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Hypersensitivity to Total Parenteral Nutrition Fat-Emulsion Component in an Egg-Allergic Child

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KEY WORDS

egg allergy, fat emulsion, hypersensitivity, total parenteral nutrition

ABBREVIATIONS

IgE—immunoglobulin E

IFE—intravenous fat emulsion

TPN—total parenteral nutrition

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abstract

Immunoglobulin E (IgE)-mediated food allergies affect 6% to 8% of children in the United States with symptoms ranging from localized hives to life-threatening anaphylaxis. Intravenous fat emulsions (IFEs) are a vital component of total parental nutrition, because they provide essential fatty acids. IFE is a sterile fat emulsion that contains egg-yolk phospholipids. Although egg allergy is listed as a contraindication, adverse reactions are uncommon. We report here the case of a hypersensitivity to IFE in a 2-year-old patient with previously undocumented egg allergy. Our patient was placed on total parental nutrition and a 20% IFE postoperatively and developed diffuse pruritus 14 days after initiation of therapy. She showed transient improvement with intravenous antihistamine, but her symptoms did not resolve until the IFE was stopped. On the basis of clinical history, including aversion to egg, we performed skin-prick testing, the results of which were positive for egg white allergy. Serum testing confirmed allergy to both egg yolk and egg white. To our knowledge, this is the first reported case of a pediatric patient with a history suggestive of egg allergy, positive skin-prick and serum testing to egg, and reaction to IFE infusion. Although ingestion of egg lecithin in cooked food is generally tolerated by egg-allergic people, administration of intravenous egg-containing lipid emulsions may cause significant adverse reactions. *Pediatrics* 2011;128:e000

Immunoglobulin E (IgE)-mediated food allergies affect 6% to 8% of children in the United Kingdom and United States,¹ and egg allergy is one of the most common food allergies in infants and young children. In addition, cow's milk, peanuts, tree nuts, and sesame seeds account for most food-induced allergic reactions in young children. Symptoms of food-induced allergic reactions range from localized hives to life-threatening anaphylaxis, and most reactions occur on the first known oral exposure, especially in the case of eggs.² Organ systems most commonly involved include the skin, gastrointestinal tract, and respiratory tract. Population-based studies have found that the prevalence of allergy to egg whites among children is between 1.6% and 3.2%.³

Five major allergens have been characterized in hen's egg and designated Gal d 1 through Gal d 5.⁴ Egg white contains several allergenic proteins including ovomucoid (Gal d 1), ovalbumin or conalbumin (Gal d 2), ovotransferrin (Gal d 3), lysozyme (Gal d 4), and ovomucin. Ovalbumin is recognized as the most abundant egg white protein (65%–68%),⁵ and ovomucoid is the most immunodominant allergen.⁶ Chicken serum albumin (Gal d 5) is the major allergen in egg yolk. Additional allergens in egg yolk include vitellin (apovitellenin I) and apoprotein B (apovitellenin VI).

Allergy to egg usually presents during the first year of life at a median age of presentation of 10 months, which is the typical age of first exposure. Most commonly, an allergic reaction to egg is cutaneous and occurs within 30 minutes of ingestion.⁷ Egg allergy accounts for <10% of all anaphylactic reactions in children.⁸ Many egg-allergic people are able to tolerate extensively heated or baked egg because of heat-labile epitopes of ovalbumin, which demon-

strate significantly reduced IgE binding after heat denaturation.^{9,10}

Intravenous fat emulsions (IFEs) are a vital component of total parental nutrition (TPN), because they provide essential fatty acids. Intralipid 20% (Fresenius Kabi AB, Uppsala, Sweden) is a sterile, nonpyrogenic fat emulsion intended as a source of calories and essential fatty acids. It is made up of 20% soybean oil, 1.2% egg-yolk phospholipids, 2.25% glycerin, and water for injection. In addition, sodium hydroxide is added to adjust the pH so that the final product pH is 8.¹¹

Although allergy to egg is listed as a contraindication to IFEs, adverse reactions are uncommon despite widespread use. The adverse effects listed in the package insert differentiate between early and delayed reactions. Most of the safety studies on fat emulsions were completed in Europe soon after a clinically acceptable soybean-oil product was developed in 1961. Adverse effects included dyspnea, allergic reactions, nausea, vomiting, headache, flushing, and irritation at the infusion site, all of which have a reported incidence rate of <1%. Most adverse reactions are described as delayed sensitivity and occur with prolonged use of IFEs and overloading syndromes associated with excessive doses of soybean oil up to 7.7 g/kg per day.¹² We report here the case of a hypersensitivity to an IFE in a patient with previously undocumented egg allergy.

CASE REPORT

This case involves a 2-year-old black girl with stage IV neuroblastoma with metastases to the bone marrow. She underwent surgery to debulk her abdominal tumor and remained nil per os after surgery. She was placed on TPN with a multivitamin and Intralipid 20%. Fourteen days after the initiation of therapy, she had diffuse pruritus without urticaria. There were no new

medications that were introduced during this time period. Her vital signs remained normal, and she did not complain of any dyspnea, lightheadedness, headache, or nausea.

