RESEARCH ARTICLE

A Clinical Perspective on Food-Related Diseases in the First Year of Life

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Abstract

Food-related disease processes can have a wide presentation picture. We present here a review of their clinical patterns in infants to allow a prompt diagnosis and appropriate management. Included in the discussion in infants from birth to 12 months includes IgE-mediated food allergy, food protein–induced allergic proctocolitis , food protein enterocolitis syndrome, atopic dermatitis, eosinophilic esophagitis, and eosinophilic gastrointestinal disease. The bibliography is updated to the past two years unless the latest guideline pre-dated 2018, or the reference was of a classic nature.

Key words: Food, allergy, food protein enterocolitis, atopic dermatitis, anaphylaxis

Introduction

Adverse food related diseases in infants can be dramatic, and often prompt immediate attention. The underlying disease process can be confusing, as true IgE- mediated disease in infants often is underappreciated. There are, however, several disease processes that over-lap IgE-mediated disease, especially when the gastrointestinal tract is involved. We review here a selection of food-related diseases and focus on their specific presentation in infants. We further divide the presentations into months 0-2, 2-6 and 6-12, presenting the reviewed processes into more classic and under-appreciated diseases. A brief overview of the diseases is presented first to highlight food-related diseases in this young age group.

Food-Associated Disease Processes to be considered in Infants

1. IgE-mediated Food allergy

Food IgE antibodies are produced after adequate exposure and with genetic pre-disposition. Food allergen, after maternal digestion, passes through the placental barrier and after birth through breast milk. The fetus has the capacity to produce IgE antibodies. After birth, breast milk can transfer food protein to the infant, allowing for the initial or continued IgE production.[1] A confluence of time and IgE levels converge to allow for an allergic reaction. The development of IgE antibodies is well recognized in toddlers and children, and food allergy is increasing, and many food allergies occur before the first year. A background of hypersensitivity reactions in children has been recently reviewed.[2]

IgE-mediated anaphylaxis to food occurs when the allergic diathesis is sufficient to result in 2 or more organ systems to be involved. The topic of anaphylaxis in children was reviewed by Simons and Sampson in 2015.[3]

2. Food protein–induced allergic proctocolitis (FPIAP)

The first study from North America to prospectively evaluate the prevalence of Food protein–induced allergic proctocolitis (FPIAP) has been recently published. Gross blood is a predominate concern, but occult blood can be occasionally present.[4] This is often accompanied by significant abdominal symptoms, with crying and colic. Milk is virtually the single most concerning food and FPIAP can also occur in breast feed babies. The elimination of milk sources drastically improves the disease, and the eventual re-introduction, without concern, supports the absence of an IgE component.

3. Food protein enterocolitis syndrome (FPIES)

A non-IgE mediated untoward reaction to an ingested food, food protein enterocolitis syndrome (FPIES) remains a dramatic but uncommon food-related disease.[5] Severe vomiting, lethargy and diarrhea starting 1-4 hours after food ingestion are the classic acute FPIES symptoms; while a chronic form presents with failure to thrive and vomiting. Acute FPIES usually occurs on an early introduction of solids (rice and oats are frequently reported). It has been reported in

exclusively breast-feed babies. Cow's milk is the predominate antigen, although a wide variety of foods have been implicated.

4. Atopic Dermatitis

Atopic dermatitis is a clinically diagnosed disease that has strong atopic concerns (IgE), but is immunologically more complex than IgE-mediated food allergy.[2] There are strong ethnic differences in the dermal and epidermal compartments, and the degree which barrier integrity and immunological dysfunction occur.[6] These marked differences have been recently outlined, but are beyond the scope of the discussion here.[6] A review of the underlying dysfunctional atopic dermatitis principals in children has been recently published.[7]

