

Eosinophilic esophagitis and anaphylaxis due to cow's milk in an infant

Erdem Topal¹, Ödül Eğritaş², Mustafa Arga¹, Sinan Sarı², Aylar Poyraz³, Arzu Bakırtaş¹, Buket Dalgıç²

Departments of ¹Pediatric Asthma and Allergy, ²Pediatric Gastroenterology, and ³Pathology, Gazi University Faculty of Medicine, Ankara, Turkey. E-mail: erdemtopal4@gmail.com

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Food allergies are often seen in infancy and usually show the clinical signs in the form of type I hypersensitivity reaction. However, a combination of food allergies can sometimes be found in the same patient. In this report, we present an 11-month-old infant who had a combination of anaphylaxis and eosinophilic esophagitis induced by cow's milk. Diagnosis of eosinophilic esophagitis is done by examination of esophageal biopsy material histologically. This is a very rare combination of food allergy. Improvement in clinical and histological findings of eosinophilic esophagitis was achieved by removal of cow's milk and dairy products from the infant's diet.

Key words: anaphylaxis, eosinophilic esophagitis, cow's milk allergy.

Food allergies are often seen in infancy and usually show the clinical signs in the form of type I hypersensitivity reaction. However, a combination of food allergies can sometimes be found in the same patient. In a baby with atopic eczema, both increment in eczema lesions and urticaria with the same food is the best example. However, a combination of anaphylaxis and eosinophilic esophagitis (EoE), which is a rare food allergy, is only mentioned in one report¹. The combination of these two clinical entities is discussed in this report.

Case Report

An 11-month-old female infant admitted to the Pediatric Gastroenterology Clinic with a complaint of failure to gain weight for six months and refusal of foods. It reportedly started when the infant was 4 months old with commencement of additional foods. The infant had a history of flushing on the face and ears, swelling of the eyelids, runny nose, sneezing, and wheezing, which had developed about five minutes after formula feeding at 5 months of age. When referred to another clinic for these complaints, she was diagnosed with anaphylaxis induced by cow's milk, and withdrawal of milk and dairy products from

the diet of both the infant and the mother had been proposed. However, the elimination diet was not adhered to completely in the infant or mother. The mother did not eliminate milk and dairy products from her diet, and the infant was given dairy products by the parents occasionally. In two of these instances, she had experienced anaphylactic episodes after cheese and pudding administration at 6 and 8 months, respectively. There was no distinctive family history. On physical examination, her weight was 8.1 kg (3-10p) and length was 71 cm (25-50p). Other system findings were normal. When anti-tissue transglutaminase immunoglobulin A (anti-tTG IgA) antibody was checked and confirmed to be positive for possible celiac disease, pediatric gastroenterology performed an upper gastrointestinal endoscopy. On endoscopy, esophageal linear shearing and trachealization were observed macroscopically, but gastric and duodenal mucosa appeared normal. On histopathologic examination of the esophageal biopsy specimens, intraepithelial dense eosinophilic infiltration (50 eosinophils/high power field [hpf]), eosinophilic microabscess formation and superficial layering of eosinophils were seen (Fig. 1). Histopathologically, the patient was diagnosed with EoE, and the Pediatric Allergy Clinic was consulted in order

