Autoimmune testing, diagnosis and treatment in gastroenterology

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Celiac disease (CD) overview

* Celiac disease versus non celiac gluten sensitivity
* Whom to test
* Serological tests
* Treatment
* Non responders

Celiac disease

- First described in 1887 by Samuel Gee
  - Immune reaction to dietary gluten
  - Affects the small bowel mucosa
  - Genetically susceptible patients
  - Resolves on a gluten free diet (GFD)
  - Relapses when gluten reintroduced
- Increasing in prevalence

Celiac disease

* Gluten sensitive enteropathy
* Non celiac gluten sensitivity (NCGS)

Celiac versus NCGS

* Nutritional deficiencies
* Malignancy risk
* Degree of adherence to GFD
* Family implications

Whom to test

- GI symptoms
  - Diarrhea
  - Malabsorption
  - Wt loss
  - Gas, bloating and distension
  - Irritable bowel symptoms

Whom to test

- Iron deficiency anemia
- Folate and B12 deficiency
- Elevated LFTs
- Pediatrics: short stature, delayed puberty, FTT
- GYN: recurrent fetal loss, low birth wt, reduced fertility
- Neuro: idiopathic neuropathy, migraine

Whom to test

- Type I DM, thyroid disease, auto immune hepatitis
- Down's syndrome
- Dermatitis herpetiformis
- First degree relatives with CD
- Osteoporosis

Diagnostic tests

- No single test can confidently diagnose CD in all patients
- Gluten rich diet
- Serological
- Small bowel biopsy
- HLA typing for DQ2/DQ8. Genetically susceptible to CD

Serologies for CD

* Anti gliadin Ab
* Anti IgA endomysial Ab (EMA)
* Anti IgA tissue transglutaminase Ab (tTG)
* Anti IgG tissue transglutaminase Ab
* Anti IgA deaminated gliadin peptide (DGP)
* Anti IgG deaminated gliadin peptide

Anti gliadin Ab

* Component of wheat protein gluten
* Low PPV
* Not recommended

IgA EMA

- Endomysium is connective tissue that surrounds smooth muscle fibers
- Target antigen is tTG
- Moderately sensitive and highly specific
- Even low titers are positive

tTG Ab

* Antigen that EMA is directed against
* Highly sensitive and specific
* ELISA test less costly than EMA

DGP Ab

- Second generation anti gliadin Ab
- Synthetic gliadin peptides that mimic tTG-modified gliadin sequences
- Highly sensitive and specific

Sensitivity and specificity

	Sensitivity	Specificity
IgA EMA	85-98%	97-100%
IgA tTG	90-98%	95-97%
IgA DGP	94%	99%
IgG DGP	92%	100%

Diagnostic approach

- IgA tTG Ab is the single preferred test
- Total serum IgA
- Alternate approach is IgA and IgG based testing

Symptoms but negative serologies

- Selective IgA deficiency
- Gluten free diet
- True false negative
- Symptoms not CD related, e.g.. wheat allergy or NCGS

Diagnosis while on a GFD

- Serological tests may become negative on a GFD
- Anti tTG, EMA and DGP antibodies
- If positive serology, proceed to small bowel biopsy
- If negative serology, HLA typing (DQ2 and DQ8). If positive, proceed to small bowel biopsy

GFD with positive serology or positive HLA typing

- Positive biopsy → patient has CD
- Negative biopsy → gluten challenge

Gluten challenge

- 3g gluten daily for 2wks
  - 68% positive biopsy
  - 75% positive serology
  - 90% either positive
- If negative, 3g gluten daily for another 6wks

Treatment

- Education
- Dietician assisted lifelong GFD
- Rx nutritional deficiencies
- Longitudinal care to monitor for complications

Gluten free diet

- Cornerstone of management
- Avoid wheat, barley and rye
- Avoid dairy initially; secondary lactose intolerance
- Oats; limit to 50-60g (2oz) a day with mild disease

Is strict adherence to a GFD necessary?

* Major life changing diagnosis
* Significant lifestyle restrictions
* Compliance is often limited

Strict GFD

- Micronutrient deficiencies
  - vitamin D deficiency and bone loss
- Increased mortality and malignancy
- Increased risk of autoimmune disease
  - Type I DM, thyroiditis, connective tissue diseases

Monitoring a GFD

- Variable response rate to GFD
- Symptom improvement in 2wks
- Blood work in 4-6wks
  - Nutritional parameters
  - CD serologies
    - Drop in titers compared to pretreatment levels
    - Baseline value in 3-12months
    - Inadvertent or intentional gluten ingestion

Monitoring a GFD

- Small bowel biopsy
  - Repeat biopsy is not routinely necessary
  - Symptoms persist or recur despite a GFD

Non responders

- Poor compliance to a GFD
  - Most common reason
- Other disorders
  - Erroneous diagnosis of CD
  - False positive serology
  - Villous atrophy not pathognomonic of CD

Non responders

- Concurrent disorders
  - Lactose intolerance
  - IBS
  - SIBO
  - Microscopic colitis
    - Assoc with more severe villous atrophy
    - Steroids and immuno suppressants

Non responders

- Intestinal lymphoma
  - Symptom recurrence
  - Fevers, hepatosplenomegaly, duodenal mass, ascites, SBO and GI bleeding
  - Enterography for diagnosis

Nutritional deficiencies

- Vitamin A, D, E, B12, Ferritin, folate, micronutrients
- Bone loss
  - Osteopenia due to vitamin D deficiency
  - DXA scanning
  - Partially reversed with a GFD

Summary

- CD is increasing in prevalence
- Diagnostic testing on a gluten rich diet
- IgA tTG Ab is single preferred test together with total serum IgA levels
- Small bowel biopsies necessary
- CD improves on a GFD and relapses with reintroduction of gluten

Summary

- Strict adherence to a GFD
- Use of serologies to assess response to dietary therapy
- Test and treat nutritional deficiencies
- Bone loss is common
- Non compliance is most common reason for lack of response