

Challenge of food allergy testing and avoidance in children with atopic dermatitis

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SUMMARY

Atopic dermatitis (AD) is a common presenting complaint by children and their caretakers to their primary care providers. On testing, children with AD frequently exhibit positive food-specific IgE levels in the absence of immediate allergic reactions. Misinterpretation of these false positive tests can lead to unnecessary food avoidance, which can have tremendous psychosocial, economic and nutritional consequences and, in some cases, facilitate the development of an immediate hypersensitivity to the food. We present a child with persistent AD who underwent broad testing that led to unnecessary food avoidance resulting in Vitamin D deficiency, growth failure and the development of an IgE-mediated food allergy. This case underscores the need for caution by primary care clinicians in using food avoidance diets as a treatment for AD and the importance of limiting allergy testing to foods only when the clinical history indicates an immediate hypersensitivity reaction.

BACKGROUND

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory and pruritic dermatitis found in 15%–20% of the paediatric population.¹ Up to 30%–40% of children with AD have IgE-mediated food allergy (FA) and almost double that are sensitised to foods, which is thought to be driven by increased penetration of food antigens through a damaged skin barrier.^{2–5} The low specificity of both skin prick testing (SPT) and food-specific IgE testing in predicting FA among patients with moderate-to-severe AD can create a diagnostic dilemma, and many of these children are prescribed food elimination diets by their primary care clinician with the goal of eradicating their AD.^{5–8} However, while foods have been identified as triggers for AD in some children, these reactions are generally non-IgE mediated and thus IgE testing is not useful to identify the culprit food(s).⁹

Herein, we describe a case of a child with severe AD who exhibited multifood sensitisation that led to extreme dietary restrictions resulting in growth failure. This case illuminates the importance of optimal skin care, nutritional interventions, caregiver education, and, if indicated, confirmatory testing for FA, while treating patients with moderate-to-severe AD.

CASE PRESENTATION

A 3-year-old African-American boy was enrolled in a natural history of FA study for the evaluation

and treatment of his severe persistent AD and multiple food sensitisations. As a previously healthy breastfed infant, at 4 weeks of age he developed an eczematous rash that was treated with emollients and intermittent low dose topical corticosteroids (TCS) (1% hydrocortisone). At 8 months, he experienced worsening flares with intense pruritus, sleep disruption and frequent daytime behavioural outbursts. His paediatric provider subsequently prescribed higher potency TCS (0.1% triamcinolone); however, his family endorsed trepidation over side effects so use was limited. At his first visit to an allergist, his parents could not identify any specific triggers that worsened his AD. History revealed that fruits, vegetables, egg, wheat, milk, soy and peanut were all introduced without incident and he had continued exposure to these foods during his first year of life. SPT revealed positive reactions to peanut and dust mite and no reactions to egg, milk, wheat, soy, orange, tomato, corn, beef, potato, chicken, shellfish and mould. The family was advised to continue peanut in his diet in the setting of sensitisation and to continue introducing new foods. In addition to the above TCS, a soak and seal plan with bleach baths three times a week was encouraged.

However, the family reported continued severe flares of AD and behavioural problems that they attributed to specific food ingestion. At 16 months, his family removed several foods from his diet without improvement of his AD or behaviour (table 1).

At 24 months, after eating fish for the first time, he had immediate wheezing and worsening AD. He was treated with diphenhydramine and strict fish avoidance. At 27 months, his paediatric provider performed an FA IgE panel which revealed an elevated total IgE, and he was advised to start avoiding all foods with positive tests, including foods he had previously tolerated (table 1).

A second allergist reiterated his avoidance of milk, egg, wheat, peanut, soy, tree nuts and shellfish (table 1). Additional food reactions were reported so supplementary SPT was performed and resulted positive for pineapple, orange, barley, corn, chicken and turkey, and he was advised to strictly avoid all these foods as well without any discussion regarding oral food challenges (OFC) to confirm FA (table 1). At this point, the patient's only immediate hypersensitivity reaction was to fish. However, 6 months after milk avoidance secondary to IgE testing, he ate ice cream with immediate vomiting and lip swelling, which resolved without treatment (table 1).



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When the child presented to our clinical centre at 46 months of age, his diet was limited to beef, beans and sweet potatoes without any supplements or multivitamins. He appeared to meet his calorie and protein goals, but vitamin D and calcium intake were only 1% and 40%, respectively, of the recommended daily allowance (RDA). All other nutrients assessed during a 3 day food diary were above 100% RDA. His current skin care included emollients and topical steroids as needed with daily hydroxyzine without use of bleach baths or wet wraps. His medical history was significant for one course of oral antibiotics for a skin infection and mild intermittent asthma. He received a total of three courses of oral prednisolone for asthma in his lifetime and never required hospitalisation. He was maintained on albuterol only as needed. He had no history of increased frequency and severity of infections that would point to an immunodeficiency.