to treat the disease and conduct follow-up. Cow's milk protein in skin prick test (SPT) and atopy patch test (APT) was 3x3 mm (negative control 0 mm, positive control 6x6 mm) and (++) positive, respectively. Total IgE (18 mg/dl) and the number of peripheric eosinophils (50 mm³, 0.7%) were within the normal limits. Cow's milk- induced anaphylaxis and EoE were diagnosed, and milk and dairy products were removed from her diet. Amino-acid based formula feeding was prescribed. The diet was created by an experienced specialist with enough calcium support. In addition, adrenalin auto-injector (Epi-pen) was prescribed, and the parents were instructed regarding an emergency action plan. In the first visit after three months, with complete compliance with the elimination diet, it was revealed that the infant attained 9 kg (10-25p) in weight and also had an improved appetite. For this reason, the elimination diet was continued alone for the treatment of the patient. In the 12th month of treatment, at the age of 22 months and with a complete clinical response in terms of EoE, follow-up endoscopy was performed to evaluate the histopathological healing. On the histological examination of the case, whose esophagus was in normal view on endoscopy, it was observed that the number of intraepithelial eosinophils dropped to 8 in each hpf, and the other pathological findings were improved (Fig. 2). Since the clinical and the histopathological responses to a year-long dietary therapy were complete and tolerance to food allergies was usually implemented around 2 years of age, the addition of milk to the diet was considered. Since the patient had a history of anaphylaxis with the same food, oral provocation test with cow's milk was planned. Before the oral provocation test, the cow's milk-specific IgE level was measured. The serum level was 15.1 kUA/L, which was higher than the recommended threshold². It was thus decided to continue with the diet as before. Furthermore, anti-tTG IgA antibody, which was checked when the patient was 22 months old, was negative.

Discussion

The prevalence of food allergy during the first 3 years of life is 6%³. EoE, which is involved in both type I and type IV hypersensitivity reactions, is a rare form of gastrointestinal food allergies. It is reported to be between

2/100,000 and 27/100,000 per year in Sweden⁴ and 1/10,000 per year in the United States⁵. EoE is mostly diagnosed in early infancy, and its coexistence with asthma, allergic rhinitis and atopic eczema is well known. However, coexistence of EoE with other forms of food allergy is seen rarely. Within the rare forms of the coexistent allergies, the most frequently reported is EoE and celiac disease, and the first case was reported in 2007 by Verzeznassi et al⁶. In the following years, the prevalence of EoE has been found to be 3.2%⁷. Lastly, Sánchez-García et al.⁸ reported the coexistence of urticaria, celiac disease and EoE in the same patient. In 6 of 17 children with EoE (35%) followed by Rizo Pascual et al.⁹, diagnosis of IgE-mediated food allergy was reported, but types of reactions were not mentioned. In the analysis of 45 children with a diagnosis of EoE by Sugnam et al¹, 24.4% were reported to have anaphylaxis, but no etiologies were mentioned. However, in our case, cow's milk was responsible for both EoE and the anaphylaxis clinic, and was found to be positive on both SPT and APT. Coexistent allergic diseases could also be seen. The majority of patients with EoE (50%–80%)¹⁰ are atopic based on the coexistence of atopic dermatitis, allergic rhinitis, and/or asthma and the presence of allergic antigen sensitization based on SPT or measurement of plasma antigen-specific IgE. Although EoE and anaphylaxis rarely occur together, their occurrence could have been expected or was just coincidental in our patient. Failure to thrive, diarrhea, refusal to eat, and vomiting could be seen as symptoms in infants with celiac disease. Even though anti-endomysium IgA antibody and anti-tTG IgA antibody were used as a screening test in the diagnosis of the disease, the definite diagnosis is reached with biopsy of the small intestines¹¹. Furthermore, transient celiac autoimmunity being reported without celiac disease in recent years¹² shows the importance of biopsy for diagnosis. In our case, anti-tTG IgA antibody was positive, but the biopsy that was performed was normal. In the follow-up, anti-tTG IgA antibody became negative. Additionally, the presence of symptoms like refusal to eat and weight loss after moving on to additional foods should be considered as a differential diagnosis in food-induced allergy.

