



**ORIGINAL RESEARCH PAPER**

**Gastroenterology**

**EOSINOPHILIC ESOPHAGITIS AND CHRONIC COUGH ORIGINATED BEYOND THE RESPIRATORY TREE**

**KEY WORDS:** Eosinophilic esophagitis, chronic cough, eosinophils, dysphagia, food impactions, intake

<b>Alejandro Raúl Gratacós Gómez</b>	MD. Sección de Alergología del Hospital General Universitario de Ciudad Real.Spain.
<b>Alberto Palacios Cañas</b>	MD. Sección de Alergología del Hospital General Universitario de Ciudad Real.Spain.
<b>Jaime Vinicio Meneses Sotomayor</b>	MD. Sección de Alergología del Hospital General Universitario de Ciudad Real.Spain.
<b>Miriam Clar Castelló</b>	MD. Sección de Alergología del Hospital General Universitario de Ciudad Real.Spain.
<b>Lucia Gonzalez Lopez</b>	MD. Servicio de Anatomia Patologica del Hospital General Universitario de Ciudad Real.Spain.
<b>Elisa Gomez Torrijos*</b>	Ph MD. Sección de Alergologia del Hospital General Universitario de Ciudad Real.Spain. *Corresponding Author

**ABSTRACT**

**Background** Chronic cough (CC) as the main symptom of eosinophilic esophagitis (EoE), associated or not with other signs of esophageal dysfunction, has been poorly studied. **Objectives** Research the frequency of CC symptoms of EoE and their characteristics. Comorbidities, adherence to treatment, and evolution. **Methods** An observational, prospective study. Variables: Epidemiological, demographics, atopic, endoscopic, histological, comorbidities, symptoms, time of evolution, endoscopic phenotype, respiratory function tests. Adherence, response to treatment, complications, and evolution **Results** Only 20 patients (5%) with EoE had CC. The mean age:24 years, male 85%. The time of evolution: 5 years. CC: recurrent during the day (never at night), worsened with food intake (during or after), improved when remission EoE and reappeared when active EoE. There were a few severe complications. **Conclusion** Although the frequency of CC as a symptom in EoE is low, it must be considered, especially if it appears in food intake.

Chronic cough (CC) affects all age groups and is a common complaint in the allergist doctor's practice. Respiratory infections and asthma are often threading causes of CC in children. In adolescence, the reasons may be like those of adults as gastroesophageal reflux disease (GERD), asthma, and upper respiratory tract syndrome (1).

Eosinophilic esophagitis (EoE) is a clinicopathologic disease characterized by esophageal symptoms, including but not limited to dysphagia and food impaction in adults and GERD symptoms in children; in addition, it is necessary for ≥15 eosinophils per high-power field (eos / HPF) in the esophagus after exclusion of other disorders with eosinophilia (2) Sometimes EoE, especially in children, courses with atypical symptoms such s vomiting, abdominal pain, swallowing disorders, and CC (3).

CC, as the main symptom of EoE, associated or not with other signs of esophageal dysfunction, has been poorly studied.

**Objectives.**

To research the frequency of CC as an atypical symptom in EoE and their characteristics (epidemiological and demographic. Clinical, endoscopic-histological, and allergic characteristics), co-morbidities, adherence to treatment, and evolution after treatment.

**METHODS**

A prospective observational study including patients in the mid-south of Spain.

All patients were diagnosed with EoE based on current consensus guidelines. In the anamnesis, all were questioned about esophageal dysfunction, swallowing disorders, and chronic cough symptoms. We're first treated with omeprazole,

and those who did not remit chose between swallowed topical corticosteroids or food elimination diets.

All (patients /or their parents) received written information about their treatment.

This study has been carried out by the principles of the Declaration of Helsinki and was approved by the Clinical Research Committee of the Hospital

**Studied variables:**

Epidemiological, demographics, symptoms, and time of evolution, allergic, endoscopic phenotype, histological, Respiratory function tests, comorbidities, adherence, response to treatment, complications, and evolution.

**Statistical Analysis:**

The SPSS statistical analysis package was used.

