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Case Report

Food Allergy Masquerading as Severe Sepsis: A Case Report

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Abstract:

Background: Among food allergies, non-IgE-mediated reactions with a more indolent and chronic course lack sufficient standardized specific lab tests to be timely identified. This is a case report of a girl with late-onset non-IgE-mediated food allergy with a fulminant course.

Case Presentation: A 16-month-old girl presented with severe gastrointestinal symptoms unresponsive to elemental formulas. At admission, poor growth and severe pitting edema were noticeable. Her clinical signs and symptoms and lab tests were improved soon after the initiation of the new elimination diet. Nine months after being discharged from the hospital, she showed noticeable catch-up growth and all allergic symptoms such as atopic dermatitis, gastroesophageal reflux, and irritability were disappeared.

Conclusion: To conclude, when a patient with chronic gastrointestinal manifestations without a specific diagnosis does not respond to conventional treatments, it is worth to consider the diagnosis of non-IgE-mediated food allergies, particularly if a history of prior atopic dermatitis exists.

Key words: food allergy; non-IgE-mediated; elimination diet

Introduction

Food allergy has become a public health problem in recent years because of its increasing global prevalence [1, 2]. The pathogenicity of food allergy resides in the immunologic pathways causing aberrant immune responses towards harmless food antigens, which are normally tolerated by healthy individuals. Food allergies are classified according to their major pathway of reaction into three main groups of IgE- and non-IgE-mediated as well as mixed [3, 4] among which IgE-mediated pathways are the most common hypersensitivity reactions characterized by the immediate manifestation of symptoms which are detected by the current laboratory tests. However, non-IgE-mediated reactions, which are not studied as frequently, have a more indolent, chronic course with late onset symptoms, and there are also insufficient standardized specific lab tests to be timely identified. Therefore, non-IgE-mediated food allergies may become a matter of diagnostic challenge with a tendency to more severe, chronic, disabling and even life-threatening course compared to IgE mediated reactions. Furthermore, because of its chronic nature, it may turn into a serious, disabling health problem in the future. While IgE-mediated reactions commonly have dermal manifestations (urticaria, itching) or appear as anaphylaxis, non-IgE-mediated reactions impact three main organs including gastrointestinal (GI) tract (e.g. evere gastroesophageal reflux, vigorous vomiting, constipation, enterocolitis, and enteropathy), skin (e.g. atopic dermatitis) and respiratory tract (e.g. asthma) [5, 6]. The most widely used approaches for diagnosis of food allergies include precise clinical history, skin prick test, specific serum IgE determination and oral food challenge as an essential test for the diagnosis [3, 4]. However, non-IgE-mediated food allergies are mainly diagnosed by physicians' high index of suspicious and awareness of such a disease and its pertinent symptoms. In order to confirm the diagnosis and manage the disease, six food-avoidance diets or elemental-based formulas are sometimes prescribed according to the extreme situations of particular patients. The current study is a case report of a 16-month-old girl with severe gastrointestinal symptoms, including hematemesis, and hematochezia as a late-onset non-IgE-mediated food allergy condition with a fulminant course, even unresponsive to elemental formulas, to make physicians aware of the fulminant course of food allergies when misdiagnosed.

Case presentation

A 16-month-old girl was admitted with hematemesis and hematochezia after receiving amino-acid based formula. She was the first child of the

