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Wheat Allergy

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Introduction

Bread wheat, also known as *Triticum aestivum*, is one of the commonly grown crops worldwide.[1] It can be grown worldwide because it grows easily in different climates, and it has a high nutritional value, high palatability, and can be processed into many foods and drinks.[1][2] However, despite these benefits, common wheat is recognized as an immune-mediated food allergen because it activates immunoglobulin E (IgE) and non-IgE immune responses.[1][2]

Etiology

The etiology of a wheat allergy is either IgE-mediated or non-IgE-mediated allergic reaction to wheat proteins.[3] The result can be life-threatening and can lead to an anaphylactic reaction. Celiac disease is a non-IgE-mediated immune response.

Epidemiology

The prevalence of confirmed (via food challenge), IgE-mediated food allergy to wheat is unknown. The prevalence of wheat-based food allergy is likely in the range of 0.2% to 1%.[1] Children have a higher prevalence of wheat allergies compared to adults and are more likely to develop an allergy if wheat is introduced after 6 months of life.[1][4] Children typically outgrow their allergy, and about 65% have a resolution by the age of 12.[5]

The prevalence of celiac disease, a non-IgE-mediated food allergy to wheat, is approximately 1% to 2% in the United States.[6][7][8]

Pathophysiology

Wheat allergy is the manifestation of mediator release, such as histamine, platelet activator factor, and leukotrienes, from mast cells and basophils.[1][9][10] The IgE production is thought to be due to a breach of oral tolerance, and as a result, of Th2-biased immune dysregulation that causes sensitization and B-cell IgE production.[11][12][13][14][15] Allergens found in wheat flour are alpha-purothionin, alpha-amylase/trypsin inhibitor, peroxidase, thioredoxin, lipid-protein transfer, serine proteinase inhibitor, thaumatin-like protein (TLP), gliadin, thiol reductase, 1-cys-peroxiredoxin, and serine protease-like inhibitor.[1]

Celiac disease is characterized by a specific autoantibody against tissue transglutaminase 2 (anti-tTG2), endomysium, and/or deamidated gliadin peptide.[16][17] When gliadin peptides pass through the epithelial barrier, they activate CD4 T-lymphocytes which produce high levels of pro-inflammatory cytokines.[6] The pro-inflammatory cytokines activate T-helper 1 pattern IFN-gamma and a T-helper 2 pattern causing an expansion of B-lymphocytes, subsequently differentiating into plasma cells that secrete anti-gliadin and anti-tissue-transglutaminase antibodies.[6][18]

Histopathology

For celiac disease, the histological changes that are expected in the small intestines are an increased number of intraepithelial lymphocytes, elongation of crypts, and partial to total villous atrophy.[16][19]

History and Physical

Clinicians should obtain a comprehensive history, including whether the patient has had a prior food allergic reaction to wheat or had a respiratory allergy to wheat flour.[5][20][21] If a patient develops symptoms anywhere from 1 to 3 hours after the exposure to wheat, the allergy to wheat should be confirmed by measuring IgE specific to wheat by skin prick test (SPT) or via serum IgE. An additional history that is important includes occupational history including current and past employment.[21]

Symptoms consistent with a wheat allergy would include urticaria, angioedema, asthma, allergic rhinitis, abdominal pain, vomiting, acute exacerbation of atopic dermatitis, and/or exercise-induced anaphylaxis.[1][22][23][24]

Patients with wheat dependent exercise-induced anaphylaxis (WDEIA) usually have symptoms that include pruritus, urticaria, angioedema, flushing, shortness of breath, dysphagia, chest tightness, profuse sweating, syncope, headache, diarrhea, nausea, throat closing, abdominal pain, and hoarseness that occurs during intense physical exercise following wheat intake in the prior 4 hours before symptom onset.[1][25]

Those with celiac disease will present with diarrhea, constipation, bloating, abdominal pain, anorexia, flatulence, weight loss, poor growth in childhood, anemia, dermatitis herpetiformis, fatigue, and even osteoporosis.[16]

Evaluation

As above, anyone who develops an allergic reaction to wheat exposure should be checked for IgE specific to wheat via a skin prick test or serum IgE.[1] A positive test for a serum IgE to wheat without a clinical history of symptoms after wheat exposure is not enough to diagnose a wheat allergy as people can be sensitive to wheat but can tolerate exposure to wheat.[1][26][27] Moreover, diagnosis of an allergy based on wheat flour extract cannot differentiate between those having a respiratory allergy versus those suffering from a food allergy to wheat.[1] The exact level of IgE that predicts whether the reaction is a true allergy in over 90% of patients is not well known.[1] Generally, children with even high levels of IgE can tolerate certain foods when undergoing an oral food challenge and thus it is difficult to correlate an IgE level to a wheat allergy.[1][5][28][29][30] Moreover, an evaluation of a wheat allergy should be done by a health care provider as there is a potential risk of anaphylaxis and the need for epinephrine.[1][22][23]

For those being worked up for WDEIA, SPT or specific IgE to wheat, gluten, and omega-5-gliadin should be ordered.[1][20][31][32]

