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Co-existence of celiac disease and eosinophilic esophagitis: Is it a coincidence for the two diseases?

Çölyak hastalığı ve eozinofilik özefajit birlikteliği: Bu iki hastalık için bir tesadüf mü?

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Abstract

Celiac disease and eosinophilic esophagitis are usually considered to be separate gastrointestinal diseases; however, it appears that they may coexist more often than would be expected. We report the case of a 5-year-old girl who had positive celiac serology and was assessed as having type 3c celiac disease according to the Marsh classification with endoscopic pathology. However, the patient's eosinophils were more than 100 per high-power field in esophageal mucosal biopsy specimens and she was evaluated as having eosinophilic esophagitis as well. The relationship between celiac disease and eosinophilic esophagitis is not clear. Nevertheless, coexistence of eosinophilic esophagitis needs to be considered in children with celiac disease.

Keywords: Celiac disease, eosinophilic esophagitis, endoscopy.

Öz

Çölyak hastalığı ve eozinofilik özefajit genellikle ayrı gastrointestinal hastalıklar olarak değerlendirilmekle beraber birliktelikleri beklenenden çok daha fazladır. Burada pozitif çölyak serolojisi olan ve endoskopik patoloji sonucunu ile Marsh sınıflamasına göre çölyak hastalığı tip 3c olarak değerlendirilen 5 yaşında kız hastayı sunmaktayız. Diğer taraftan hastanın özefagus mukoza biyopsi örneklerinde her sahada 100 den fazla eozinofilisi mevcuttu ve hasta eozinofilik özefajit olarak da değerlendirildi. Çölyak hastalığı ve eozinofilik özefajit arasındaki ilişki kesin değildir. Bununla birlikte çölyak hastalığı olan çocuklarda eozinofilik özefajit birlikteliğine dikkat edilmesi gerekmektedir.

Anahtar Sözcükler: *Çölyak hastalığı, eozinofilik özefajit, endoskopi.*

Introduction

Eosinophilic esophagitis (EE) and celiac disease (CD) are considered to be distinct immunologic diseases of the gastrointestinal tract. It is a rare case in the literature of children who underwent upper gastrointestinal endoscopy for suspected CD, which was confirmed histologically, were also found to have endoscopic and histological evidence of EE. Recent case reports and cohort studies have suggested an association between CD and EE in pediatric populations (1,2). This case report aims to make a contribution to the literature by showing the rare co-existence of the two diseases.

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Case Report

A 5-year-old girl with abdominal pain was admitted to our clinic 3 months earlier. The patient had a history of suffering from constipation. Her weight was 15.6 kg (10-25th percentile) and height was 107 cm (25-50th percentile). On physical examination, there was no abdominal tenderness. The white blood cell count was 14.400/mm^3, hemoglobin 12 g/dL, hematocrit 35%, platelet count 554.000/mm^3, aspartate aminotransferase 60 IU/l, alanine aminotransferase 28 IU/L, gamma-glutamyl transferase 9 U/L, total bilirubin 0.45 mg/dL, direct bilirubin 0.09 mg/dL and other biochemical values were normal. Celiac serology revealed an IgA antigliadin antibody titer of 92.8 AU/mL, IgG antigliadin antibody titer of >200 AU/mL, an IgA tissue antitransglutaminase titer of 234.1 AU/mL as positive.

Upper gastrointestinal tract endoscopy revealed reduced duodenal folds, pale duodenal mucosa, evident scalloping, fissures of duodenal mucosa and normal

esophageal mucosa. The pathological examination of endoscopic duodenal biopsy specimens showed total villous atrophy, elongation of the crypts, flattened mucosa and infiltrations of mononuclear cells in the lamina propria (Figure-1a). There was an increased number of intraepithelial CD3-positive T-lymphocytes in the surface epithelium. These findings were consistent with CD and the patient was evaluated as having CD type 3c according to the Marsh classification. Eosinophils were more than 100 per high power field in esophageal mucosal biopsy specimens (Figure-1b). The patient was also evaluated as having EE.

