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Dear Editor

Eosinophilic Gastroenteritis Treated with a Multiple-Food Elimination Diet

Primary eosinophilic gastrointestinal disorders (EGIDs) include eosinophilic esophagitis (EoE), gastroenteritis (EGE), and colitis.[1,2] Recently, an empiric diet, preferentially devoid of the 6 most common food-allergens, milk, soy, egg, wheat, peanuts/tree nuts, and shellfish/fish (6-FED) has been used for EoE.[3,4] The 6-FED induced a significant improvement, which was equivalent to that of topical steroids in EoE.[5] In contrast to EoE, 6-FED has never been employed for the treatment of EGE as far as we know.

Here, we report a case of a patient with EGE successfully treated with the elimination of these 6 foods and other the patient's historically causative foods (multiple foods elimination diet; MFED).

CASE REPORT

A 5-year and 11-month-old boy was referred to our institution because of urticaria, abdominal pain, diarrhea, and bloody stool starting 3 months prior. He frequently experienced abdominal pain and vomiting after eating various foods, especially chicken, pork, and beef. He was treated with oral steroids and antihistamines for urticaria in another institution. However, only temporary remission in digestive symptoms as well as urticaria was observed. He had been treated for asthma as an outpatient. He had a history of colon-polyps and bloody stool associated with lymphoid hyperplasia at 2 and 3 years of age, respectively. After visiting our institution, he underwent upper gastrointestinal endoscopic examination, which revealed circumferential redness, edema, and erosion of the duodenum (Fig. 1A-a). The biopsy showed hyperemia and bleeding with eosinophil and lymphocyte infiltration in the duodenal lamina propria (Fig. 1 A-b). Eight days after upper gastrointestinal endoscopy, the patient was admitted to another institution because of sudden abdominal pain and diarrhea soon after eating Sichuan-style bean-curd containing soybean, chicken, and pork and then referred to our hospital owing to the computed tomography findings: extensive bowel wall edema. Rectal wall thickening was also evidenced by ultrasound (Fig. 1B-a). Sigmoidal biopsies revealed hypereosinophilia (36 eosinophils/high-power-field, Fig. 1A-c). Therefore, the patient was diagnosed with EGE.[6,7] There was a wide variety of possible causative foods, which made it difficult to pinpoint each food. The antigen-specific IgE antibody

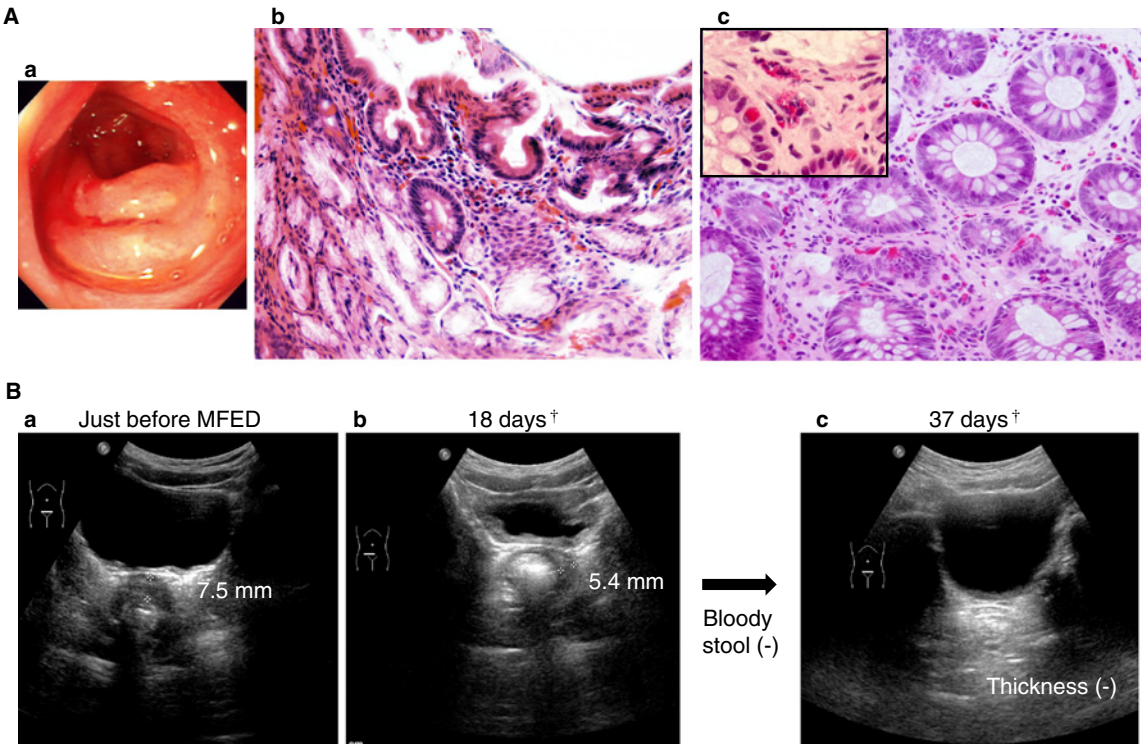

Fig. 1 Endoscopic findings of duodenum (**A-a**). Histological findings of duodenum (**A-b**) and sigmoidal colon (**A-c**) in hematoxylin and eosin-stained sections (Optical magnifications: **A-b** and **c**, ×200, inset in **c** ×400). Ultrasound findings of rectum (**B-a-c**, †days after first ultrasound). MFED, multiple foods elimination diet.