INVESTIGATIONS

On physical examination, excoriated, eczematous lesions covered his face, trunk, arms and legs. He had a prominent costochondral junction without metaphyseal widening, frontal bossing or leg bowing. His growth chart revealed normal growth velocity until about 17 months of age, at which point his height and weight began crossing percentiles downward to the 10th

and 15th percentile, respectively (figure 1A,B). By 25 months of age, he met the clinical criteria for linear growth failure. At presentation to our clinical centre, his height, weight and body mass index (BMI) percentiles were 2nd, 12th and 70th, respectively (figure 1A,C).

Initial labs revealed eosinophilia of 1.63 K/uL (NR 0.03–0.53 K/uL), elevated total IgE and food-specific IgE levels (table 1), extreme vitamin D deficiency with a vitamin D, 25 OH level of 5 ng/mL (<10 ng/mL associated with osteomalacia or rickets), and elevated parathyroid hormone of 194.8 pg/mL (NR 15.0–65.0 pg/mL). Other cell counts and nutritional labs (alkaline phosphatase, vitamins A, E, B₁₂, iron, folate, zinc, copper, selenium, albumin, prealbumin) were within normal limits.

He was evaluated by endocrinology who found no physical or laboratory findings of rickets. Further work up revealed normal thyroid functions and IGF-1 levels, ruling out other endocrine causes of short stature including hypothyroidism and growth hormone deficiency. His short stature was felt to be due to chronic inflammation secondary to his AD, chronic TCS use, limited diet and severe Vitamin D deficiency.

Table 1 Timing of food introduction and elimination with reaction and testing history

Food	Age at introduction	Age 27 months at paediatrician sIgE (kU/L)	Age at removal	Reaction attributed to food	Age 46 months at clinical centre sIgE (kU/L)
Total IgE		3626 IU/mL (NR 0–90 IU/mL)			18261 IU/mL (NR 0–90 IU/mL)
Egg	<1 year	>100	27 months	Tolerated without any adverse reactions	>100
Cow's milk	<1 year	32.9	27 months	Accidental exposure at 33 months with vomiting and lip swelling	68
Peanut	<1 year	>100	27 months	Tolerated without any adverse reactions	>100
Almond	Never eaten	ND	NA		97.8
Brazil nut	Never eaten	ND	NA		32.1
Cashew	Never eaten	ND	NA		>100
Hazelnut	Never eaten	ND	NA		45.1
Pistachio	Never eaten	ND	NA		>100
Pecan	Never eaten	ND	NA		1.34
Pine nut	Never eaten	ND	NA		14.0
Walnut	Never eaten	6.3	NA		14.8
Sesame seed	Never eaten	ND	NA		27.2
Soybean	<1 year	26.8	27 months	Tolerated without any adverse reactions	86.8
Codfish	24 months	26.8	24 months	First exposure at 24 months with wheezing, pruritus, erythema	44.8
Crab	Never eaten	ND	NA		>100
Shrimp	Never eaten	>100	NA		>100
Meat (except beef) and poultry	<1 year		16–24 months	Mouth pruritus	
Wheat	<1 year	9.24	27 months	Tolerated without any adverse reactions	58.7
Corn	<1 year	ND	16–24 months	Behavioural issues, rash, pruritus, erythema	22.8
Other grains	<1 year		16–24 months	Behavioural issues, worsened AD, erythema	
Tomato	<1 year	6.34	16–24 months	Behavioural issues, rash, pruritus	ND
Other fruits and vegetables (except sweet potato)	<1 year		16–24 months	Behavioural issues, worsened AD, mouth pruritus, stuttering	

AD, atopic dermatitis; NA, not applicable; ND, not done; NR, Normal Range; sIgE, specific Immunoglobulin E.

OUTCOME AND FOLLOW-UP

The patient received intensive nutritional counselling, and calcium and vitamin D supplementation were prescribed. A nutritionally complete elemental based formula was again recommended, however, was not implemented due to familial concerns regarding corn syrup and maltodextrin derived from corn. Over the next 6 months, his AD improved along with his sleep and behaviour on a strict regimen of hydrolatum (Dennison Pharmaceuticals) after a nightly bath and 14 day bursts of mid-to-high potency TCS. He was started on a calcium and Vitamin D fortified pea-protein-based drink, and several fruits and vegetables were reintroduced. Since he had tolerated many of the foods he was avoiding without a history of immediate reaction (except for milk and fish), the recommendation was made to reintroduce foods back into his diet either with at-home reintroduction of most low-allergenic foods or monitored OFCs to egg, peanut, tree nuts, wheat, soy and shellfish. However, his diet remained quite limited as the family declined OFCs. His eosinophilia resolved, vitamin D deficiency corrected to optimal levels, his height and weight increased to the 5th and 30th percentiles, respectively, and his BMI increased (figure 1A,C).

