have also been described in EoE, although those are less frequent. Some of them are aerodigestive as CC (2,3).

In a study on the prevalence of extraesophageal symptoms in patients with EoE, it detets CC in 7–46% (4). It is rare but it can happen (2) that the main symptom of EoE is CC (5.1% de our patients), with the disadvantage that it is underdiagnosed, or its diagnosis is delayed of EoE. In other study son recurrent croup in children, thank you 7.3% were found to suffer from EoE.

We had not found studies which had evaluated the characteristics of the patients' CC with EoE. There is lower or no evidence on the characteristics of this atypical symptom. Instead, we have observed that cough in EoE triggering during day (worsening or starting during or after food intakes)

As CC may be caused by an underlying EoE or merely coexistence with other diseases. We have carried out the differential diagnosis of CC requesting several complementary tests (Table 2). Most of the studies on EoE and CC have performed in children (5,6), whereas in our serie, the children are only 10%. Therefore, it is the first time that it has been studied CC, and its characteristics in adults with EoE. Excluding symptoms, rest of the characteristics are like other patients with typical EoE symptoms. (1).

Almost half of de our patients had a fibrostenotic endoscopic phenotype, compatible with a long evolution of the disease that can lead to oesophageal structural and functional alterations (1) and provoke serious complications (15% of our patients). CC could be influence as the main symptom of EoE in the diagnostic delay, and we forced us to carry out the differential diagnosis with respiratory diseases.

We highlight the good adherence to PPIs drugs of our patients, probably because they are eager to find a remedy for their CC.

CC improved in all patients who did treatment with PPIs dugs, but it only completely disappeared in the patients with EoE in remission. In subsequent reviews, several patients have acknowledged the reappearance of the cough upon cessation of adherence to treatment and its disappearance within three months of performing it again.

This study has its limitations, we present data from an Allergology Service, so it is possible that the results do not coincide with other settings. One strength would be that it is a prospective study that characterise CC secondary to EoE.

In conclusion, despite the frequency of the CC in EoE as a major symptom is low, the doctors should consider EoE in the differential diagnosis of CC in children and adults. Above all if it is diurnal, in relation with food intakes to avoid delays in diagnosis and treatment which can triggering complications that they reduce in the quality of life of patients

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Authors contribution

AR Gratacos: Made substantial contributions to the conception, design of the study, and writing of the article

J Meneses: Made substantial contributions in the data acquisition

L Gonzalez: Has performed the histological study of all the biopsies of the study patients

J Joyanes: Realization of the study tables

A Palacios: Search of the bibliography

E Gomez: Supervision, and submission of the manuscript

All the authors have reviewed all the patients during the years of the study.

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Table 1. Descriptive study of multiple variables studied in patients with chronic cough as the main symptom at the beginning and / or reactivation of eosinophilic esophagitis

Patients with CC Total Patients with EoE	20 386 5.1%
Frequency of the CC as principal symptom	
Age Age <14 14-18 >18	X:24 SD 12.47 Me 20 Mo: 22 R: 43, I (4-47) 2 6 12
Sex	Men: 17 (85%)
Family history of atopy	11 (55%)
Personal history of atopy	17 (85%)
Rhinoconjunctivitis	16 (80%)
Asthma	10 (55%)
Atopic Dermatitis	5 (30%)

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Food allergy LTP Profilin Milk Egg	7 (35%) OAS 6 (86%) 4 (20%) 2 (10%) 2 (10%) 2 (10%)
Disphagia	15 (75%)
Food impact - Spontaneous resolution **- E**ndoscopic resolution	13(66%) 10 (77%) 3 (23%)
Chronic Cough - During food intake - After food intake **-** Daytime CC that worsens during or after food intake (no night CC)	20 (100%) 7 (35%) 5 (25%) 8 (40%)
Time of evolution of symptoms (months)	X:62.42. SD:77.48, Me:48, Mo:36 R:359, I (1-360)
Sensitization to aeroallergens: - Pollens - Epithelia - Fungi - Mites	1 (85%) 6 (31%) 4 (21%) 1 (5%)
Endoscopic phenotype: Inflammatory Fibrostenotic	12 (60%) 8 (40%)
Eosinophils in the uesophagus	X:49.88. SD:38.20 Me and Mo:60 I: 0-120
Spirometry (Fev1 y CVF>80%) 2 patients, did not collaborate	18 (100%)
Fractional exhaled nitric oxide levels - <35 ppb - 10 patients	10 (100%)
Methacholine test 8 patient	8 (100%), Negative

CC: Chronic cough. OAS: Oral allergy syndrome. Fev1: Second maximal expiratory volume. CVF: Force d vital capacity.

X: Arithmetic mean. SD: Standard deviation. Me: Median.Mo: Mode R: RanK. I: Interval. Ppb: parts per billion

Table 2 Adherence, response to treatment, evolution, and complications of chronic cough in patients with EoE

Response to PPIs (R-PPIs) Non-adherence to treatment with PPis	9 /20 (45%) 0 (0%)
Response to food elimination diet (R-FED) (They had had no response to PPIs) Non-adherence to treatment with FED	7 /10 (70%) 1
Response to swallowed topical corticosteroids (R-STCs) (They had had no response to PPIs or FED) Non-adherence to treatment with stcs	3/4(75%) 1 (The same patient who also did not adhere to FED)
Evolution of CC -Adherence to treatment -No Adherence to treatment	Disappeared when EoE remitted The cough persisted
Evolution of cough in patients with EoE not responding to PPIs	All patients improved but did not remit in any of them
Adherence to maintenance treatment	14/19 (74%)
Non-Adherence to maintenance treatment	5/19 (26%) 1-PPIs 2-FED 2-STCs
Evolution of CC after stopping treatment	Reappearance of the CC along with other symptoms of esophageal dysfunction within 4 months
Complications	3 (15%) 2 Esophageal perforations 1 Severe asthma and Aspiration pneumonia in the same patient

CC: Chronic cough. R-PPIs: Response to proton-pump inhibitor drugs. (R-FED): Response to food elimination diet. R-STCs: Response to swallowed topical corticosteroids

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