For patients being evaluated for bakers asthma, the lower limit with a positive predictive value of 100 percent was 2.32 kU/L for specific wheat IgE and 5.0 mm for wheat on SPT with wheat flour extracts.[1][33] The gold standard to confirm the diagnosis of wheat-induced occupational allergy is a bronchial challenge test which consists of a nebulized aqueous flour solution in increasing concentrations (0.01, 0.1, 10, and 100 mg/mL) or by inhaling wheat flour dust.[1] Bakers asthma is diagnosed if a bronchial challenge test induces at minimum a 20% decrease in forced expiratory volume in one second (FEV1) or a 3-fold increase in bronchial hyperreactivity with an increase in sputum eosinophilia.[1][34]

For celiac disease, measurement of serum IgA antibody to tissue transglutaminase (anti-tTG) should be the first screening test ordered.[16] For those with IgA deficiency, deamidated gliadin peptides-antibody of the IgG class can be used as an initial screening test.[16] An IgA antiendomysial antibody has a 98% specificity for active celiac disease and should be ordered as a confirmatory test.[16][35]

Treatment / Management

Primary treatment and management of wheat allergies is avoidance of both food and inhaled wheat allergens.[1] For celiac disease, a lifelong, gluten-free diet is the current treatment option.[6]

In cases of exposure and an anaphylactic reaction, the administration of epinephrine is the lifesaving treatment. Epinephrine comes in either a 0.15 or 0.3 mg intramuscular injection and is typically injected into the lateral thigh. All patients should go to the emergency room for further evaluation and antihistamines, glucocorticoids, and beta-agonist are additional secondary treatment options.[1][23] Additional treatments include immunotherapy such as oral immunotherapy (OIT), sublingual immunotherapy (SLIT) and epicutaneous immunotherapy (EPIT).[1][36] OIT and SLIT both utilize the principle of gradually increasing the amount of food ingested leading to desensitization and thus hopefully helping to avoid experiencing an allergic reaction. EPIT utilizes a skin patch to deliver an allergen to the patient. Those with WDEIA require epinephrine and can avoid symptoms by, avoiding exercising within 4 to 6 hours

after wheat ingestion, avoid exercising alone or in hot weather/pollen season, and carrying emergency medication.
[1][20]

Differential Diagnosis

The differential diagnosis for a wheat allergy is broad and includes non-IgE-mediated food allergy (food protein-induced enterocolitis), flush syndrome (carcinoid, postmenopausal, chlorpropamide-alcohol, autonomic epilepsy), restaurant syndromes (sodium glutamate, sulfites, scombroid), non-anaphylactic shock (hemorrhagic, cardiac, endotoxic, monoclonal gammopathy), syndromes with excessive endogenous production of histamine (idiopathic angioedema, mastocytosis, urticaria pigmentosa, basophil leukemia, promyelocytic acute leukemia, hydatid cyst), nonorganic syndromes (panic attack, Munchausen, vocal cord dysfunction, hysteric bolus, anorexia nervosa), and miscellaneous (hereditary angioedema, anaphylaxis due to progesterone, urticarial vasculitis, pheochromocytoma, hyper IgE syndrome, seizures, strokes, pseudo-anaphylaxis, red man syndrome, constipation, irritable bowel syndrome).[1]

Prognosis

For those with celiac disease, adherence to a gluten-free diet might prevent morbidity and mortality associated with celiac disease.[16]

Complications

Conditions associated with celiac disease include type 1 diabetes, autoimmune thyroid disorders, autoimmune hepatitis, and neurological disorders such as epilepsy.[6] Complications of celiac disease can include but are not limited to anemia, anxiety, arthralgia, arthritis, dental enamel hypoplasia, delayed puberty, depression, fatigue infertility, osteoporosis, pancreatitis, peripheral neuropathy, and short stature.[16] Other complications of celiac disease can include enteropathy-associated, intestinal, T-cell lymphoma, small bowel adenocarcinoma, and non-Hodgkin lymphoma.[6]

Consultations

Important consultation for a wheat allergy includes an allergy and immunology physician, gastroenterologist, and nutritionist. If a patient is having gastrointestinal (GI) symptoms, a gastroenterologist can help determine differential diagnoses, conduct further testing, and determine the etiology of the symptoms. An allergist can do skin and blood testing to make the diagnosis and guide treatment options, such as immunotherapy. Additional consultations that would be helpful would be a nutritionist who can guide dietary changes that need to be made to avoid wheat from one's diet.

Deterrence and Patient Education

Patients who have signs or symptoms of a wheat allergy should see a doctor as soon as possible as it can be a life-threatening disease. Those that are already diagnosed should make sure they avoid wheat and to always carry epinephrine. Following up with an allergist can offer treatment options such as immunotherapy. Those with celiac disease should maintain a gluten-free diet to avoid symptoms and follow up with a gastroenterologist.

Pearls and Other Issues

A wheat allergy can be life-threatening, and it is vital that patients carry epinephrine. Patients should follow up with an allergist for treatment goals. Patients will also benefit from a gastroenterology followup as patients frequently have GI symptoms, especially if they have celiac disease.

Enhancing Healthcare Team Outcomes

Wheat allergies are just one of the many allergic reactions that a patient can face. A multidisciplinary allergy clinic can improve families' ability to manage allergies and reduce allergic reactions.[37] (Level II)

Questions

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