



Food Allergies Versus Intolerance: How to Tell the Difference?

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Case Study – Are the Symptoms Due to Adverse Reactions to Food?

21 yr old female

- Diarrhea, cramping with dairy products including some yoghurts, but lactose free diet of no benefit
- Tomatoes give oral swelling, vomiting
- Past history of skin rashes, otitis as a child with similar foods and some reactivity to food antigen skin testing
- Some atopic features (nasal congestion with mowing grass) but no eczema or asthma in patient or family
- Recently tried a gluten free diet that helps

Case Study – Are the Symptoms Due to Adverse Reactions to Food?

Differential Diagnoses:

- Irritable Bowel Syndrome
- Lactose intolerance
- GI food allergy
- Eosinophilic gastroenteritis
- Celiac disease

Adverse Reactions to Food (ARF)

Food allergy or hypersensitivity:

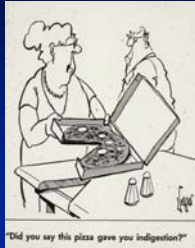
- Immediate hypersensitivity
- Allergic eosinophilic gastroenteritis
- Food protein induced enterocolitis syndromes (FPIES)
- Celiac disease

Food intolerance (non-immune):

- Food toxicity or food poisoning
- Anaphylactoid (pseudo-allergic)
- Pharmacologic
- Metabolic
- Idiosyncratic
- Psychologic

Bischoff & Crowe, Gastroenterology, 128: 1089, 2005

Adverse Reactions to Food



Food Toxicity or Poisoning

- Staphylococcal enterotoxins
- *Shigella*, *Salmonella*, *Campylobacter*
- *E. coli*
- Botulism
- Hepatitis A
- *Vibrio*

Anaphylactoid Reactions

Foods that mimic the effects of mast cell degranulation (pseudoallergic reactions)

- Strawberries
- Shellfish

Pharmacological Food Reactions

- Histamine
 - » swiss cheese
 - » tuna
- Amines
- Caffeine
- Sulfites
- Tartrazine
- MSG

Immunological Reactions to Food

- Food hypersensitivity (IgE-mediated)
- Celiac disease
- Food protein enteropathies
 - » Hypersensitivity
 - » Immune complexes
 - » T-cells

Manifestations of Adverse Reactions to Food

Symptoms

- Isolated GI tract or Multisystem

Duration

- Acute/subacute or Chronic/persistent

Incidence of ARF

- Many report adverse reactions to food but most involve non-immune mechanisms
- Individuals with functional disorders more likely to report adverse reactions to foods and drugs
(Aliment Pharmacol Therapeutics, May 2002)
- Actual incidence of food allergy unknown
 - Estimate: 1-4% of adult population
 - Higher in children (4-8%), atopic individuals
 - Increasing in developed nations

GI Disorders and ARF

- GI food allergy
- Food protein enteropathies (milk, soy)
- Celiac disease
- Eosinophilic gastroenteritis
- Lactose intolerance
- Irritable bowel syndrome
- Inflammatory bowel disease
- Dyspepsia, GERD, peptic ulcer



Manifestations of Food Allergy

- GI symptoms (in 30-70%):
 - edema of oropharyngeal mucosa
 - nausea/vomiting, diarrhea, abdominal pain, bloating
- Other manifestations:
 - urticaria, eczema
 - asthma, rhinitis, otitis
 - anaphylaxis
 - ?? rheumatologic, CNS

Common Food Allergens

- Peanuts
- Tree nuts
- Cows milk protein (casein, BLG)
- Eggs
- Wheat
- Soya protein
- Corn
- Shellfish
- Fish

Risk of Anaphylaxis

Food allergy is now the major cause of anaphylaxis in western countries

Those with increased risk include those:

- with past history of anaphylaxis
- with reactions with respiratory tract symptoms
- with reactions to peanuts, tree nuts, fish, seafood
- taking B-blockers or ACE inhibitors

Peanut Allergy

- Increasing prevalence
- Occurs in 1 in 150-200 individuals
- Varying presentations
- Major cause of anaphylaxis
- Varying dose sensitivity
- Most react on first recognized exposure
- Up to 20% may lose sensitivity
- Associated with other food allergy, atopy

