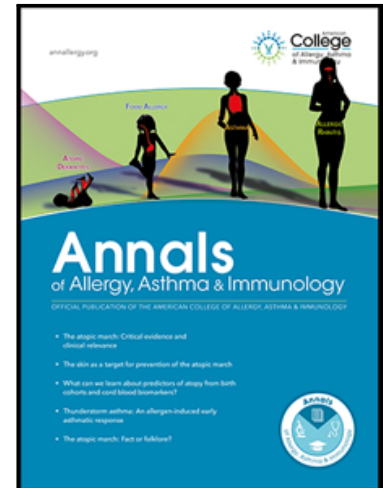


Concomitant Cow's Milk and Beef food protein-induced enterocolitis syndrome in young infant

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Title Page

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FPIES: food protein-induced enterocolitis syndrome

CMb: Cow's Milk-based

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Acute food protein-induced enterocolitis syndrome (FPIES) is a non-IgE cell mediated food hypersensitivity. Common causes include cow's milk (CM), soy, rice, and oat, though any food can be a potential culprit¹.

Acute FPIES is defined as repetitive, profuse emesis within 1-4 hours after ingestion of the culprit food leading to dehydration and occasionally shock ². Diarrhea may follow, usually 5-10 hours after. Symptoms should resolve within 24 hours of removing the food from the diet. Patients are asymptomatic as long as the trigger food has been eliminated. Oral food challenge is often performed to confirm diagnosis, or to determine if a patient has outgrown their sensitivity¹. While there are many case reports and studies on CM FPIES, limited information is available on the prevalence of beef induced FPIES³. We present a patient who has developed FPIES to both cow's milk and beef and explore mechanisms of cross reactivity that may be responsible.

A generally healthy 8-month-old male first presented to our clinic following an episode of severe gastrointestinal symptoms soon after introduction of cow's milk-based (CMb) yogurt. He presented to our clinic and based on the criteria established in the current consensus guidelines⁴ a diagnosis of FPIES was made. The family was advised to avoid feeding the patient dairy but to introduce other allergenic foods.

The patient remained asymptomatic until 10 months when he had his first introduction to beef and pork upon eating hot dog containing both. Of note the hot dog did not contain dairy, nor did the patient eat any other foods at the time. Four hours following ingestion he developed profuse voluminous vomiting. After three episodes, ondansetron was administered and EMS was called. Parents reported pallor and lethargy as well. The child was taken to the ER, by which time he had returned to baseline. The hot dog company was contacted and denied any possible cross contamination with dairy products. Following this episode, the baby was given a diagnosis of suspected beef or pork FPIES, and a food challenge was scheduled.

Per the international consensus guidelines⁴, inpatient challenges to both meats were performed. The challenge to pork was passed with no adverse events. Four hours following beef introduction, the patient had large volume emesis in multiple repeated, forceful episodes. He then had one smaller episode an hour later. Ondansetron was given. The patient was later discharged after ensuring he was tolerating oral fluids. IV hydration was not deemed necessary. No further beef was given to the patient; he had no further episodes. Patient was discharged home and instructed to avoid beef.

We presented a patient with FPIES to both cow's milk and beef, a phenomenon that has only been mentioned once previously as part of a larger report². The concomitant reaction suggests cross reactivity that puts patients with FPIES to one food at higher risk for FPIES to the other. Cross-reactivity between foods is known to play an important role in IgE mediated food allergies, but its role in FPIES remains unclear.

There are emerging data in the existing literature that may suggest a potential link between these two foods, especially as it pertains to IgE mediated allergies. Bovine serum albumin (BSA), a protein found both in CM and in beef, is a potential link. Foremost, BSA is present in both CM and beef in sufficient quantities to produce allergic reactions⁵. Though BSA is considered a minor allergen in CM and a major allergen in beef, one study of CM allergic children found that the highest allergens for study participants were primarily casein (57%) and BSA (51%)⁶. Allergic reaction to BSA has a variety of manifestations; there is evidence via case reports that BSA hypersensitivity predisposes to allergic reactions to various animal products, often showing skin prick test positivity to meats including beef and cow's epithelia as well as IgE positivity for CM and cow dander⁷. Furthermore, one study of CMA identified 13%-20% of the CMA cohort as also allergic to beef whereas 93% of those with beef allergy also reacted to cow's milk on OFC⁸. Another study identified that children tolerant to beef became reactive with less well-cooked beef, implicating heat labile proteins such as BSA as possible allergens³. This evidence suggests BSA as the major link connecting CM and beef FPIES. Future studies should pursue BSA as well as other albumins as potential molecular triggers of FPIES.

CM allergy and beef were first connected when Kanny et al reported a case of a 19 y/o with IgE mediated reaction to BSA, who tested positive for BSA on SPT and whose symptoms resolved with an elimination diet of undercooked dairy and beef.⁹ Animal albumins thus do in fact link certain foods, and hence can influence a patient's immunological, physiologic, and clinical response^{3,8}.

Finally, a study by Martorell et al 2006, showed that children with beef allergy had a high rate of clinical activity to CM. Interestingly, of their participants with beef allergy, only two of them did not show sensitivity to BSA (authors theorized sensitivity to a different beef protein). Those same two patients were also the only two patients with confirmed beef allergy that did not have concomitant reaction to CM challenge¹⁰. This finding in itself further emphasizes the likely overlap of these two conditions, and begs the question that such a link may also exist in non-IgE mediated food allergies such as FPIES.

While much of this pertains to IgE mediated reactions it is plausible to suggest that such a link may exist with FPIES as well. In theory, reaction to BSA in the gut could produce T-cell mediated inflammation in the intestine, leading to intestinal permeability, and, ultimately, the symptoms characteristic of FPIES. This case brings to light that more research is needed to further elucidate the pathophysiology of FPIES and potentially find a link between CM and beef FPIES.

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