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Case Report

Neonatal Food Protein Induced Enterocolitis Syndrome to Cow's Milk with Delayed Diagnosis in Two Pediatric Patients

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Abstract

We present a case of 3-year-old pediatric Lebanese patient who initially presented to the clinic because of severe and persistent cow's milk allergy since age of 3 days, and a 6-month-old Belgian pediatric patient with the same symptoms since the age of 3 months. Symptoms were consistent of only gastro-intestinal manifestations in the Lebanese patient, but the symptoms were more severe in the Belgian patient with hypoglycemia, eczema, and failure to thrive. Investigations showed IgE sensitization for milk and egg in the Belgian child and only to milk in the Lebanese child and both patients were diagnosed initially with Cow's milk protein allergy until the diagnosis of food protein induced enterocolitis syndrome was made.

Keywords: Food Protein Induced Enterocolitis Syndrome; Cow's Milk Allergy; Immunoglobulin E; Recurrent Vomiting

Introduction

The term Food Protein Induced Enterocolitis Syndrome (FPIES) refers to an immunologic delayed non IgE food allergy with mainly gastro-intestinal manifestations [1]. It can be found in two forms, acute or chronic. Despite the serious potential for reactions, the education of FPIES is weak. High-quality studies providing insight into pathophysiology, diagnosis, and management are lacking, and clinical outcomes are poorly established.

Case Report

In this study, we present 2 cases of a 3 year and 2 months old Lebanese child and a 6-month-old Belgian pediatric patient initially diagnosed with cow's milk protein allergy before being diagnosed with FPIES by the allergist.

Both patients are full-term infants born to non-consanguineous parents. The Lebanese child was born by normal vaginal delivery to a smoker mother and the Belgian child was born by C-section with twin pregnancy. Both had good neonatal adaptation without the need for neonatal intensive care unit admission.

For the Lebanese patient, he was breastfed for only 3 days and the same day of introduction of the formula, he was hospitalized for recurrent vomiting and diarrhea. He was suspected to have cow's milk allergy and was started on extensive hydrolyzed formula till 6 months of age. At the moment, he was started again on regular formula with reappearance of episodes of vomiting, recurrent diarrhea and fever. Upon that presentation, patient was put again on extensive hydrolyzed formula. Note that, at this time, allergic blood test was done and showed class 2 alpha and beta lactoglobulin and class 1 casein. Patient was symptoms free, until solid food introduction which was delayed due to parenteral anxiety and with each food containing small amount of dairy products the same symptoms (fever, vomiting and diarrhea) reappear. Patient was

diagnosed with severe cow's milk protein allergy until 3 years and 2 months, where skin prick test was done in the clinic, and was negative for different types of fresh milk/formula with positive control of 5 mm. Moreover, he was found also to have poor weight gain (-1.5 Standard deviation for age).

Based on the skin prick test result, and on the symptoms, patient was diagnosed with FPIES with delayed cow's milk tolerance. Dietician consultation was advised with exclusion of dairy products till 5 years of age.

For the Belgian patient, he was breastfed till 3 months of age and after that he was started on regular age-appropriate formula. He presented with repetitive non bloody diarrhea for which he was hospitalized and treated as simple gastro-enteritis. Few days later, he presented to the emergency room (ER) for the same repetitive diarrhea but associated to hypoglycemia and 10% loss of weight. After initial bolus and glycaemia control in the ER, he redeveloped another hypoglycemia few minutes post feeding. During this hospitalization, a full endocrinology and metabolic work up was done and turned out normal. Allergic test was done and showed total IgE of 15 kU/L with IgE cow's milk of 0.66 kU/L and IgE betalactoglobulin of 0.42 kU/L. The patient was started on hypoallergenic formula and discharged home.

Few days later, a third hospitalization was done due to dehydration and malaise, reversible with hydration only. He was found to have Norovirus infection and suspicion of cow's milk protein allergy. So he was started on extensive hydrolyzed formula and due to good tolerance in hospital setting he was discharged home. Again, few days later a fourth hospitalization was done due to the same symptoms and allergist consultation was done. Skin prick test was done and was negative for milk. Patient was diagnosed with severe FPIES, non-responsive to extensive hydrolyzed formula and was started on amino acid-based formula.

