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Severe Malnutrition Resulting from Use of Rice Milk in Food Elimination Diets for Atopic Dermatitis

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ABSTRACT: **Background:** Alternatives to cow's milk and soy milk are often necessary for children with food allergies. Although hydrolyzed and elemental formulas are appropriate replacements, other milk products such as rice and almond milk are insufficient protein sources for children under 2 years of age. A chart review on three patients treated for protein malnutrition in association with multiple diagnosed food allergies that resulted in refractory eczema revealed adverse outcomes that resulted from elimination diets. The use of rice milk resulted in hypoalbuminemia and poor weight gain in all cases, and multiple secondary infections in one patient. These cases illustrate the need for careful nutritional guidance in the management of food allergy, as well as the importance of cautious use and interpretation of testing for food allergies in the absence of a clear clinical history of reaction.

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KEY WORDS: eczema, atopy, food allergy, malnutrition, hypoalbuminemia

Eczema is a chronically relapsing inflammatory skin disease and one of the most common skin disorders of childhood, affecting up to 17% of children [1]. It is commonly associated with respiratory and/or food allergy [2,3], and previous studies have suggested that in roughly one-third of children with eczema the condition resolved with food avoidance [4,5]. However, eczema can rarely be managed with dietary changes alone, and hypoallergenic diets carry a significant risk for nutritional deficits in young children. Thus, the evaluation for food allergy should be limited to children with moderate to severe eczema not controlled by topical steroids [6-8] and should be performed by allergists with experience in food allergy and diet management in children. Both skin testing and specific immunoglobulin E testing for food allergies are complicated by low positive predictive values in the general population, making these tests imperfect for diagnosis of food allergy in the absence of a clear reaction history [9]. Moreover, in children under 2 years of age, cow's milk and soy are both common allergens [10] and also one of the primary sources of protein and calories. Though hydrolyzed and elemental formulas meet recommended protein and nutrient requirements, they are both costly and not very palatable, which often causes parents to opt for other alternatives such as rice, coconut or almond milk. Though they may be vitamin fortified and comparable in calories, these are not suitable substitutes for cow's or soy milk due to their lower protein and fat content, and long-term use may result in significant protein malnutrition and poor weight gain in infants and toddlers.

The following cases describe three incidences of severe hypoalbuminemia resulting from the use of rice milk for eczema, which was thought to be secondary to food allergy.

PATIENT DESCRIPTIONS

A chart review was performed at the host institution. Results of allergy skin-prick testing were obtained from outside facilities, and follow-up tests were performed at the Allergy Clinic of the Children's Hospital of Philadelphia. Specific IgE testing was obtained from commercial laboratories.

PATIENT 1

A 19 month old girl was hospitalized due to severe hypoalbuminemia and concern for refeeding syndrome. Eczema appeared at age 3 months and was treated with emollients and topical steroids with only slight improvement. She was diagnosed with eczema herpeticum at age 8 months and was treated with acyclovir. At 1 year of age, she underwent allergy skin-prick testing to a variety of foods due to her refractory eczema. She was positive to milk, soy, egg, peanut, tree nut, lentil, oat, pork, tomato, wheat, melon, and negative to beef and chicken.

The child had been breastfed for 6 months and then transitioned to soy formula. She was fed lentils, rice, beans, and carrots prior to allergy testing. She had rarely eaten dairy products and never exhibited any reactions. She had never ingested egg, peanut, tree nut, oat, or pork. Following skin testing, a brief trial of a hydrolyzed formula failed due to refusal to drink the formula, and the child was given only rice milk, rice, potato, and carrot. Chicken was also offered but refused. She had no symptoms of gastroesophageal reflux or diarrhea.

IgE = immunoglobulin E

Despite diet restriction, the eczema persisted with frequent flares and was treated with antibiotics, topical steroids, and brief courses of oral steroids. Her weight remained at the 25th percentile for age, but her height fell to below the 3rd percentile. At 18 months, edema of the face and extremities developed, and her albumin level was 1.6 g/dl and total protein 3.3 g/dl, with no proteinuria. She was hospitalized at 19 months due to kwashiorkor.

She required central access due to severe edema and electrolyte abnormalities, and developed line infections with both *Pseudomonas aeruginosa* and *Candida glabrata*. Her hospitalization was further complicated by infections with influenza A (H1N1) and *Clostridium difficile*, as well as respiratory failure and acute renal failure. Further investigation revealed mild hypogammaglobulinemia (332 mg/dl) in the setting of overall hypoproteinemia, and she was given intravenous immunoglobulin due to her multiple infections. Lymphocyte flow cytometry was normal, and genetic sequencing of STAT3 revealed no mutations.

She was discharged home on an elemental formula. She unfortunately suffered a left tibial fracture secondary to osteopenia 3 weeks after discharge. Repeat skin testing was positive to egg, peanut, wheat, lentil, and pea, and negative to milk, soy, oat, and tomato. Milk and soy were reintroduced without reaction. Her eczema flares have been managed with topical steroids. Her weight and height have continued to track at the 25th and 3rd percentiles for age respectively, and she has not had further infections of note.

PATIENT 2

This patient was born at term and developed eczema in infancy. He was breastfed for 6 weeks but developed moderate gastroesophageal reflux and refused to feed. He was transitioned to a hydrolyzed formula and showed improvement. At age 12 months, cow's milk was introduced, but the child developed vomiting and diarrhea after exposure. Soy milk and goat's milk were offered, both of which worsened his eczema. Finally, he was placed on rice milk, as well as chickpeas, lentils, and olives to further supplement protein. In spite of this, the child developed failure to thrive, and at 16 months of age experienced gradual onset of facial and lower extremity edema.