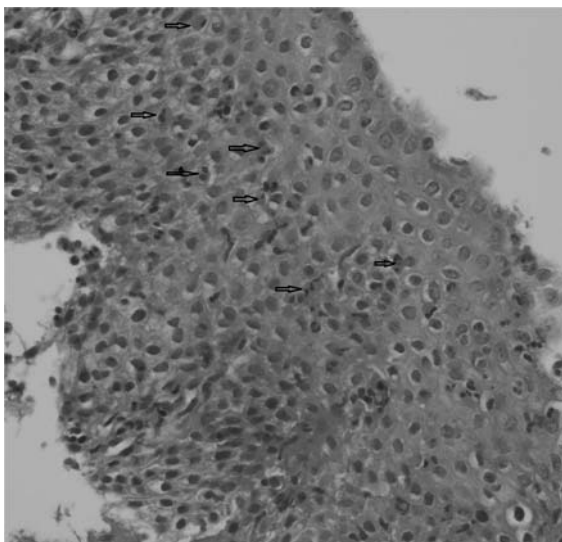


Fig. 1. Intraepithelial dense eosinophilic infiltration and eosinophilic microabscess formation.

The basic approach in the treatment of food allergies is to avoid the responsible foods. The treatment of EoE consists of dietary and/or medical therapy. Dietary therapy can be administered in three ways: elementary diet (amino acid-based formula), six empirical elimination diet (milk, egg, soy, wheat, peanuts, seafood) and specific elimination diet (identified with SPT and/or APT). In studies, complete remission has been reported to be 96-100% with elementary diet^{13,14} and 50-70% with empirical diet^{15,16}. Spergel et al.¹⁷ reported a 77% remission rate with the elimination of foods from the diet detected by SPT and/or APT.

It may be interesting to have histopathological findings concordant with EoE in our case, although the parents were advised to apply a milk elimination diet 6 months before reference to our clinic. However, the mother, who was breastfeeding the patient at that time, stated that she never stopped drinking milk or eating dairy products. In addition, the parents did not give milk or milk-based formula to the patient but tried dairy products like cheese and yoghurt occasionally. As a result, mild urticaria and pruritus were experienced, and two of these cases occurred as an anaphylactic reaction. Therefore, we think that the patient was exposed to milk and dairy products by breastfeeding, which led to persistence of histopathological findings of EoE at the time of the diagnosis. In our case, clinical and

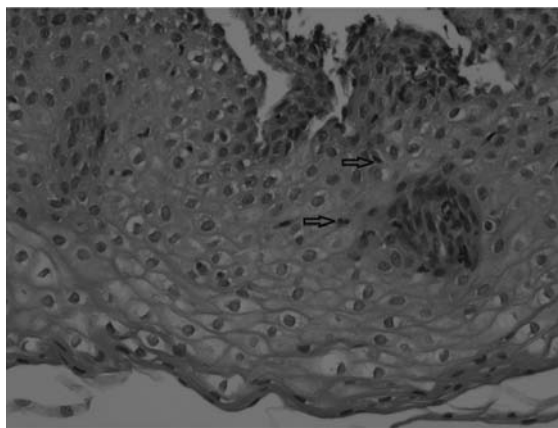


Fig. 2. Esophageal mucosa after dietary treatment.

histological remission was obtained with full adherence to the milk elimination diet. In the 562 case series of Spergel et al.¹⁸, it is reported that all 11 patients in complete remission had food hypersensitivity, and they recovered with specific elimination diets without any other medical treatment. In these cases, it is reported that foods found to be sensitive are mostly those such as egg and milk, to which tolerance develops with advancing age. In the same study, it was also observed that the average number of sensitive foods was lower in the remission group than the non-remission group (2.4 vs 6.9). In our case, there was single food sensitivity, and removal of this food from the diet provided clinical and histological remission. As in previous studies, this result supports that sensitization against a small number of foods increases to complete remission.

In conclusion, this is a case report of EoE, which is already a rare phenomenon, and coexistence of anaphylaxis with the same food. Elimination of cow's milk, which causes both conditions, from the diet was sufficient to achieve the clinical and histological remission.

Therefore, while bearing in mind that different spectra of food allergies can be found together in the same patient, we believe it is appropriate to question the cases in this regard and stress the importance of diet in terms of treatment compliance.

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