Table 1 Total and antigen-specific IgEs before MFED

Total IgE (IU/ml)	1145
Antigen-specific IgEs (U_A/mL)	
Milk	<0.35
Egg white	0.80
Wheat	0.51
Soybean	0.40
Peanuts	0.54
Sesame	1.03
Crab	<0.35
Shrimp	<0.35
Mackerel	<0.35
Scallop	<0.35
Pork	<0.35
Chicken	<0.35
Beef	<0.35
House dust	>100
Mite	>100
Cedar pollen	17.7

test results are shown in Table 1. In addition, oral steroids yielded poor results as mentioned above. Therefore, he was recommended a MFED, which involved the 6-FED as listed above and meats when combined with an elemental diet (ED). Antihistamines and suplatast tosilate were also administered. One month later, the bloody stool and urticaria resolved, although transient exacerbation of urticaria due to respiratory infection occurred, and the rectal wall thickening was improved (Fig. 1B-b, c). One month later, the patient presented vomiting due to accidental consumption of sweets, including chocolate and wheat. To minimize the eliminated foods and shorten the elimination period, challenge tests were scheduled immediately. About 2.5 months after treatment initiation, a soybean challenge test was blindly performed using 1 g of bean curd. The patient developed erythema, facial swelling, and urticaria within 30 minutes. Two weeks later, milk challenge tests were blindly performed. One milliliter of cow's milk induced mild urticaria and erythema within 1 hour. To confirm these results, 5 ml of cow's milk was administered the next day. The patient developed emesis within 30 minutes of milk consumption followed by generalized erythema and urticaria. Diarrhea and bloody stool persisted for a few weeks. Approximately 5 months after the beginning of MFED, serial reintroduction was initiated after the discontinuation of anti-histamines and suplatast tosilate, as the patient had been asymptomatic for almost 4 months except when consumed accidentally. The reintroduction phase consisted of the addition of 1-food group every 1-2 weeks (Fig. 2). Mild symptoms were presented but not exacerbated. Therefore, we were able to continue with the reintroduction phase, except when the patient presented with influenza. Foods were successfully reintroduced. Peanuts/tree nuts and shellfish were not challenged, as they were not necessary for his nutrition. Bloody stool recurred 1 month after the completed reintroduction. In addition, he had presented vomiting after eating dairy products, eggs, bean-curd, and sausages and more varied foods behind the back of his mother. Subsequently, a colonoscopy was performed, which indicated sigmoidal wall edema. The biopsy presented eosinophilic infiltration. MFED was initiated again. Symptoms disappeared in a few weeks and sigmoidal wall edema was improved. Therefore, the reintroduction phase was initiated once more. As the symptoms were milder than before, foods were reintroduced every 3 days. The reintroduction phase was completed without any major symptoms (shown in Fig. 2 until this point). About 4 months later, the patient presented with intermittent vomiting with mild abdominal pain, which were mostly self-limited and occasionally required antihistamines. Subsequently, symptoms were accompanied with urticaria. According to the medical history, the symptoms were exacerbated by cow milk, and thus dairy products were eliminated from his diet. Colonic mucosal edema and eosinophilic infiltration with lymphoid hyperplasia and Charcot-Leyden crystals were observed. Swollen mesenteric lymph nodes were identified by ultrasound. These symptoms resolved a month after elimination of dairy products. The improvement of swollen mesenteric lymph nodes was also confirmed. Subsequently, the patient achieved symptom remission while maintaining a dairy product-free diet.

