



DIAGNOSIS OF GLUTEN SENSITIVITY AND WHEAT RELATED ALLERGIES

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OUTLINE

- ▶ Introduction to Gluten sensitivity
- ▶ Definition of terms
 - ▶ Coeliac disease
 - ▶ Wheat allergy
 - ▶ Non coeliac gluten sensitivity
- ▶ Clinical manifestations of gluten related disorders
- ▶ Initial testing for gluten related disorders
- ▶ Confirmatory tests for gluten related disorders
- ▶ Summary
- ▶ Questions

Introduction to gluten sensitivity



Introduction to gluten sensitivity

- ▶ How many have heard of someone who is excluding gluten (or wheat) from their diet?
- ▶ 30% of people in the US are limiting gluten ingestion₁. It's here too.
- ▶ The gluten related disorders account for a small percentage of those following a gluten free diet and the vast majority has no medical necessity for doing so.

Introduction to gluten sensitivity

- ▶ Gluten related disorders include
 - ▶ **Coeliac disease**
 - ▶ **Wheat allergy**
 - ▶ **Non coeliac gluten sensitivity**

Definition of terms

1. Coeliac disease.

Coeliac disease is an **immune-mediated systemic disorder** triggered by **gluten and related prolamines present in wheat, barley and rye** that occurs in **genetically susceptible individuals**.

Definition of terms

immune-mediated systemic disorder – Inflammatory process mediated by T-cells leading to mucosal damage of the small bowel.

What are gluten and related prolamines? –Gluten is a protein component of wheat. Contains glutamine and prolamines. Prolamines also found in barley and rye.

genetically susceptible individuals – HLA-DQ2 and/or HLA-DQ8 haplotypes.

Definition of terms

2. Wheat allergy.

Wheat allergy is a **hypersensitivity reaction** to **wheat proteins** mediated through **immune mechanisms and involving mast cell activation**. It is most commonly a **food allergy**, but wheat can become a sensitizer when the exposure occurs through the skin or airways.

Definition of terms

- ▶ The immune response can be Ig E mediated, non Ig E mediated or a combination of both.
- ▶ Reaction to insoluble gliadins, particularly ω -5 gliadin.
- ▶ Usually not allergic to other prolamines containing grains such as rye and barley, and therefore diet less restrictive.

Definition of terms

▶ 3. Non coeliac gluten sensitivity.

This is a poorly defined syndrome characterized by a variable combination of intestinal and extra-intestinal symptoms, typically occurring soon after ingestion of gluten-containing foods and disappearing quickly upon their withdrawal.

Definition of terms

- ▶ **3. Non coeliac gluten sensitivity.**

Occurs in individuals where both coeliac disease and wheat allergy have been excluded.

Clinical manifestations

There is a lot of overlap of symptoms between the three conditions.

1. Coeliac disease

▶ Intestinal manifestations. –

- ▶ Malnutrition
- ▶ protein losing enteropathy
- ▶ abdominal pain and distention
- ▶ diarrhoea
- ▶ steatorrhea
- ▶ severe constipation.

*severe manifestations have become progressively less common.

Clinical manifestations

1. Coeliac disease

▶ Extraintestinal manifestations. –

- ▶ Lethargy, hypotension and electrolyte disturbances.
- ▶ Anaemia- iron deficiency.
- ▶ Linear growth failure
- ▶ Dermatitis Herpetiformis
- ▶ Dental enamel hypoplasia

Clinical manifestations

1. Coeliac disease

- ▶ Extraintestinal manifestations. –
 - ▶ Recurrent aphthous ulcers
 - ▶ Arthritis/ arthralgia
 - ▶ Increase in headaches, peripheral neuropathy and seizures.
 - ▶ Psychiatric issues including anxiety, recurrent panic attacks, hallucinations, depression and increased suicidal behaviour

Dermatitis herpetiformis



- ▶ Common in adults or older children.
- ▶ Symmetrical, pruritic blisters.
- ▶ Lead to erosions, excoriations
- ▶ Commonly elbows, knees, shoulders, buttocks.
- ▶ Diagnosed on Ig A deposits in skin biopsies.