Oral Allergy Syndrome

- Initial sensitization to pollens results in IgE that cross reacts with fruit and vegetables
- Those with seasonal allergic rhinitis are at increased risk
- Pollen-food associations:
 - Birch pollen – apple, peach, pear, almond, hazelnut, potato, carrot
 - Ragweed pollen – melons, banana, gourd family
 - Mugwort pollen – celery, carrot, spices
 - Grass pollen - tomato

Latex – Food Allergy Syndrome

- Sensitization to latex results in IgE that cross reacts with fruit and vegetables
- Exposure to foods give same symptoms as latex
- Natural Rubber Latex contains over 200 proteins, 10 bind IgE (HEV b 1-10)
- Food associations:
 - Kiwi (5)
 - Potato, tomato (7)
 - Avocado, chestnut, banana (6)

Celiac disease

- Immune disorder in which gluten causes intestinal damage
- Gluten found in wheat, rye, barley
- Not rare - occurs as frequently as 1 in 100 to 300 Americans, Europeans!
- Often presents as non-GI problems (osteoporosis, fatigue, depression, miscarriages) and is associated with other autoimmune conditions

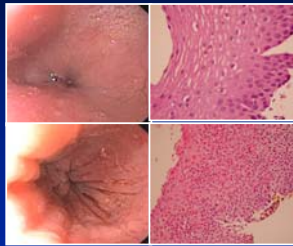
Eosinophilic Gastroenteritis

- Affects adults and children
- Can involve all layers of gut wall
- Various GI manifestations
- May have food allergies, specific IgE
- Increased peripheral eosinophils
- Varying response to elimination diets, anti-allergic therapies

Eosinophilic Esophagitis

- Affects children, teens, adults
- More common in males
- Heartburn, dysphagia, vomiting, food impaction
- May have food and inhalant allergies
- Endoscopy findings – rings (felinezation), stricture
- Diagnosis – mucosal biopsy

Endoscopic and Histologic Findings



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EE: Management

- Varying response to acid suppression
- Elimination or hypoallergenic diets
- Inhaled corticosteroids (fluticasone)
- Oral steroids
- Dilation of strictures – higher risk of tears, perforation
- Newer therapies - anti-allergic biologic therapies (anti-IL-5, anti-IL-13)

Pediatric Gut Food Allergy

- Food hypersensitivity
- Food protein enteropathies
 - Cow's milk, soya
 - Enteritis, colitis, proctitis
- Gastroesophageal reflux with CMA
- Eosinophilic esophagitis
- Eosinophilic gastroenteritis
- Chronic constipation due to CMA
- Celiac disease

Cows Milk Protein Enteropathy

- Occurs in 0.3 -7.5% of infants
- Onset within first 6 months
- Diarrhea, failure to thrive, anemia, protein-losing enteropathy
- Typical gut pathology
- Improvement with dietary elimination
- Worsening with CMP challenge

Lactose Intolerance

Most common ARF worldwide

- Congenital deficiencies - rare
- Constitutional lactase insufficiency
 - » Common in native NA, Asians, Africans, those from Mediterranean areas
- Secondary lactase insufficiency
 - » Gastroenteritis, Crohn's disease, celiac disease

ARF and IBS

- Controversial area with studies for and against a role for food allergy in IBS
- Most patients have food intolerance with nonspecific reactions to food
- Presumed neurohormonal mechanisms

ARF and IBS

- 150 outpatients with IBS with serum IgG to various food antigens
- Randomized to 3 month of specific elimination versus sham elimination diet
- Primary outcomes of IBS symptom severity (10% reduction) and global rating scores were significantly improved with specific diet
- Trend to benefit with secondary outcomes including QOL

W. Atkinson et al, Gut, 53: 1459, 2004

ARF and IBD

- No evidence that food-induced immune responses play a causal role in IBD
- Some patients may benefit from special diets (e.g., low residue, low lactose, elemental) or bowel rest
- Diets high in meat, alcoholic beverages, sulfur/sulfates associated with exacerbations
(SL Jowett, Gut; 53: 1479, 2004)
- Not all IBD patients are lactose intolerant!
- Cow's milk allergy very rare in IBD

ARF and Upper GI Disorders

- Not uncommon
- Usually due to pharmacologic or physiologic reactions to:
 - food content (fat, caffeine)
 - additives
 - osmolality
 - quantity