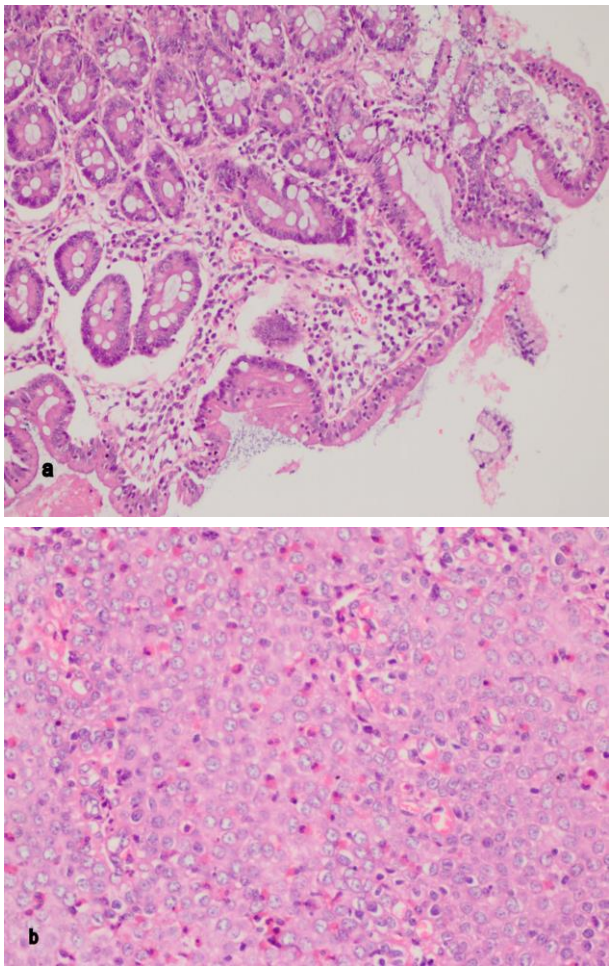

Figure-1. a. Total villous atrophy, elongation of the crypts, flattened mucosa and infiltrations of mononuclear cells in the lamina propria of duodenum (H&E stain; x20). **b.** Eosinophils were more than 100 per high power field in esophageal mucosal biopsy specimens (H&E stain; x40).

The patient's skin prick test was negative for all allergens. There was no peripheral blood eosinophilia and total IgE was normal (20.3 IU/mL). Specific IgE was negative for cow's milk and food panel was normal. Thyroid function tests and thyroid autoantibodies were normal, glucose 91 mg/dL and hemoglobin A1c were 5,7%. There was no acid reflux in 24-hours-esophageal pHmetry. The patient was started on a gluten-free diet. Follow-up endoscopy of the patient revealed regression of the endoscopic and histological findings of celiac disease, but no decline of the findings of eosinophilic esophagitis following the gluten-free diet after 6 months. We continue to follow-up the patient, whose abdominal pain and constipation have ended, in our clinic.

Discussion

CD and EE are distinct disorders with specific clinicopathological characteristics. EE is an immunoallergic disease that characteristically presents with acute or chronic dysphagia, food impaction, gastroesophageal reflux symptoms unresponsive to acid suppression, though it may be asymptomatic. Endoscopy may reveal longitudinal furrowing, circular rings, white exudates or normal mucosa in the esophagus. The pathogenesis of EE includes a T-helper (Th) 2-type immunological reaction, which is triggered by exposure to dietary allergens causing infiltration of the esophageal mucosa by T lymphocytes, mast cells and eosinophils (3).

On the other hand, CD is a Th 1-mediated autoimmune disease of the small intestine induced by the ingestion of gluten (4). CD has classically been diagnosed when duodenal biopsies have shown typical histologic alterations and a favorable response has occurred to a gluten-free diet (4). Patients with CD are known to be at higher risk for coexisting autoimmune diseases, such as type 1 diabetes mellitus and autoimmune thyroiditis, but their risk of developing atopic diseases remains unclear (5).

In the last few years, some studies have suggested an association between CD and EE in pediatric populations. Ooi et al. (1) reported the prevalence of EE to be 3.2% among 221 children with CD. Leslie et al. (2) reported the prevalence of EE to be 4% among 250 children with CD and in this study 3 of 10 children were reported to have symptoms of CD and EE, esophagus appeared normal at endoscopy, but biopsies showed evidence of EE similar to our case. Another study showed that approximately 30% of children diagnosed as having EE had normal-appearing esophageal mucosa at endoscopy (6). Our patient presented with only abdominal pain and constipation. Leslie et al. (2) reported that 1 of 10 children with CD and EE presented with only abdominal pain and normal-appearing esophageal mucosa at endoscopy but biopsies showed evidence of EE, as in our case. However, other diseas that are associated with esophageal eosinophilia were also excluded for our patient with clinical and laboratory findings.

CD and EE are two manifestations of food allergy with different pathogenic mechanisms. A gluten-free diet was started for the patient. There was no food allergy in our

case so other food elimination diet was excluded. The effect of a gluten-free diet on EE in children with both CD and EE is varied in the reported studies. In two studies, children who had undergone repeated endoscopic examinations showed recovery of their duodenal mucosa but no resolution of esophageal eosinophilia on a gluten-free diet alone, as in our case (1,2). However, Quaglietta et al. (7) reported that 6 children with CD and EE who primarily had the symptoms of EE had all improved symptomatically on gluten-free diet, and 3 children's second endoscopy showed significant reduction in intraesophageal eosinophils. Studies have also shown that eosinophils may play a role in gliadin-induced intestinal damage (8). Increased intestinal permeability in CD may facilitate the exposure of the intestinal immune system to various antigens and transport of these antigens to various body sites leading to hypersensitivity reactions in genetically predisposed individuals (9). Although studies have suggested an inverse association between Th1- and Th2-related disorders, they have shown that autoimmune and atopic diseases share risk factors that increase the propensity of the immune system to generate both Th1- and Th2-mediated inappropriate responses to nonpathological antigens (10).

Clinical symptoms of EE and CD vary with age. The relationship between these two diseases is not clear. Nevertheless, coexistence of EE needs to be considered in children with CD. In these cases, irrespective of whether the esophagus appears normal or abnormal at endoscopy, biopsies should be taken from distal, medium and proximal esophagus to investigate the association EE.

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