

Chronic Food Protein-Induced Enterocolitis Syndrome Caused by Cow's Milk Proteins Passed through Breast Milk

Stefano Miceli Sopo^a Serena Monaco^a Monica Greco^a Guglielmo Scala^b

^aDepartment of Pediatrics, Agostino Gemelli Hospital, Catholic University of the Sacred Heart, Rome, and

^bAllergology Unit, Loreto Crispi Hospital, Naples, Italy

Key Words

Breast milk · Cow's milk allergy · Food protein-induced enterocolitis syndrome

Abstract

We describe 2 cases of food protein-induced enterocolitis syndrome (FPIES) caused by cow's milk (CM) passed through breast milk. The onset in both cases was characterized by chronic symptoms (regurgitation, colic, diarrhea, failure to thrive); in one patient, two acute episodes due to the direct consumption of CM formula by the infant were also reported. The diagnosis of FPIES through breast milk can be easily overlooked, especially in milder cases. We also discuss some important issues concerning the general management of the disease. In conclusion, (1) the diagnosis of chronic FPIES should be taken into account even in exclusively breast-fed infants who present suggestive symptoms such as persistent regurgitation, small amounts of vomiting, lethargy, failure to thrive, dehydration, diarrhea (sometimes bloody) and abdominal distention. A 2-week maternal elimination diet should be considered even in apparently mild cases. (2) CM seems to be the most frequently reported culprit food. (3) In those cases in which acute FPIES is elicited by the direct consumption of the culprit food in breast-fed infants, maternal diet may be unrestricted.

© 2014 S. Karger AG, Basel

Introduction

Food protein-induced enterocolitis syndrome (FPIES) is likely a non-IgE-mediated food allergy that can express itself both in acute and chronic forms. The former is the commonest type and usually presents with acute profuse and repetitive vomiting, lethargy, pallor and episodes of diarrhea that start 2–4 h after ingestion of the culprit food and resolve within a few hours. The chronic form is rarer and is usually observed in young infants who have been fed with cow's milk (CM) or soy-based formula daily from their early days of life. Chronic FPIES is characterized by persistence of symptoms, which are less striking (although they may be severe) than those of the acute form. The most reported symptoms are intermittent emesis, diarrhea (that can sometimes be bloody), lethargy, dehydration, abdominal distension and failure to thrive [1]. FPIES is typically caused by direct ingestion of the culprit food by the child. However, 2 cases of FPIES have been described even in exclusively breast-fed infants in which symptoms occurred after maternal ingestion of CM or soy, likely due to the passage of food proteins through the breast milk [2, 3].

Since FPIES caused by protein passed through maternal milk is very rare, we report and describe 2 cases from our experience, and focus on its peculiarities and characteristics.

Clinical Cases

Clinical Case 1

D.L. is an exclusively breast-fed infant suffering from atopic dermatitis. He has a family history positive for atopy and beginning in the first month of life he presented on a daily basis with 6–7 episodes of colic, diarrhea and mild lethargy. The episodes did not have a precise temporal association with meals and were of moderate severity. After some time, he also began to lose weight. A diagnosis was made of viral gastroenteritis. At the age of 3 months, D.L. additionally showed persistent hypotonia, pallor and bloody diarrhea. D.L.'s mother decided to eliminate both CM and egg from her diet and in a few days the infant's symptoms disappeared. Afterwards, an allergist made the diagnosis of FPIES and confirmed strict avoidance of CM and egg in the maternal diet. Prior to the CM elimination diet, D.L.'s mother used to eat on average 100 g of dairy products (cheese, butter) and to drink 250 ml of milk daily. She did not replace the milk protein consumption with any alternate milk such as soy milk, but took vitamin D and calcium supplementation. In the course of a few weeks, height-weight growth increased, bloody diarrhea totally resolved and the child appeared more active and dynamic. D.L. was referred to our clinic at the age of 5 months. Skin prick tests with raw egg, albumen and yolk egg extracts, raw CM, α -lactalbumin, casein and β -lactoglobulin were negative. As egg-induced chronic FPIES is unusual, we decided to consider CM first as the causative food. We suggested to reintroduce egg in the maternal diet and to submit D.L. to an oral food challenge (OFC) with CM. However, before the OFC was performed, D.L.'s mother accidentally ate some pasta flavored with butter sauce. Later on, she breast-fed D.L. as usual and no additional foods were given to the baby. In the following hours, the child appeared disturbed and about 14 h after the maternal ingestion of butter, he developed lethargy, grayish skin and repetitive diarrheal episodes, the last of which was bloody. No vomiting was reported. D.L. fully recovered 12 h later. At this point we decided not to perform the OFC and we confirmed the definitive diagnosis of chronic FPIES caused by CM passed through breast milk. At the age of 6 months, in partial agreement with Sicherer's recommendations [4], D.L. underwent an OFC with a mixture of legumes including soybean, cereals (including rice) and poultry, and the baby did not have any adverse reaction. At the age of 12 months, D.L. still remained breast-fed and his mother still followed a strict CM-free diet. She ate hen's egg several times without any problem for her child.