At 17 months old his albumin was 1.2 g/dl and he was hospitalized. Urine studies revealed no proteinuria. He was also found to be anemic with hemoglobin 7 g/dl, and he received a transfusion. The child was given elemental formula, which he tolerated well, and the edema gradually resolved. Specific IgE testing during his hospitalization was positive to egg and cow's milk and negative to soy.

On follow-up, the skin-prick test was negative to milk, soy, peanut, wheat, and a variety of fruits and meats. He has continued on elemental formula pending future food challenges to cow's milk and soy to rule out food protein-induced enterocolitis syndrome. His eczema was managed with topical steroids.

PATIENT 3

The patient was born at term and developed eczema at 2 months of age while being fed a cow's milk-based formula. She underwent skin testing at age 6 months due to ongoing rash and was positive to egg, cow's milk, and wheat. She was transitioned to a soy formula but her eczema did not subside. She was subsequently transitioned to rice milk by 7 months of age. She was also fed oatmeal and a variety of fruits. Meats were offered to supplement her protein-poor diet, but were refused. She had no gastroesophageal reflux symptoms or diarrhea.

Within 5 months the child's weight had dropped from the 50th percentile to the 7th percentile. Skin testing at age 12 months was positive to egg and dog, but negative to milk, soy, peanut, tree nut, and wheat. Laboratory evaluation demonstrated albumin of 2.9 g/dl, and an elemental formula was started. Specific IgE to cow's milk was negative, and it was slowly reintroduced without difficulty. Her eczema was managed via topical steroids and avoidance of the family dog. Within several months her weight had rebounded to the 25th percentile for age. She remains on an egg-free diet, as accidental exposure to egg has caused hives.

DISCUSSION

Though eczema and food allergies commonly coexist, previous studies suggest that only a small fraction of eczema cases are triggered by food allergies [4,5]. In these instances, the interpretation of food allergy testing via skin-prick testing and/or specific IgE must be interpreted with caution as positive results do not necessarily correlate with clinical symptoms [9]. Furthermore, positive predictive values vary dramatically by food. A study of skin and blood testing compared to double-blind placebo-controlled food challenges found that the positive predictive values of skin testing to milk and soy were 66% and 33% respectively [11].

As demonstrated by these cases, elimination diets in the absence of nutritional counseling can lead to severe malnutrition and associated complications [Table 1]. Similar cases of severe hypoalbuminemia resulting from rice milk have been described [12]. In all three of these cases the malnutrition resolved on elemental formula, and their eczema was managed via topical treatments.

In cases of eczema worsened by food allergies, careful dietary management is essential for preventing malnutrition. Cross-reactivity between mammalian milks (cow, sheep, goat) has been shown to be high [13]. Though allergy to soy in patients with IgE-mediated allergy to cow's milk is relatively low [14], confirmatory testing is recommended in these cases. Alternatives to cow's milk [Table 2] such as rice or almond milk, in spite of fortification, are

Table 1. Patient characteristics and complications of elimination diets

Patient	Age at onset of hypoproteinemia (mos)	Length of elimination diet (mos)	Albumin at presentation (g/dl)	Absolute eosinophil count	Infectious complications	Other complications
1	19	6	1.6		Bactermia: *Pseudomonas aeruginosa*	Acute renal failure
					H1N1;	osteopenia
				265–1065	Fungemia: *Candida glabrata*	Left tibial fracture
2	16	4	1.2	422–539	None	Anemia
3	12	5	2.9	104–182	None	Failure to thrive

Table 2. Nutritional values for milk/milk substitutes

	Calories	Protein (g)	Fat (g)	Calcium	Vitamin D (IU)
Cow's milk	150	8	8	300	120
Soy milk	100–130	6	3-4	300–350	100–133
Rice milk	120–130	1	2.5	300	0–100
Coconut milk	80	1	5	100–450	100–133
Hemp milk	100	4	6	300	100
Oat milk	120–130	4	2.5	100	0-100
Potato milk	70–110	0	0	300	60
Almond milk	60–90	1	2.5	200–450	100
Elemental formula (infant)	160	4.5–5	7.2–8.6	154–199	82–98
Elemental formula (pediatric)	240	6–8.4	8.4–12	149–288	74–146
	Numbers above refer to a serving size of 240 ml (8 oz)				

not a sufficient protein source. In the case of significant dietary restrictions, guidance from a nutritionist is essential. The recommended protein intake for children aged 0–6 months is 1.5 g/kg, 1.2 g/kg for children aged 7–12 months, and 1.1 g/kg/day for children aged 1–3 years. Hydrolyzed or elemental formulas provide a safe alternative for children allergic to cow's milk or soy.

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Capsule

A novel immunodeficiency disorder characterized by genetic amplification of interleukin-25

Many primary immunodeficiency disorders of differing etiologies have been well characterized, and much understanding of immunological processes has been gained by investigating the mechanisms of disease. Green et al. have used a whole-genome approach, employing single-nucleotide polymorphism and gene expression microarrays, to provide insight into the molecular etiology of a novel immunodeficiency disorder. Using DNA copy number profiling, the researchers defined a hyperploid region on 14q11.2 in the immunodeficiency case associated with the interleukin (IL)-25 locus. This alteration was associated with significantly heightened expression of IL-25 following T cell activation. An associated dominant type 2 helper T cell bias in the immunodeficiency case provides a mechanistic explanation for recurrence of infections by pathogens met by Th1-driven responses. Furthermore, this highlights the capacity of IL-25 to alter normal human immune responses.

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