Summary of ARF

Type of ARF	Immune mediated	Tissue damage	Genetic factors
Food hypersensitivity	Yes	Transient	Yes
Food protein enteropathy	Yes	Long term	Yes - celiac, unclear for CMPE
Food intolerance	No	No	Yes for lactose, no for others

Case Study: How to Evaluate for Causes of Adverse Reactions to Food

- History - ? co-factors (exercise, drugs)
- Assess for lactose intolerance
- Skin testing for food allergens / RAST
- Eosinophil count
- Celiac serology and/or HLA DQ assay
- Diet diary
- Hypoallergenic diet trial*
- Endoscopy and biopsy

Crowe, Current Gastroenterology Reports, 3: 351, 2001

Double-Blinded Placebo-Control Food Challenge

- Considered the gold standard for diagnosing food allergy
- Food antigens administered in blinded fashion by NG or gelatin capsules
- Not available in most centers

Laboratory Tests

- CBC, eosinophil count
- Quantitative immunoglobulins
- Specific IgE levels (RAST, ELISA)
- ? Serum IgG to foods
- Basophil histamine release assay
- Basophil leukotriene release assay
- Others for non-IgE mediated reactions

Bischoff & Crowe, Gastroenterology, 128: 1089, 2005


Food Antigen Challenges

- Skin prick testing
 - Excellent negative predictive value
 - Poor positive predictive value
- Skin patch testing for food allergens
- GI tract by endoscopic mucosal testing
 - Limited studies but appears useful
- Other sites unproven or not accepted
 - Sublingual
 - Neuromuscular

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Unorthodox Diagnostic Methods



- Sublingual testing
- Neuromuscular testing
- Electromyography
- Iridology

Case Study – Are the Symptoms Due to Adverse Reactions to Food?

Approach to this patient:

- Assess for lactose intolerance
- Skin testing for food allergens
- Eosinophil count
- Celiac serology and/or genetic testing
- Diet diary
- ? Hypoallergenic diet trial
- ? Endoscopy and biopsy

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Management of Food Allergy

- Avoidance of food allergens
 - Antihistamines
 - Mast cell inhibitors
 - Cromolyn sodium, Ketotifen
 - Corticosteroids
 - Injectable epinephrine
- No proven role for oral desensitization



"How much longer did he tell you to stay on this banana diet?"

Management of Food Allergy

- Patient education
 - Understand food allergen groups
 - Since Jan 2006 labeling for the 8 major food allergens in the USA
 - Recognize warning symptoms
- Information networks, newsletters
 - The Food Allergy and Anaphylaxis Network (www.foodallergy.org)
- Injectable epinephrine

Prevention of Food Allergy

Recommended in atopic families:

- Delayed introduction of solid foods in early childhood
- Breast feeding
- Hypoallergenic (not soy) formulas
- ? Hypoallergenic diets for mother during pregnancy and breastfeeding
- ? Probiotics during pregnancy and in infants

New Therapies for Food Allergy

- Tolerogenic peptides
- Recombinant proteins
- Anti-IgE vaccines
- DNA vaccines
- Th1 cytokines
- Inhibition of Th2 cytokines (e.g., IL-4)
 - Neutralizing antibodies
 - Receptor antagonists

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Future Directions in Food Allergy

- Improved diagnostic methods
- Identification of individuals at risk
- Improved treatments
- Development of hypoallergenic foods

These advances will require a greater understanding of food allergens and basic immunopathogenetic mechanisms

**Case Study Follow-up:
Results of Tests and Management**

Results of evaluation for ARF:

- Lactose hydrogen breath test negative
- CBC, eosinophil count normal
- Total IgA and tTG IgA within normal range
- HLA DQ 2 and 8 by PCR negative
- Diet diary suggests tomatoes and fatty foods induce symptoms
- Skin testing for food allergens showed positive reaction to tomato antigen
- Trial of low fat diet helps GI symptoms and avoiding tomatoes stopped oropharyngeal symptoms: educated about cross reactivity of grass pollen and tomato

**Take Home Message on Dealing with
Possible GI Food Allergies**

Lactose intolerance is common and easily treated
Celiac disease is common and easily screened for
Food allergies are not rare and can be identified with subsequent dietary elimination providing benefit

Patients can have a specific ARF and IBS
Identifying specific food intolerances can also be beneficial for IBS patients

Patients appreciate the assessment even if it turns out to be negative and they have the non-specific food sensitivity common to most IBS patients