5. Eosinophilic enteritis

Although severe FPIAP can have colonic eosinophilia, the true eosinophilic enteritis diseases are considered in the atopic disease family.[2, 8-10] The atopic march has now been updated to include eosinophilic esophagitis (EOE) the most common eosinophilic enteritis.[8] Eosinophilic infiltration into any gastrointestinal compartment, including stomach, duodenum, jejunum, ileum, cecum or colon can occur (EGID).[10] These eosinophilic processes have been recently discussed.[2] As food exposure is considered a paramount concern, especially in EoE, a reasonable time of exposure is required to generate an eosinophilic infiltration. The fact that milk protein can appear in breast milk may provide a temporal issue with exposure time, as milk itself is the critical protein in many young EoE children. Infants do develop EoE, but exceedingly rarely in the other segments of the gastrointestinal tract (EGID).[10-11]

Food-related diseases by age group

By dividing the food-related disease presentation into 0-2 months, 2-6 months, and 6-12 months it is possible to present clinical presentation and frequency of occurrence in a time of life dependent fashion. Interestingly, intrauterine life for the infant has immunological skewing towards a TH2 milieu, with a rapid shift after birth towards emphasis on bacterial and viral exposures, dominated by a TH1 immune response. The usual question is why an infant might present with an food-related disease with minimal to no exposure prior to the reaction? It's clear, therefore that food protein in intrauterine life, through breast feeding, and in environmental transdermal contact within home life all has potential for sensitization.

A second issue is the national emphasis on earlier infant ingestion of food, including allergenic foods.[12] Therefore, the infant with non-ingestion sensitization (skin, trans-uterine) has the opportunity to present earlier with an IgE-mediated food reaction. The presumption is early introduction of foods shifts the immune system to a tolerance state, which does happen (with or without sensitization), but the initial ingestion of allergenic foods allows for the earlier presentation of a IgE reactions, as *non-ingestion* IgE sensitization had already occurred.

1. Food-related diseases 0-2 months

IgE mediated food allergy is uncommon, and anaphylaxis to the food is rare in this age group. Cow's milk would be the most likely culprit and the protein come through the breast milk, and the reaction would occur soon after ingestion. Other proteins passing through the breast milk could cause food IgE reactions, but are at the case report stage. The biggest problem is identification, and without hives the identification will likely be difficult. Blood pressure deterioration has become a hallmark of infant anaphylaxis.

Food- protein-induced allergic proctocolitis (FPIAP) is probably the most common food-related disease in this age group. The exposure of milk protein via breast milk or bottle is necessary; other foods are virtually never seen. Most primary care doctors recognize the beginnings, and formula changes occur relatively quickly. The protein intolerance likely begins de-novo at birth, although data is scarce in that regard.

Food protein enterocolitis (enteropathy) syndrome (FPIES) has had case reports less than 2 months. The relatively rarity less than 2 months also suggests a de-novo intolerance beginning after birth, with milk being the almost the exclusive food in very young infants.

Eosinophilic esophagitis and EGID diseases are virtually non-existent; again suggesting a protein needs to touch the gastrointestinal tract for a while to induce the complex gene modifications that occur in EoE and EGID.

Atopic dermatitis is a clinical diagnosis.[13] Biopsies done in research protocols and strikingly abnormal cytokine profiles (TH2 driven). [6] Diffuse infantile seborrhea dermatitis is the most likely mimic, and is almost always accompanied by scalp involvement. Atopic dermatitis is accompanied by positive allergy tests in at least a third of patients.[1] In the young infant cow's milk and/or breast milk transferred protein might result in the demonstration of a positive IgE test. The clinician experienced with AD in infants could recommend a short-term elimination diet of one allergen (when the child's test is positive), making sure adequate protein and caloric needs of the child and mother (when breast feeding) are met. Only when clear evidence exists of benefit should a food (or foods) be used as primary AD therapy. It's also critical to know that if systemic tolerance co-existed to the food eliminated, re-introduction can result in a more profound allergic reaction. The time frame from tolerance to non-tolerance is likely longer than 2 to 3 weeks, but is unknown.

2. Food-related disease 2-6 months

Advancing age predominately allows for a larger repertoire of foods for adverse reactions. Age breakdown for the reviewed conditions is generally not emphasized, but the early introduction of foods, especially allergenic foods could allow their oral presentation to present as adverse reactions. The hypothesis for early introduction appears valid, based on with-in study data.[12]

Immediate, IgE reactions with or without anaphylaxis, can occur as foods are introduced. Milk, eggs and peanuts are the most likely in this age group, but any food

can occur. Confirmation by allergy testing is valuable, and an epinephrine prescription is mandatory. Long term management is required. The subsequent plan is best managed by an allergist, and baked milk or baked egg can often be challenged successfully. Protocols for peanut desensitization using a commercial product are emerging.