Dental enamel hypoplasia



Clinical manifestations

- ▶ **2. Wheat allergy**
 - ▶ Swelling and itching of the lips or mouth
 - ▶ Atopic dermatitis
 - ▶ Hives
 - ▶ Allergic rhinitis
 - ▶ Asthma
 - ▶ Angioedema
 - ▶ Anaphylaxis

Clinical manifestations

- ▶ **2. Wheat allergy**
 - ▶ Abdominal pain
 - ▶ Bloating
 - ▶ Diarrhoea
 - ▶ Nausea
 - ▶ Vomiting
 - ▶ Constipation
 - ▶ Eosinophilic esophagitis
 - ▶ fatigue

Clinical manifestations

- ▶ **2. Wheat allergy**

- ▶ Wheat dependent, exercise-induced anaphylaxis (WDEIA)
- ▶ Baker's asthma

Clinical manifestations

▶ 3. Non coeliac gluten sensitivity.

- ▶ Multisystemic, characterized by a variable combination of intestinal and extra-intestinal symptoms.
- ▶ Latency period may be between hours to days.
- ▶ Irritable bowel syndrome- bloating, abdominal pain and change in bowel consistency and frequency of bowel movements.

Clinical manifestations

- ▶ **3. Non coeliac gluten sensitivity.**
 - ▶ Headache, migraine, foggy mind
 - ▶ Chronic fatigue
 - ▶ Joint and muscle pain

Who should be tested for gluten related disorders?

▶ **Symptomatic individuals.**

- ▶ The three conditions cannot be distinguished from each other on the basis of symptoms.
- ▶ Test for CD in those with chronic diarrhoea, abdominal pain, distension and weight loss.
- ▶ Consider tests in those with unexplained constipation, linear growth failure, anemia, fatigue, arthralgia, and elevated liver enzymes.

Who should be tested for gluten related disorders?

- ▶ **Symptomatic individuals.**

- ▶ Test for WA if there are symptoms occurring shortly, or within a few hours, after consuming wheat products.
- ▶ No test to identify NCGS. Rule out CD and WA first.
- ▶ A gluten challenge should be considered in those who initiate a Gluten Free Diet prior to confirmatory diagnosis testing.

Who should be tested for gluten related disorders

▶ **Asymptomatic individuals**

- ▶ Those belonging to groups known to be at increased risk for CD
 - ▶ Children who are first degree relatives of an index case
 - ▶ Trisomy 21
 - ▶ Turner's syndrome
 - ▶ William's syndrome
 - ▶ Ig A deficiency
 - ▶ Those with other autoimmune conditions.
 - ▶ Type 1 diabetes

Initial testing for gluten related disorders

- ▶ Coeliac disease. (Ensure adequate exposure to gluten).
 - ▶ Anti tissue transglutaminase Ig A antibody – to identify people who **may** have coeliac disease. Also obtain serum Ig A to identify those who have selective Ig A deficiency. Sensitivity 90-100%, specificity 95-100%.
 - ▶ In Ig A deficiency, and Ig –G based TTG, Endomysial antibody or deamidated gliadin peptides assay is required.

Initial testing for gluten related disorders

- ▶ Coeliac disease
 - ▶ In <2years combine anti TTG with DGP IgG to improve accuracy.
 - ▶ People with associated autoimmune conditions may have transient elevation of anti TTG. Do anti EMA-Ig A before proceeding to biopsy.
 - ▶ Transient elevations of Anti TTG can occur during an acute infectious process.

Initial testing for gluten related disorders

- ▶ Coeliac disease

- ▶ HLA tests.

- ▶ Not specific to people with Coeliac disease. 40% in general population in the developed countries.
 - ▶ Used as a screening tool for asymptomatic children who are family members of an index case.
 - ▶ Useful when there is a discrepancy between serological tests and histology or when a gluten free diet has been started prior to any testing.