family born from consanguineous parents. At admission, poor growth (body weight = 7 kg, height = 67 cm) and severe pitting edema were noticeable. Both parents had a history of urticaria. She was exclusively breast-fed up to the age of 6 months, and then custard, porridge, carrot and potato soups were gradually added to her diet. There was a history of diarrhea, vomiting and fever at 9 months with a fever lasting for 10 days leading to her first hospitalization with the diagnosis of viral gastroenteritis. After 2 days of persistent diarrhea and vomiting, she was transferred to PICU due to severe dehydration. Meanwhile, she developed electrolyte disturbance (hyponatremia =119 meq/L and hypokalemia=2.2meq/L) and coagulopathy (PT and PTT > 120 sec & Platelet = 137000/µl) in PICU. CBC was indicative of anemia (WBC=8700/ µl, Hb=9.6g/dl, Lym=54.7%, Neut=32.8%, others =12.5%). Therefore, she received fresh frozen plasma (FFP) as well as packed cell. Anti-diphtheria antibody, anti-tetanus antibody, and also peripheral blood CD flowcytometry were within normal limits, but her immunoglubolin profile revealed hypogammaglobulinemia (IgG=89mg/dl, IgA=21 mg/dl, IgM=1 mg/dl, IgE=16 IU). In addition, stool calprotectin was as high as 2433mg/kg. Abdominal distension with a suspected intussusception was her next complication after a month of hospitalization. Therefore, a surgical procedure with laparascopic examination was performed for her but the diagnosis was not confirmed. After 10 days, she developed generalized maculopapular rash with urticarial lesions through her body. Five days later, her condition was suddenly deteriorated, so she was transferred to Mofid Children's Hospital with an altered level of consciousness, respiratory distress, hypoxia, generalized edema and maculopapular eruptions. Again, she was admitted to PICU, intubated, and mechanically ventilated. Broad spectrum antibiotics, in addition to IVIG, platelets, packed RBCs, FFP and albumin were administered to her. Although she was sedated, an amino-acid-based formula (Neocate, Nutricia) was initiated via a nasogastric tube, which soon worsened the patient's conditions, the result of which was gastrointestinal bleeding (hematemesis and hematochezia). In light of the patient's symptoms and signs including chronic gastroesophageal reflux, poor weight gain, persistent, severe diarrhea and vomiting, and atopic dermatitis, food allergy was strongly suggested. The amino-acid formula was therefore discontinued immediately, and thin vegetable soup, containing rice and pumpkin, was prepared for her, which was well tolerated. Her clinical signs and symptoms and the lab tests results were improved soon after the initiation of the new elimination diet and her immunoglobulins levels increased to normal range (IgG=611mg/dl, IgA=35 mg/dl, IgM=75 mg/dl). The patient was discharged and recommended to avoid all kinds of formulas and major food allergens including milk and dairy products, egg, beef, lamb, chicken, wheat, soy, barley, tree nuts and peanuts, and sea foods. The patient was fed with the above-mentioned vegetable soups and a new kind of vegetable was added to her soup each week. Four months later, her body weight increased to 9 kilograms. Nine months after being discharged from the hospital, the patient showed noticeable catch-up growth, weighing 11.5 kg at the age of about 2 years old (50th percentile for body weight). Surprisingly, all the previous allergic symptoms such as atopic dermatitis, gastroesophageal reflux, and irritability were completely disappeared.

Figure 1: The patient: A) at the time of admission B) At present.

Discussion

In this case, a patient with history of atopic dermatitis, gastroesophageal reflux, FTT and recurrent hospitalization due to severe diarrhea and vomiting leading to dehydration was reported. The patient had a constellation of symptoms suggestive of food allergy such as significant eczematous skin lesions, allergic hives, and recurrent episodes of gastroenteritis accompanying gastroesophageal reflux and failure to thrive. Other serious manifestations were fever and coagulopathies, which were related to the release of several inflammatory cytokines due to the chronic severe inflammation originating from prolonged food allergy turning it into a potentially life-threatening disorder. Furthermore, not only was the patient unresponsiveness to amino acid-based formula, but her condition also deteriorated. Although it is an uncommon occurrence, it was predictable for us as we had already experienced the same scenario in our previous reported case study. Therefore, we first initiated an

exclusive elimination diet including rice and vegetables, such as pumpkin, gradually followed by quince and boiled grape juice. The patient's condition dramatically improved as a result of such a diet without prescribing any medications. This delayed presentation of the features could be attributed to two types of non-IgE mediated food allergies with dominant gastrointestinal presentations.