Food- protein-induced allergic proctocolitis (FPIAP) is likely waning in this age group, although the later introduction of milk may trigger a start; while other foods, such as eggs, are exceedingly rare.

Food protein enterocolitis (enteropathy) syndrome, exclusive of milk, has rice or oats as a common food; therefore the introduction of these two foods would coincide with the infant older than 2 months. Many other foods have been implicated, and recently reviewed.[14]

Eosinophilic esophagitis (EoE) and very less possibly gastroenteritis (EGID) may rarely occur in the infant less than 6 months. Significant vomiting will be the predominate symptom, and the eventuality that a food which triggered the condition required time of exposure. The role of initiation of proton pump inhibitors as ameliorating (temporizing) therapy, and the early natural history of EoE are all unknown factors. Cow's milk will be a high suspicion food.

The development of atopic dermatitis (AD) after 2 months is common, and the moderate to severe infants may seek specialty care. The potential that an infant with moderate to severe AD will have a co-morbidity with a true food IgE-mediated allergy is reasonably low, but the likelihood of IgE-sensitization to a ingested food is common. The role for selective avoidance of a food(s) as a trial of co-management of significant AD is controversial, as discussed previously.

3. Food-related diseases 6-12 months

Reaching toward the one year mark, hopefully, most food have been introduced, and have been eaten multiple times. New foods might include tree nuts, due to concerns for choking at early ages, more exotic fruits or vegetables, and seafood, such as shrimp. Adding finger foods can generate concerns, as many packaged foods contain multiple food dyes, shelf life and rancidity extenders, and multiple micro-nutrients for flavor enhancement (spices and natural flavors).

Immediate facial hives to a new complex food (see above) often presents in this age group. Elimination of specific IgE to the main ingredients is often easy, as milk, wheat or soy are eaten elsewhere. The multiple dyes, flavor enhancers, and shelf-life extenders is an issue. Ranch dressing is a common culprit. Localized hives in this situation can be clinically managed, with avoidance and no emergency medication required for home. The development of a food allergy to a frequently eaten food by this age is uncommon. Foods less eaten at earlier age can occur, (i.e. tree nuts), and appropriate testing and planning follows the same as food allergens developed at young ages (milk, eggs).

Food protein enterocolitis (enteropathy) syndrome can emerge if oats and rice were

not added till this age. The wide variety of uncommon FPIES foods can occur, but generally the peak is about 6-7 months in infants.[15]

Food- protein-induced allergic proctocolitis (FPIAP) is virtually never seen group, although the later introduction of milk may trigger a start; while other foods, such as eggs, are exceedingly rare, as they were added, hopefully by 6 months.

Eosinophilic esophagitis (EoE) and very less possibly gastroenteritis (EGID) are emerging as new diagnosis in the 6-12 month timeframe, based, likely, on time from food start to generation of esophageal (and extra-esophageal) inflammatory change and development of symptoms. EGID is very rare, as compared to EoE, but isolated cases have been reported. Any child with food IgE concerns, or atopic dermatitis who develops new gastrointestinal concerns (vomiting, diarrhea) should be considered a EoE or possibly EGID candidate for evaluation.

Significant atopic dermatitis (AD) continues to present in this age group, but later development likely decreases clear-cut food related associations, but increases concomitant food IgE sensitization. A rationale approach is to provide short-term avoidance for IgE-positive high ingested foods, but not expect significant benefit. Long-term avoidance is not encouraged and clinical food reactions have occurred when that approach is allowed. Nutrition concerns also emerge for critical protein avoidance.

Summary

Food-related diseases rank from common to exceedingly rare in infants. The epidemiology evidence including incidence or prevalence data is virtually absent, and is largely experiential from a long-standing academic pediatric allergy practice. Specialty care can be extremely beneficial, as infants can have dramatic emergency-based presentations.

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