Clinical Case 2

C.P. is an exclusively breast-fed infant suffering from mild atopic dermatitis. She has a family history of atopy and beginning in her second month of life, she was observed to present on a daily basis with 8–9 episodes of abundant regurgitations, colic and diarrhea. The episodes did not have a precise temporal association with meals and were of moderate severity. Her growth parameters remained within the normal values. At the age of 4 months, C.P. developed two reproducible episodes of projectile vomiting, hypotonia, pallor, lethargy, profuse sweating and diarrhea 2 h after consumption of 70–80 ml of CM formula. These symptoms lasted about 3 h. Afterwards, C.P. did not have any more CM formula. No further acute episodes occurred, but the baby went on suffering from colic, diarrhea and regurgitation, although her growth was regular. When C.P. was 5 months old, her mother drank about half

a liter of CM (much more than her normal consumption) and she breast-fed her infant as usual. 12 h later, C.P. developed pallor, strong crying and diarrhea (5 episodes, 2 of which were bloody). The clinical picture improved within 6–8 h. A diagnosis of FPIES was made and the mother was prescribed a diet with strict exclusion of milk and dairy products. Prior to the CM elimination diet, C.P.'s mother used to eat on average 50 g of dairy products (cheese, butter) and to drink 200 ml milk daily. She did not replace the milk protein consumption with any alternate milk such as soy milk, but took vitamin D and calcium supplementation. Since the beginning of the CM-free diet, episodes of diarrhea, regurgitations and colic fully resolved. We met C.P. when she was 6 months old. Skin prick tests with raw CM, α -lactalbumin, casein and β -lactoglobulin were all negative. We decided not to perform an OFC with CM because of the suggestive clinical history. In partial agreement with Sicherer's recommendation [4], we performed an OFC with a mixture of legumes (including soybean), cereals (including rice) and poultry, and C.P. passed it without any problem. At the age of 9 months, C.P. was still fed with breast milk, his mother still followed a strict CM-free diet and the baby had not experienced any further FPIES episodes.

Discussion

CM was the culprit food in 3 of the 4 reported cases of FPIES through breast milk [2, 3] (2 of them are those herein described) and the clinical presentation seems to be the same of chronic FPIES, at least at the initial stages. This is probably due to early, daily consumption of CM proteins passed through maternal milk. We hypothesize that the daily and early contact with the culprit food are necessary for the development of chronic FPIES. We firmly believe that the most probable initial presentation of FPIES through breast milk is the chronic form caused by CM proteins (or other food which should be eaten daily by breast-feeding mothers).

Diagnosis of chronic FPIES through breast milk is not easy. The disease is quite rare and symptoms are vague, not striking and not well defined, at least in the milder forms. In our 2 cases, the diagnosis was made only after the clinical conditions clearly worsened (see D.L.'s case) or following two acute episodes (see C.P.'s case). Guidelines [5] suggest that a 2-week food elimination, followed by a supervised OFC, may be necessary for a conclusive diagnosis of chronic FPIES because of the nonspecific nature of its symptoms. Actually, we believe that OFCs might be avoided in some conditions such as a severe relapse due to accidental consumption as we observed in D.L.'s case. It is noteworthy that there are criteria for acute FPIES that have recently been updated [6], i.e. at least two typical episodes and the exclusion of alternative diagnosis, that provide a correct diagnosis even without

OFC. However, OFC is always needed for the diagnosis of chronic FPIES whatever the clinical presentation.