Follow up after 4 months showed absence of symptoms with amelioration of weight curve from less than 3 standard deviation to 3 standard deviation. In addition, control of his allergic test showed total IgE of 23 kU/L associated to egg sensitization with IgE egg white of 0.2 kU/L and milk sensitization of 0.23 kU/L. He was advised to continue on amino acid based formula with egg exclusion from diet for possible oral provocation test later.

Discussion

We reported in this article two cases of food protein induced enterocolitis syndrome with delayed diagnosis.

FPIES non-IgE cell-mediated allergy, is one of the poorly described and often undiagnosed allergies worldwide. It was described for the first time around the years 1973-1977 [2].

The prevalence of FPIES differs from one country to another due to different diets [3-5]. The best-known foods are cow's milk, soy, rice and wheat as well as eggs, fish and other vegetable grains with FPIES for cow's milk protein and Soy present more often in children under 6 months of age whereas that FPIES for solid foods occur between 6 and 12 months of age [3,6,7] and those for fish and seafood tend to occur in adults. The chronic form often due to cow's milk protein and or soy is frequently found in Asian countries like Japan and Korea compared to America. The prevalence of FPIES differs between 3 out of 1000 newborns in America [8] and 21 out of 10,000 in Japan [9,10]. This syndrome is still sometimes associated with other atopic disorders such as atopic dermatitis and IgE-mediated food allergy [4].

FPIES can be presented as 2 different phenotypes: the acute form, which presents between 1 to 4 hours and typically 2 hours after ingestion of the trigger food, and the chronic form, when the trigger food is ingested repetitively, and the time relation is missed [11].

The usual symptoms upon presentation consist of gastro-intestinal manifestations with mainly profuse, repetitive vomiting that develops within 1 to 4 h following ingestion of the trigger food in addition to diarrhea which might be bloody and or mucoid about 5–10 h after ingestion [11]. Some patients might have even more severe reactions, with some episodes of lethargy, pallor, hypotonia, cyanosis and even methemoglobinemia.

As for the pathophysiology, FPIES mechanism is still unclear despite recent advances. But the reaction is suspected to affect different pathways including:

- Cellular mechanism by activating T cells through increased IL2, IL 17 with Th 17 [12], TNF alpha in addition to increased Neutrophils secondary to stress induced cortisol

stimulation [13]. Also researches showed a potential role of tissue eosinophilic infiltration mediating gastro-intestinal inflammation [14].

- Autonomic nervous system due to the extra-intestinal manifestations related possibly to serotonin activation and secretions by mast and entero-chromaffin cells. This theory is fortified by the role of Ondansetron (selective serotonin receptor antagonist) effective role in the treatment of FPIES [15].

Treatment for FPIES is supportive. Maintaining good hemodynamic stability with volume resuscitation in case of dehydration or shock. Plus, Ondansetron is used even in oral form (in cases of mild vomiting) at home or as intra-muscular or intra-venous form in hospital settings. In addition, Methylprednisolone with a dose of 1mg/kg is used due to the potential role of cell mediated inflammatory reaction even there is no proven efficacy in mitigating reaction severity or hastening recovery [11].

Patients with cow's milk as food trigger for FPIES, breast feeding should always be encouraged and dairy products restriction in the mother diet is usually not necessary unless there are signs of reactions. In case of formula feeding extensive hydrolyzed formula are usually well tolerated but 10 to 20 % of infant may require amino acid-based formulas. In the case of other food trigger or group of trigger food, a dietician consultation is always advised due to high burden of stress and anxiety in parents and their tendency to eliminate multiple food groups.

Finally, psychosocial considerations should be considered due to worse quality of life found in parents of patients with multiple vs single food trigger and with FPIES over IgE mediated food allergy [16].

Conclusion

FPIES is one of the non-IgE-mediated allergies. As illustrated in our clinical cases, the diagnosis is sometimes difficult to evoke and to differentiate it from IgE-mediated allergy essentially with the presence of co-sensitizations towards the same allergens and sometimes other allergens. FPIES can still cause failure to thrive, mainly in infants in its chronic form, as in the case of our Belgian patient. The essential treatment remains the total eviction of the allergen and in the case of FPIES with cow's milk, the use of amino acid-based milks is sometimes necessary as indicated above. Follow-up must always be ensured both for allergies and the possibility of the appearance of co-sensitizations and the evolution towards IgE-mediated allergies and by a nutritionist to ensure an adequate diet and a balanced ratio. Finally, in case of doubt of the diagnosis or in case of decision to reintroduce the allergen in question, an oral provocation test must be established in an intra-hospital environment.

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