**RESULTS**

Of the 386 patients diagnosed with EE, only 20 (5%) had CC as the main symptom of EoE. Therefore, an atypical sign in EE appears in 5%. The improvement in CC was parallel to the remission of the disease, and the CC related to intake reappeared in the patients who stopped treatment unilaterally. A minority of patients had severe complications that required emergency treatment (Table1)

**DISCUSSION**

Some gastrointestinal diseases can lead to CC, such as GERD (the most frequent cause), esophageal anatomic abnormality, esophageal dysmotility, and EoE. (4)

In EoE, there are differences in the symptoms have been identified in varies according to age, evolving from non-

specific symptoms such as abdominal pain and rejection of food in pediatric patients to symptoms of esophageal dysfunction (dysphagia, choking, and food impaction) in adult patients (2,5) Atypical symptoms have also been described in EoE, but they are few CC, recurrent croup, and hoarseness (3,6).

Orenstein et al. and her colleagues were the first to report on the association between EoE and extraesophageal symptoms. Since then, several other authors have reviewed the prevalence of different esophageal symptoms in patients with EoE. Symptoms consistently reported include cough in 7-46% (7).

It is rare, but the main symptom of s EoE maybe CC, with the disadvantage that it is underdiagnosed, or its diagnosis is delayed, as in our patients. In a study, one hundred and ten children underwent a flexible esophagoscopy with biopsies as an additional investigation for recurrent croup (CR). Eight children (7.3%) were found to suffer from EoE. Another 19 children (17.3%) were diagnosed with GERD (8). In another study, 3.7% of children with aerodigestive symptoms refractory to medical treatment had EoE; of these, almost 43% had a cough (9). Other researchers found that in 80 patients, 6.25% had EoE (10). In a retrospective study on CC and CR with 40 children, 27% met EoE criteria (11)

In the literature, the authors do not evaluate the characteristics of the patients' CC, which explains the scant or no current evidence on this atypical symptom of EoE. Instead, we have observed that cough in EE is daytime manifests or worsens with food intake. The cough is the main symptom of the patients since it was the one that worried them the most and for which they consulted. After ruling out the respiratory origin, by conducting a thorough history, we found that most of the patients in the study had digestive symptoms except for three patients who only reported CC. Sometimes patients with EoE only have CC (3), and typical gastrointestinal symptoms are absent.

CC may be caused by an underlying EoE or merely coexistence since the patients with EoE may have atopic diseases that can cause CC (3). For this reason, we have carried out the differential diagnosis of CC in the 20 patients in the study by requesting several complementary tests (Table 1)

The CC of our patients usually appears during the day with the food intake either during or after the same (during the night, the patients are asymptomatic). They may also have irritating cough during the day that is exacerbated by food intake.

According to the biography, most patients with EoE who have cough as an atypical symptom are children (9,12), whereas, in our series, we only have 10% of patients <14 years of age. Therefore, this symptom, and its characteristics in adult patients, have hardly been studied.

The epidemiological, allergology, endoscopic-histological, and therapeutic aspects are very similar in patients whose main symptom is cough and those who do not present CC as a symptom (13).

Despite the youth of our patients, almost half had a fibrostenotic endoscopic phenotype; this is compatible with the long evolution of the disease and can lead to oesophageal structural and functional alterations (14). The diagnostic delay was possibly influenced by having CC as the primary symptom because he forced us to make the differential diagnosis with respiratory diseases that occur with CC.

Patients with fibrostenotic endoscopic phenotype are more likely to trigger severe complications than those with the

inflammatory endoscopy phenotype. In our study, 15% of the patients suffered them (2 esophageal perforations (15) and one aspiration pneumonia that was complicated by a lung abscess)

We highlight the perfect adherence to the first therapeutic modality indicated -Proton-pump inhibitor (PPIs) drugs-. The patients Were eager to find a remedy for their CC. Only one patient who did not respond to PPI became discouraged and did not adhere to other treatments, such as a food elimination diet.

Cough improved in all patients treated with PPIs, but it only wholly disappeared in the patients with EoE in remission EoE (<15 eos / HPF). In subsequent reviews, several patients have acknowledged the reappearance of the cough upon cessation of adherence to treatment and its subsequent 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 those of other services, nor can they be generalized to different settings. One strength would be that it is a prospective study that includes a large cohort of EE casin es; only 5% have a CC with food intake.

In conclusion, despite the frequency, the CC in EoE, like the main symptom, is low; it should be considered EoE in your differential diagnosis, especially if it is diurnal and with food intake, to avoid delays in diagnosis and treatment, which can trigger complications that they reduce in the quality of life of the patients.