She was treated with intravenous antihistamine and showed transient resolution of symptoms. Her pruritus continued despite intermittent antihistamine use. The IFE was stopped because it was suspected to be the etiology of her reaction. At the time of her reaction, she was receiving 3 g/kg per day of lipid. In the days leading up to her reaction, there was no change in the lipid dose or the infusion rate. The TPN and the multivitamin component continued to be infused because it was not thought to be a contributing factor of her symptoms. Within a few hours, she had complete resolution of her symptoms and continued to do well off the IFE.

A food history was obtained at the time of admission and did not reveal any food allergy or intolerances. After further discussion with her mother, it was found that the patient was averse to eating plain egg and would have emesis after ingestion. Her symptoms occurred without urticaria or pruritus. She was able to tolerate baked egg without difficulty. There was no family history of atopic disease, and the patient did not express any additional atopic symptoms. She was hemodynamically stable without symptoms and her examination was unremarkable.

On the basis of history, we performed skin-prick testing for peanut, soy, and egg (Greer, Lenoir, NC). She had positive skin-test results to egg white and histamine, but all others were negative. We were unable to skin test for the IFE because the IFE had been discarded and it is made by a third party not located within the hospital. The IFE continued to be held, and there was no further incident. Serum testing with ImmunoCAP (Phadia, Uppsala, Swe-

den) confirmed allergy to both egg yolk (0.60 kU/L) and egg white (1.23 kU/L). Total IgE was also measured and noted to be 10.7 IU/mL.

There are limited data available detailing TPN and particularly IFE hypersensitivity. The literature becomes even more restricted in regards to IFE hypersensitivity and food allergy, which may be because of the noted contraindication to both egg protein and soy listed on the prescribing information.

There have been a few isolated cases described in the allergy and nutrition literature. Most of the cases involved adults; only a handful of the reports described hypersensitivity to IFEs in the pediatric population. One case report described a 9-year-old boy with IFE sensitivity.¹³ It only documented that the results of all skin testing were negative. Another case report described a pediatric patient with an allergic reaction with wheezing, erythema, wheals, and urticaria after 11 days of soybean-oil emulsion therapy.¹² According to the report, there was no testing completed to identify the specific allergen.

One case report described hypersensitivity to IFEs in a 36-year-old black man with AIDS.¹⁴ In addition, Darryl et al¹⁵ presented the case of a patient with known legume hypersensitivity who reacted to an IFE and had positive in vitro testing to soy. In a case report from the adult literature, an IFE has also been implicated in adult respiratory distress syndrome, as described in a 68-year-old man with bronchogenic carcinoma.¹⁶

DISCUSSION

To our knowledge, this is the first case report of a pediatric patient with a his-

tory suggestive of egg allergy, documented positive skin-prick and serum testing to egg, and documented reaction to IFEs. One case report in the pediatric literature, as described above, documented allergy to soy protein and reaction to IFEs. There have only been a few cases that were suggestive of allergy to IFEs in the adult population without identification of a specific allergen. The limited data may suggest the general tolerance of TPN and, more specifically, IFEs. Alternatively, given the contraindication to IFEs in egg-allergic people, there may be an awareness to avoid IFEs altogether.

Although ingestion of small amounts of egg lecithin in cooked foods is generally tolerated by egg-allergic people, administration of intravenous egg-containing lipid emulsions may cause significant adverse reactions or even anaphylaxis. It was suggested by Hansen et al¹² that some of the reactions related to IFEs could be related to an overload syndrome correlating to excessive IFE doses. This is unlikely in our case, because the patient was receiving therapeutic doses of an IFE and had no other sequelae of IFE intolerance. In addition, postoperative sedation may have delayed symptom presentation. Because her only manifestation was pruritus, it is our thought that the patient was unable to display signs of pruritus until the sedation was weaned. At that time, her IgE-mediated symptoms were exposed. Because the IFE formulation contains both egg-yolk phospholipids and soybean oil, its use is contraindicated in patients with hypersensitivities to these components.

Currently, there are no available egg-free IFE products for use in egg-allergic patients who require an IFE. The same is true for soy-allergic pa-

tients, because there is no soy-free IFE product that has been approved by the US Food and Drug Administration. There is 1 case report that documented the use of a fish-oil-based lipid emulsion in the treatment of a soy-allergic patient with essential fatty acid deficiency who was receiving parenteral nutrition.¹⁷ It was further discussed that the fish-oil-based product is used mostly as a supplement for patients receiving parenteral nutrition whose underlying disease may benefit from an increased intake of ω -3 fatty acid formulations and not as a sole source of fat calories. However, the authors noted in the aforementioned case report that the fish-oil-based lipid emulsion was used as the sole source of lipid, and the outcomes were positive. This therapy would not have been an option for our patient, because the product contained egg-yolk phospholipid and, therefore, would have been contraindicated. This presents a difficult situation for a patient who requires parenteral nutrition, and the clinician is left with limited options. The infusion can be discontinued, as we did for our patient, which represents the safest and most conservative approach. Ultimately, resuming enteral feeds as soon as possible would be the goal to prevent essential fatty acid deficiency.

CONCLUSIONS

This case is presented to make physicians aware of egg-yolk protein within the IFE component of TPN and the potential for allergic reactions. We reiterate the need for a complete patient assessment that includes a detailed food-allergy history before the use of parenteral products.

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