



Eosinophilic Esophagitis due to Gluten without Celiac Disease and Unusual Comorbidities

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Abstract

In recent years, it has become recognized that patients with eosinophilic esophagitis (EoE) have an increased risk of multiple autoimmune diseases. Possible shared genetic aetiologies have been observed between EoE and autoimmune diseases. Currently, it is believed that EoE is not associated with a higher risk of neoplasms since such published cases are very rare and there are only isolated reports. Herein, we describe a unique case of EoE due to gluten without coeliac disease. The patient presented some unusual comorbidities, such as hypothyroidism (autoimmune disease) and essential thrombocythemia (neoplasm of haematologic origin).

Introduction

Polycythemia vera, essential thrombocythemia and myelofibrosis are clonal disorders collectively identified as myeloproliferative neoplasms. The incidence and prevalence rates of myeloproliferative neoplasms, in general, have increased in the last decade,¹ as has eosinophilic esophagitis (EoE).^{2,3} Moreover, studies of patients with EoE have uncovered an increased risk of multiple autoimmune diseases among this population. Possible shared genetic aetiologies have been observed between EoE and autoimmune diseases. Currently, however, it is believed that EoE is not associated with a higher risk of neoplasms, and this is primarily based on the fact that such published cases are very rare and there are only isolated reports in the medical literature.⁴

Case report

We report here the case of a 52-year-old male patient with a personal history of non-allergic bronchial asthma. He reported having

experienced dysphagia with solid foods over the previous 9 years and isolated episodes of food impaction, which resolved spontaneously.

An esophagogastroduodenoscopy with biopsies was performed, and samples were obtained from each targeted organ and from the three sections of the oesophagus. More than 30 eosinophils/high power field (eos/hpf) were found in the upper, middle and lower oesophagus, but no eosinophils were detected in the stomach or duodenum. No atrophy of intestinal villi was observed in the duodenum.

After being treated with omeprazole (40 mgs bid) for 2 months, a new oesophagoscopy was performed with biopsies using sections that detected >20 eos/hpf in the three oesophageal sections analysed.

Skin prick tests and specific IgE tests for wheat, milk, egg, lentils, peanuts, hake and shrimp were all negative. The patient was therefore diagnosed with EoE and subsequently treated with a food elimination diet. We instructed the patient how to follow the six-food elimination diet (6FED) with slight modification: we removed all cereals (with and without gluten) for 6 weeks. After the diet, the EoE remitted (0 eos/hpf in the oesophageal biopsies).⁵ The eliminated foods were then introduced sequentially (one-by-one), with biopsies performed at 6 weeks after the introduction of each food in order to detect the food responsible. The disease became reactivated only following the introduction of cereals. In order to reduce the number of cereals to be excluded from the diet and to improve the patient's quality of life, we offered the patient a gluten-free diet that maintained the EoE in remission.

Three months later, the patient returned for a check-up and reported that he had lost 3 kg with the 6FED, but had not regained the weight. He also reported eating all foods except those containing gluten. He made complaint of asthenia and a right upper quadrant abdominal pain that had lasted for 1 month. Blood test (Table 1) and chest/abdominal computed tomography scan were performed.

Keywords: Eosinophilic esophagitis; Gluten; Essential thrombocythemia; Autoimmune disease; Dysphagia.

Abbreviations: 6FED, Six-food elimination diet; EoE, Eosinophilic esophagitis; Eos/cga, eosinophils/high power field.

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Table 1. Blood tests made to the patient

Items	Results
Blood	605,000 platelets/mcL
RBC and WBC counts	Normal
Coagulation	Normal
Except fibrinogen	775 mg/mL
ESR	40 mm
Lupus anticoagulant	Positive
GGT	262 U/L
LDH	700 U/L
Alkaline phosphatase	259 U/L
Tyroid Tests	TSH:1.26 mcu/ml; T4:N
Antibodies of connective tissue diseases	All Negative

The computed tomography scan showed hepatosplenomegaly and pleural effusion with atelectasis of the lower lobe of the left lung due to ischaemia and left portal vein thrombosis. The patient was admitted and given a final diagnosis of chronic myeloproliferative syndrome, of the essential thrombocytopenia type (JAK2-positive, calreticulin-negative), and deemed at high risk of thrombosis and hypothyroidism.

Discussion

Our patient suffered from classic EoE, very similar to the cases previously described (male, onset of symptoms in the 4th decade of life).⁶ In our patient, the EoE did not subside with high doses of IBPs, and, after explaining to him the possible treatments (corticosteroids or diet), he chose the elimination diet.⁷ Since results of allergy testing against the most frequently involved foods were negative, the patient was prescribed a 6FED.⁵ In order to improve the quality of life of the patient, we followed what other authors have done with other foods, such as milk,⁸ and offered him the opportunity to test whether gluten was responsible for his EoE.

The patient agreed to adhere to the same diet as if he were a patient with coeliac disease. After performing oesophagoscopy, we found that gluten was the responsible protein for the patient's EoE. Therefore, even if he had to follow the diet indefinitely, he could eat rice and corn and gluten-free cereals, for which many supermarkets have wide selections of currently. Although in this patient, gluten produced an eosinophilic inflammation of the oesophagus, it did not produce inflammation of the stomach or duodenum; in addition, we ruled out coeliac disease in this patient, as villous atrophy was not detected in the duodenal biopsies.

We know from our experience that when patients adhere to the 6FED diet they lose at least 2–3 kg in 6 weeks, but this weight is quickly recovered. In this patient, however, this did not happen and, instead, he complained of other symptoms. The subsequent studies showed at least one autoimmune disease (hypothyroidism), an increasingly common finding in patients with EoE.⁹ Our patient also had developed an associated haematologic malignancy, which is rare in patients with EoE. We have reviewed the literature and only found isolated cases of EoE as a paraneoplastic syndrome. These include a patient with ganglioneuroblastoma and another case of an oesophageal tumour compatible with the "classical variant" of inflammatory myofibroblastic tumour, with prominent

eosinophilic infiltrate from the lesional to the extralesional area consistent with EoE.^{4,10} We believe that patients with EoE have a risk of developing malignancies similar to that in the general population.

In conclusion, this is the first report of a case of EoE due to gluten without coeliac disease that presents the unusual comorbidities of hypothyroidism (an autoimmune disease) and essential thrombocytopenia (a neoplasm of haematologic origin).

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study concept and design (JRS), acquisition of data (YMD, LML, AEO), analysis and interpretation of data (JMS), drafting of the initial and final manuscript (JFFB), critical revision of the manuscript (RGR), study supervision (EGT), translation to English (YMD, LML, AEO).

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