Initial testing for gluten related disorders

- ▶ Wheat allergy
 - ▶ Sensitization can be demonstrated by measurement of circulating Ig E specific antibodies and skin sensitivity testing.
 - ▶ Specific Ig E- sensitivity 83% and specificity 43%
 - ▶ Skin sensitivity- skin prick, skin patch or intradermal injection. Sensitivity 73% and specificity 73%.
 - ▶ Many children with eczema have a positive SPT yet do not display an allergic reaction when ingesting wheat

Initial testing for gluten related disorders

- ▶ Non-coeliac gluten sensitivity.
 - ▶ There are no initial tests to identify people who may have NCGS.
 - ▶ ? Elevated Anti Gliadin Antibodies/ HLA DQ2 or HLADQ8.
 - ▶ Consider after excluding Coeliac and Wheat allergy.

Confirmatory tests for gluten related disorders.

- ▶ The diagnosis of Coeliac disease is confirmed on demonstration of the characteristic changes in the histology of the small intestinal mucosa.
- ▶ These include infiltration of lymphocytes in the epithelium, increased density and depth of the crypts and progressive flattening of the villi.
- ▶ Marsh classification of histological changes in CD.

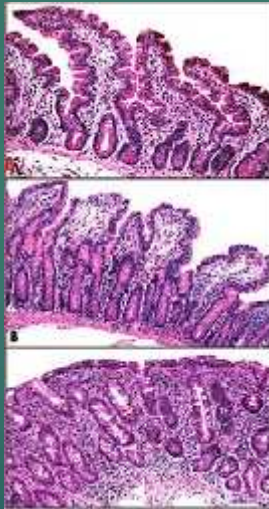
Confirmatory tests for gluten related disorders.

- ▶ These changes are not unique to CD.
- ▶ Can be in autoimmune enteropathy, food allergies, inflammatory bowel disease and infections.
- ▶ Clinical history, serological tests, and response to Gluten free diet are important.
- ▶ Exceptions: ESPGHAN recommends foregoing the biopsy in patients with classical symptoms, anti TTG > 10 times normal, positive EMA-Ig A and presence of HLADQ2/HLADQ8. (not universally accepted).

Confirmatory tests for gluten related disorders

- ▶ When serological tests are positive and histology fails to confirm CD
 - ▶ Check if patient on adequate amount of gluten.
 - ▶ Site of biopsy.
 - ▶ Adequate biopsies due to patchiness of CD.
 - ▶ HLA typing useful.

Histology in coeliac disease.



Confirmatory tests for gluten related disorders

- ▶ Wheat allergy
 - ▶ Confirmation of wheat allergy requires an oral food challenge.
 - ▶ A double blind, placebo controlled (DBPC) challenge is the most accurate.
 - ▶ This is difficult to undertake.
 - ▶ In clinical practice symptom resolution in response to dietary elimination of wheat is usually regarded as confirmation of the suspected diagnosis.

Confirmatory tests for gluten related disorders

- ▶ Non coeliac gluten sensitivity

- ▶ Confirming a diagnosis of NCGS is twofold

1. For those on unrestricted diet, observe the clinical response to the gluten free diet
2. Measuring the effect of ingesting gluten in those patients on a gluten free diet.

Evaluate using a questionnaire assessing baseline intestinal and extra-intestinal symptoms. Evaluate after 6 weeks and assess difference in the scores. Currently a change of >30% is considered a symptomatic response.

SUMMARY

- ▶ Gluten related disorders are divided into 3
 - ▶ Coeliac disease
 - ▶ Wheat allergy
 - ▶ Non coeliac gluten sensitivity.
- ▶ Clinical symptoms, though differing somewhat, are not diagnostic due to a lot of overlap.
- ▶ Coeliac disease requires a histological diagnosis
- ▶ Wheat allergy requires an oral challenge for diagnosis.
- ▶ Non Coelian Gluten Sensitivity is a diagnosis made after excluding the other two.

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QUESTIONS