**REFERENCES**

- Kantar A. 2017. Phenotypic presentation of chronic cough in children. *J Thorac Dis.* 9(4):907-913. DOI: 10.21037/jtd.2017.03.53.
- Gonsalves NP, Aceves SS. 2020. Diagnosis and treatment of eosinophilic esophagitis. *J Allergy Clin Immunol*;145(1):1-7. DOI: 10.1016/j.jaci.2019.11.011.
- Kumar S, Choi S, Gupta SK. 2019. Eosinophilic Esophagitis-A Primer for Otolaryngologists. *JAMA Otolaryngol Head Neck Surg*; 145 (4): 373-80. DOI: 10.1001/jamaoto.2018.4177.
- Naime S, Batra SK, Fiorillo C, Collins ME, Gatti M, Krakovsky GM, Sehgal S, Bauman NM, Pillai DK. 2018. Aerodigestive Approach to Chronic Cough in Children. *Curr Treat Options Pediatr*;4(4):467-479. DOI: 10.1007/s40746-018-0145-9
- Dellon ES, Hirano I. 2018. Epidemiology and Natural History of Eosinophilic Esophagitis. *Gastroenterology*;154(2):319-332. DOI: 10.1053/j.gastro.2017.06.067
- Ballart MJ, Monrroy H, Iruretagoyena M, Parada A, Torres J, Espino A. 2020. Diagnosis and management of eosinophilic esophagitis. *Rev Med Chil*;148(6):831-841. DOI: 10.4067/S0034-98872020000600831.
- Rubinstein E, Rosen RL. 2018. Respiratory symptoms associated with eosinophilic esophagitis. *Pediatr Pulmonol.*;53(11):1587-1591. DOI: 10.1002/población.24168
- Duval M, Tarasidis G, Grimmer JF, Muntz HR, Park AH, Smith M, Asfour F, Meier J. 2015. Role of operative airway evaluation in children with recurrent croup: a retrospective cohort study. *Clin Otolaryngol*;40(3):227-33. DOI: 10.1111/coa.12353
- Hill CA, Ramakrishna J, Fracchia MS, Sternberg D, Ojha S, Infusino S, Hartnick CJ. 2013. Prevalence of eosinophilic esophagitis in children with refractory aerodigestive symptoms. *JAMA Otolaryngol Head Neck Surg*;139(9):903-6. DOI: 10.1001/jamaoto.2013.4171
- Cooper T, Kuruvilla G, Persad R, El-Hakim H. Atypical croup: association with airway lesions, atopy, and esophagitis. 2012. *Otolaryngol Head Neck Surg*;147(2):209-14. DOI: 10.1177/0194599812447758
- Greifer M, Santiago MT, Tsirilakis K, Cheng JC, Smith LP. 2015. Pediatric patients with chronic cough and recurrent croup: the case for a multidisciplinary approach. *Int J Pediatr Otorhinolaryngol*;79(5):749-52. DOI: 10.1016/j.ijporl.2015.03.007
- Duval M, Tarasidis G, Grimmer JF, Muntz HR, Park AH, Smith M, Asfour F, Meier J. 2015. Role of operative airway evaluation in children with recurrent croup: a retrospective cohort study. *Clin Otolaryngol*;40(3):227-33. DOI: 10.1111/coa.12353
- Gómez Torrijos E, Sánchez Miranda P, Donado Palencia P, Castro Jimenez A, Rodriguez Sánchez J, Mendez Diaz Y, Moreno Lozano L, Garcia Rodriguez R. 2017. Eosinophilic Esophagitis: Demographic, Clinical, Endoscopic, Histologic, and Atopic Characteristics of Children and Teenagers in a Region in Central Spain. *J Investig Allergol Clin Immunol*;27(2):104-110.
- Biedermann L, Straumann A, Greuter T, Schreiner P. 2021. Eosinophilic esophagitis-established facts and new horizons. *Semin Immunopathol*;43(3): 319-335. DOI: 10.1007/s00281-021-00855-y
- Donnet C, Destombe S, Lachaux A, Michaud L, Triolo V, Heissat S, Stephan JL, Patural H. 2020. Esophageal perforation in eosinophilic esophagitis: five cases in children. *Endosc Int Open*;8(7): E830-E833. DOI: 10.1055/a-0914-2711