DISCUSSION

EGIDs are recognized as a result of combined IgE and non-IgE mediated hypersensitivity. Consequently, the majority of patients have positive antigen-specific IgE antibody tests and/or skin-prick tests to multiple food-allergens but their symptoms lack the typical immediate response, which is considered to be delayed food hypersensitivity.[1] In fact, the symptoms occur at a variety of times, from minutes to days. This also indicates the difficulty of identifying the causative foods.[8] As a result, ED and systemic steroids have often been chosen for the treatment of EGE.[1,9] However, ED reduces quality of life[4] and systemic steroids are often accompanied by undeniable side effects. Therefore, we designed MFED for EGE based on those of EoE.[3,4] There is the possibility that the MFED against EGE allows the identification of possible causative foods during the reintroduction period as well as significant improvement of symptoms.[4] Indeed, the present case of EGE represents a significant improvement after MFED and the reintroduction process was helpful to identify the causative foods. Consequently, MFED could result in the unnecessary removal of foods and/or might not include

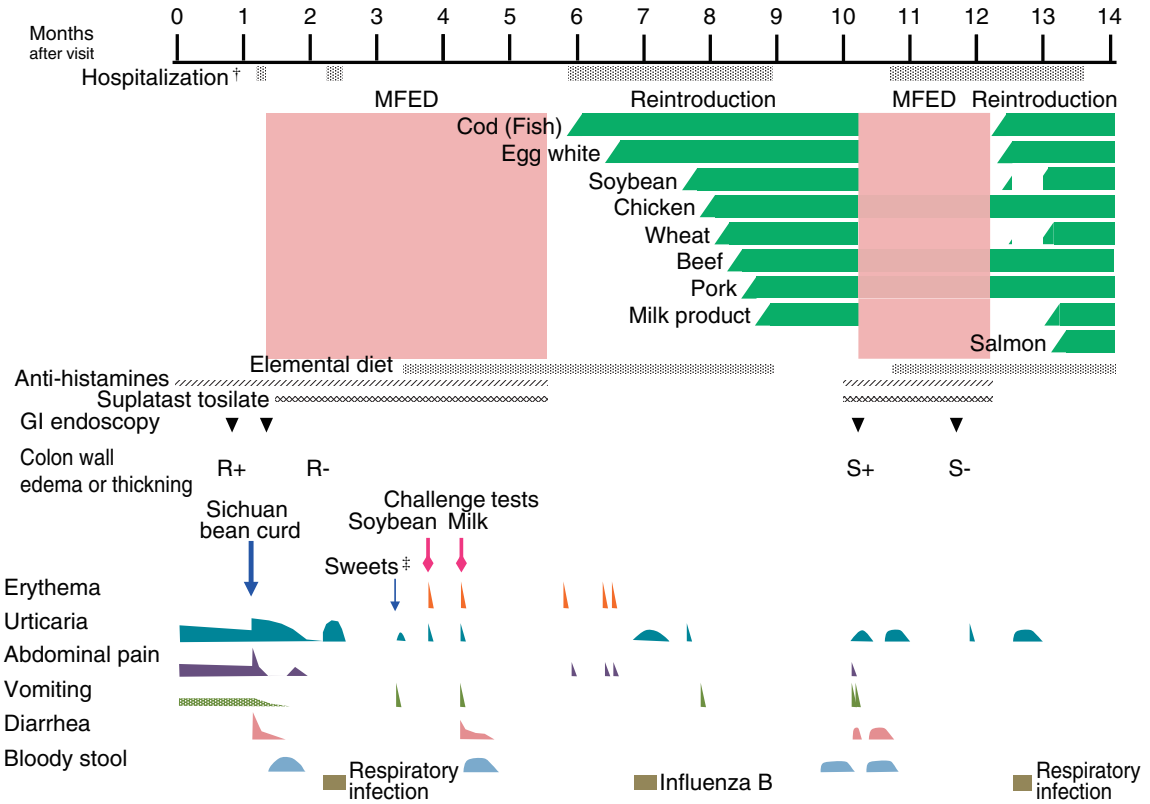

Fig. 2 Clinical course after visit of our institution containing 1st MFED, 1st serial reintroduction, 2nd MFED, and 2nd serial reintroduction. MFED, multiple foods elimination diet; GI, gastrointestinal; R, rectal wall thickning; S, sigmoidal colon edema. †Hospitalization due to treatments; ‡containing chocolate and wheat.

the true causative foods responsible for disease development. Therefore, ongoing efforts to identify the true causative foods and shorten the food elimination period are necessary. Herein, challenge tests for soybean and milk were performed in the first few months after initiating the MFED for earlier reintroduction. Challenge tests in preparation for reintroduction and accidental ingestion indicated that the patient was thought to be allergic at least to cow milk, soybean, and wheat in the early remission phase. In addition, cow milk was the most susceptible antigen for the patient as was indicated by the long-term follow-up. Nonetheless, elimination of his historically allergy-causative foods such as meats in addition to 6-FED could be effective, although the symptoms induced by these foods were not repeated, since they apparently induced symptoms in the early phase. Interestingly, long-term MFED induced successful reintroduction of the foods, suggesting that complete remission may take longer time. Moreover, when mildly relapsed, MFED with short-term reintroduction may be possible.

In conclusion, compared to ED, MFED can be easily applied and it demonstrates similar efficacy in identifying causative foods. Further, apparent side effects were not detected in the follow-up period. MFED is thought to be a promising alternative approach for EGE.

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