When diagnosis of FPIES through breast milk is made, the culprit food must be excluded from the maternal diet. However, should this advice be followed even by breast-fed patients who had an acute FPIES episode caused by the direct ingestion of culprit food by the child? In these cases, Monti et al. [2] proposed to eliminate the culprit food from the maternal diet if the acute episode of FPIES was severe. On the other hand, Tan et al. [3] wrote: ‘... we would only advocate the removal of the trigger food(s) from the maternal diet if there is a history supportive of breast-milk-triggered reactions.’ Järvinen and Nowak-Węgrzyn [7] are of the same opinion, and we agree with them, too. In fact, we have never suggested removing the causative food from the maternal diet and in our acute FPIES clinical records [8] there are no reports of any adverse reaction caused by this behavior.

If culprit food avoidance from the maternal diet is necessary, is elimination too rigorous? Our case 1 presented an adverse reaction when their mother ate some pasta flavored with butter sauce. However, Monti et al. [2] reported that for their patient, ‘bakery products containing more extensively heated milk in the mother’s diet had

been tolerated’. And Tan et al. [3] wrote that ‘our case did not have clinical features consistent with chronic FPIES despite the mother continuing to ingest soy in processed foods.’ In fact, it has been reported how the different ways of cooking may influence the reduction of egg’s allergenic properties [9]. However, as opposed to IgE-mediated CM allergy [10], the ingestion of baked milk is not recommended in FPIES [7], as high temperatures cannot destroy sequential allergenic epitopes recognized by T cells. However, we found some children suffering from CM-FPIES, who tolerated baked CM [11]. This observation, jointly with Monti et al. [2] and Tan et al. [3], highlight the importance of better exploring this important nutritional aspect. It might be useful to perform an OFC with baked food in patients with less severe forms of FPIES who may be more likely to tolerate the baked food. Unfortunately, as opposed to research in using basophil allergen testing as a potential marker of severity in IgE-mediated food allergy, there are no in vitro tests currently being studied for predicting severe FPIES reactions [12].

In conclusion, we hope that our 2 cases of FPIES through breast milk will lead pediatricians to think more often of this condition.

References

- 1 Leonard SA, Nowak-Węgrzyn A: Manifestations, diagnosis, and management of food protein-induced enterocolitis syndrome. *Pediatr Ann* 2013;42:135–140.
- 2 Monti G, Castagno E, Liguori SA, et al: Food protein-induced enterocolitis syndrome by cow’s milk proteins passed through breast milk. *J Allergy Clin Immunol* 2011;127:679–680.
- 3 Tan J, Campbell D, Mehr S: Food protein-induced enterocolitis syndrome in an exclusively breast-fed infant – an uncommon entity. *J Allergy Clin Immunol* 2012;129:873.
- 4 Sicherer SH: Food protein-induced enterocolitis syndrome: case presentations and management lessons. *J Allergy Clin Immunol* 2005;115:149–156.
- 5 Boyce JA, Assa’ad A, Burks AW, et al: Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol* 2010;126:S1–S58.
- 6 Miceli Sopo S, Greco M, Monaco S, Tripodi S, Calvani M: Food protein-induced enterocolitis syndrome, from practice to theory. *Expert Rev Clin Immunol* 2013;9:707–715.
- 7 Järvinen KM, Nowak-Węgrzyn A: Food protein-induced enterocolitis syndrome (FPIES): current management strategies and review of the literature. *J Allergy Clin Immunol Pract* 2013;1:317–322.
- 8 Miceli Sopo S, Giorgio V, Dello Iacono I, Novembre E, Mori F, Onesimo R: A multicentre retrospective study of 66 Italian children with food protein-induced enterocolitis syndrome: different management for different phenotypes. *Clin Exp Allergy* 2012;42:1257–1265.
- 9 Nowak-Węgrzyn A, Bloom KA, Sicherer SH, et al: Tolerance to extensively heated milk in children with cow’s milk allergy. *J Allergy Clin Immunol* 2008;122:342–347.
- 10 Liu X, Feng BS, Kong X, Xu H, Li X, Yang PC, Liu Z: Food-cooking processes modulate allergenic properties of hen’s egg white proteins. *Int Arch Allergy Immunol* 2013;160:134–142.
- 11 Miceli Sopo S, Buonsenso D, Monaco S, Crocco S, Longo G, Calvani M: Food protein-induced enterocolitis syndrome (FPIES) and well cooked foods: a working hypothesis. *Allergol Immunopathol (Madr)* 2013;41:346–348.
- 12 Homšak M, Silar M, Berce V, Tomazin M, Skerbinjek-Kavalar M, Celesnik N, Košnik M, Korošec P: The relevance of basophil allergen sensitivity testing to distinguish between severe and mild peanut-allergic children. *Int Arch Allergy Immunol* 2013;162:310–317.