DISCUSSION

Our case showcases the complex interactions between AD and FA and highlights the challenges of diagnosis and treatment. Throughout this patient's life, increasing emphasis was placed on food as the cause for his AD flares. As a result, he underwent broad testing for FA by his primary care clinician which revealed

multiple sensitivities to foods that were interpreted as indicative of allergy despite the absence of clinical reactivity. This resulted in an unnecessarily restrictive diet, contributing to his growth failure and a high level of anxiety in both the patient and his parents. More worrisome, after the removal of milk that he had previously tolerated, he developed clinical symptoms suggesting the development of an immediate IgE-mediated FA. Despite his restricted diet, his skin did not improve until his skin care regimen was optimised.

As AD is the most common chronic inflammatory skin disease to affect children and typically develops very early in life, paediatric clinicians are often the first healthcare providers to advise parents on a treatment plan. Infants with severe AD have the highest risk of developing FA, which may, in part, be due delayed introduction of foods and incorrect diagnosis of FA based only on sensitisation.¹⁰ US guidelines from 2010 recommend that a limited FA evaluation be considered only when patients have persistent moderate to severe AD despite optimal skin care and/or a clinical history of immediate reaction to a specific food.¹¹ However, it should be noted that specific SPT has a positive predictive value <50%, and current food-specific IgE threshold levels (32 kU_A/L for milk, 7 kU_A/L for egg, and 15 kU_A/L for peanut) with 95% positive predictive value for allergy may not be applicable in patients with moderate-to-severe AD.^{5 12 13} For example, although very high peanut IgE levels are often associated with clinical peanut allergy in AD patients, this was not the case in our subject who had a peanut IgE of >100 kU_A/L but was tolerating peanut in his diet. Unfortunately, the recommendation