1.Eosinophilic gastroenteritis disorders (7)

Since eosinophilic gastroenteritis is a frequent comorbidity of atopic dermatitis and encompasses the entire presentations of the infant, it was considered the first diagnosis to start elimination diet. Subsequent disappearance of the symptoms following the commencement of the diet was certainly due to the correct diagnosis. The diagnostic work-up was limited by the severity of the symptoms leading to PICU admission of the infant, so we could not perform invasive diagnostic procedures, or defer the elimination diet in order to confirm the diagnosis. However, the resolution of the symptoms, which soon occurred after the beginning of the elimination diet was indicative of the appropriate diagnosis and management. Respiratory failure and the need for mechanical ventilation was attributed to the GERD and its complications as well as RDS (Respiratory distress syndrome) due to the release of cytokines in the course of chronic food allergy. On the whole, we described the child's presentations as "atopic march" with atopic dermatitis preceding food allergy and food allergy prior to airway disease, the subsequent result of which was deterioration of the child's condition.

2. Food protein induced entrocolitis (FPIES)

Another suggested diagnosis was food protein-induced enterocolitis syndrome (FPIES). FPIES is a non-IgE-mediated food allergy, which has similar symptoms to eosinophilic gastroenteritis requiring an endoscopic examination in order to rule out other possible diagnoses [8]. However, because of the lack of specific laboratory tests to confirm the diagnosis, most cases of non-IgE-mediated food allergies are being increasingly recognized based on the existence of the compatible clinical symptoms and the disappearance of the symptoms once the elimination diet is introduced [9]. Since there was no clear distinction between the two major diagnoses mentioned above, the elimination diet appeared as the best treatment strategy, which is a common approach in both of these maladies, although in both conditions systemic corticosteroids could also be administered. Since endoscopy, colonoscopy, skin prick rest, patch test, and OFCs were not practical for this patient at the time of hospitalization because of her poor condition, a six-food elimination diet was initiated as an empirical treatment and the above-mentioned vegetables were added to the child's regimen, after being discharged, one by one every two weeks, if tolerated. Acute episodes were treated by intravenous fluid resuscitation and anti-emetics. Because of the dangerous nature of oral food challenges (OFCs), they were not repeated to assess their tolerance development or to identify potential triggers [6].

Conclusion:

To conclude, this patient was a case of non-IgE-mediated food allergy with GI presentations, leading to growth impairment and several life threatening complications. The most important finding in this patient was the variable presentation of multiple food allergies and development of allergic reaction even after consumption of amino-acid-based formulas. Timely diagnosis and nutritional intervention was an effective treatment modality in this patient leading to growth recovery. Therefore, primary care physicians should have a high index of suspicion and need to be aware of these conditions. Administering antibiotics to patients with recurrent or persistent episodes of gastroenteritis may be harmful by disrupting gut microbiome. It is proven that gut microbiome has a central role in balancing the activities of Th1 and Th2 cells and consequently facilitating the development of allergic diseases. When a patient with chronic gastrointestinal signs and symptoms without a confirmed diagnosis after specific investigations does not respond to conventional treatments, it is worth to consider the diagnosis of non-IgE-mediated food allergies as a highly probable diagnosis, particularly in those with a history of prior atopic dermatitis. In this case, the critical condition of the patient did not allow us to perform endoscopic investigations for documented pathological evaluations, but our previous experiences [1, 10] were sufficient to initiate a limited hypoallergenic diet with careful monitoring of the patient's clinical situation in short-term. The bottom line is that unresponsiveness to amino acid-based formulas does not exclude food allergy, as in this patient with a normal growth and development pattern after the optimal treatment. Finally, it should be emphasized that food allergies may sometimes appear with unusual manifestations such as high fever in the forms of acute infections, intestinal obstruction, hypogammaglobulinemia (probably due to protein losing enteropathy mimicking primary humoral immunodeficiency), as well as the activation of coagulation cascade (as a result of immense cytokine release secondary to allergic and eosinophilic inflammation).

Declarations:

Ethics approval and consent: This case study has been approved by the ethics committee of Mofid Children's Hospital.

Consent for publication: Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data: All data and the patient's caregivers' consent are available by Dr. Mahboubeh Mansouri, the corresponding author.

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Authors' contribution:

- Analysis or interpretation of data: all authors
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