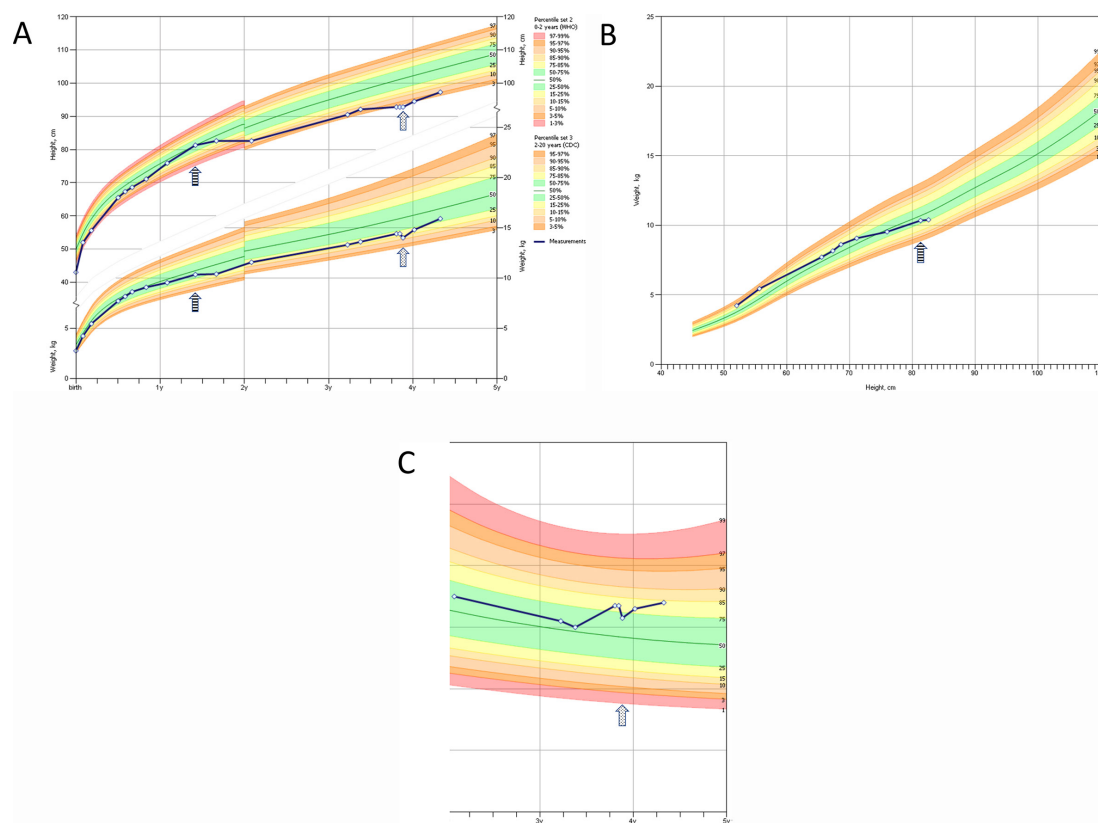


Figure 1 Growth charts. (A) Weight and height for age: Note the transition from World Health Organization (WHO) Child Growth Standards (2006) to Centers for Disease Control and Prevention (CDC) growth charts (2000) at 2 years of age. Striped arrow corresponds with introduction of the elimination diet and subsequent reduction in growth velocity. Dotted arrow corresponds with introduction of treatment for vitamin D deficiency and nutritional supplementation with consequent rise in growth velocity. (B) Weight for length (who: 0–2 years). Striped arrow corresponds with introduction of the elimination diet and subsequent reduction in growth velocity. (C) BMI (CDC: 2–20 years). Dotted arrow corresponds with introduction of treatment for vitamin D deficiency and nutritional supplementation with consequent rise in growth velocity. BMI, body mass index.

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was made to remove peanut from his diet because of the high positive peanut specific IgE level alone. A recent retrospective study found that AD subjects with a milk IgE of 43 kU_A/L, egg IgE of 28 kU_A/L and peanut IgE of 34 kU_A/L had at least a 50% chance of not being allergic to the food.⁵ Therefore, sIgE testing may have utility in predicting FA in patients with moderate-severe AD and high total serum IgE levels, but the decision points may be much higher than those that apply to a less atopic population.

Adverse reactions to food can be characterised by severity and by immunological mechanisms of action. They can be categorised into immediate (IgE) reactivity, delayed eczematous reactions (non-IgE mediated) and combined immediate-type and late eczematous reactions.¹² While it is true that elimination of certain foods may improve AD in some patients with true food-triggered AD, this process can also lead to the future development of IgE-mediated FA, including anaphylaxis.¹² Recent studies have underscored the benefits of keeping the food in the diets of infants sensitised to common FAs. In a landmark study, consumption of peanut in peanut sensitised infants with AD and/or egg allergy led to a 70% relative reduction in acquiring peanut allergy, supporting the hypothesis of oral tolerance induction.¹⁴ Thus, strict elimination of foods to which an infant is sensitised but clinically tolerant may elicit development of FA and anaphylaxis on subsequent exposure. Interestingly, the inclusion of peanut in these sensitised infants' diets did not alter the trajectory of their AD nor did they find that IgE was predictive for development of peanut allergy.¹⁴ More recent guidelines on the primary prevention of FA recommend that SPT/IgE screening is not required prior introduction in all infants, and if completed after discussion with the family, should only lead to the decision of where an introduction should be attempted (at home vs under clinical supervision).¹⁰ IgE testing is not diagnostic for FA, and an OFC is an imperative step to validate the clinical significance of sensitisation.¹⁰ However, parents and clinicians may become reluctant to perform OFCs for fear of inducing anaphylaxis after encountering high levels of IgE that are not necessarily predictive of true allergy.¹⁴

In addition to development of FA, the child in our case was profoundly vitamin D deficient and met the clinical criteria for growth failure. Correction of vitamin D deficiency led to only a modest increase in height velocity over the short observation period. This is not surprising, as he had other ongoing causes for growth failure, including continued inflammation and steroid use.^{15–17} It has been shown that children who eliminate two or more foods from their diet are more likely to reach lower height percentiles and to be vitamin D deficient.¹⁸ This is most likely due to the fact that many of the most allergenic foods (milk, egg, peanut, tree nut and soy) include common sources of protein and other nutrients essential for proper growth of infants and toddlers.^{9 19} Consequently, national FA guidelines recommend nutritional counselling and growth monitoring for children on elimination diets.¹¹

The evaluation and treatment of children with moderate-severe AD who are suspected to have FA is incredibly complex and optimally involves a multidisciplinary team comprising of paediatric providers, allergists, dermatologists, dietitians and psychologists. In the absence of a convincing clinical history for an immediate FA, skin barrier creation and protection should be the primary focus. Elimination diets and IgE allergy testing have been historically part of the workup of children with AD, but their roles are clinically limited and clearly not benign. As illustrated in this case, unnecessary testing and removal of previously tolerated foods can compromise nutrition and growth, and

promote the development of an immediate FA, increasing the risk of anaphylaxis. Those children who undergo elimination diets for their AD likely can benefit from consultation with an allergist and dietitian as OFCs remain the gold standard to diagnose FA.

Learning points

- Optimal skin moisturisation and barrier creation and protection are essential for the management of atopic dermatitis.
- While children with atopic dermatitis are more likely to have a food allergy, food allergy is rarely a primary cause of atopic dermatitis.
- Elimination diets after extensive testing are not always benign, especially when infants and children are growing and developing.
- All food avoidances due to a concern for allergy should be confirmed by a convincing history of a type I hypersensitivity reaction following ingestion of the food or with an oral food challenge by a board-certified allergist.
- If a true food allergy is confirmed, patients and their families should consult with a registered dietitian.

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