Conflicts of Interest

• None to disclose
• Format
  • Present a case
  • Do a pretest about the evaluation
  • Review case
  • Discuss the questions & answers
The patient is a 40 year old female being seen because of crampy abdominal discomfort and diarrhea. The discomfort is generalized and mild. There are no obvious precipitating or relieving factors. The diarrhea consists of one to two slightly loose stools a day. She only rarely has formed bowel movements.
She denies rectal bleeding, nocturnal diarrhea, or malodorous stools. She has had both symptoms for several years, but they have become somewhat more pronounced recently. Her GI history and ROS are otherwise unremarkable.
PMH – Neg.

SH, FH, & ROS – Neg.

PE – Normal

Labs
Recent labs done in the ER were all normal, including: CBC, CMP, TSH, & ESR

KUB – nonspecific bowel gas pattern
Question #1

She tells you that she has been hearing a lot about gluten sensitivity and wants to know if she has celiac disease. What is the best first test or set of tests?

1. Anti-gliadin antibody
2. Tissue transglutaminase (tTG) Ab - IgA class
3. Tissue transglutaminase (tTG) Ab - IgA class & Total IgA level
4. Empiric trial of a gluten free diet
5. EGD with small bowel biopsy
She asks you if Celiac disease is very common in the United States.
Question #2

The prevalence of celiac disease in the United States is currently thought to be approximately:

1. 10%
2. 1%
3. 0.1%
You order a tissue transglutaminase (tTG), and it comes back positive.

She has a follow-up appointment two weeks later. Her history and exam are unchanged.
Question #3

What do you do next?

1. Recommend a gluten-free diet
2. Recommend EGD with small bowel biopsies
She doesn't want an EGD and requests a referral to a nutritionist for dietary counseling regarding a gluten-free diet.

She comes back in two months and has been following the diet very carefully. However, she wasn't able to keep the appointment with the nutritionist.

Her symptoms are only slightly better.
She now tells you that she and her husband are having marital problems. This has been extremely upsetting. In the past she has had a change in bowel habits and similar abdominal discomfort when under stress. Several years ago she was told that she might have irritable bowel syndrome.

She asks you if her lack of response to the diet means that she has irritable bowel syndrome (IBS) and not celiac disease.
Question 4

She might have celiac disease but is not following a strict gluten-free diet.

• True
• False
The initial tTG could have been a false positive, and she might not have celiac disease.

- True
- False
You have a medical student observing you. She has just finished reviewing clinical epidemiology and asks you to explain what the positive predictive value (PPV) of a tTG is.
Question #6

Assuming the prevalence of celiac disease is 15%, and the sensitivity and specificity of the tTG are both 98%, the PPV will be:

1. 95%
2. 90%
3. 50%
When you tell the patient that it is hard to know at this point whether or not she has celiac disease, she says she is willing to undergo an EGD if that will help. However, she wants to keep her invasive testing to a minimum and is even willing to go back on a gluten-containing diet if that will help make the diagnosis.
In order to follow her wishes and keep the testing to a minimum as well as maximizing the chance of having a conclusive test, you suggest that she resume a gluten-containing diet and then have an EGD. She agrees.
Question 7

How long should she be on a gluten-containing diet before having an EGD?

1. She hasn't been on the gluten-free diet long enough to affect the biopsies. You can do the EGD and SB biopsies now.

2. Wait four weeks. That is probably enough for most patients.
Some patients can take years before having a relapse after resuming a gluten-containing diet.

- True
- False
You eventually make the diagnosis of celiac disease by small bowel biopsy on a gluten-containing diet. On a follow up appointment, she says that she has been reading on the Internet that her children and other first degree relatives may be at increased risk for celiac disease. She requests that you call their pediatrician to discuss this issue.
Question 9

Her children have an increased risk of developing celiac disease.

- True
- False
Question 10

Her children's pediatrician reports that your patient is insisting her children be tested. He tells you that they are asymptomatic. He wants to know the best first test to order.

You suggest:
1. Tissue transglutaminase (tTG) IgA
2. EGD with small bowel biopsy
3. HLA Testing to determine if they have DQ2 or DQ8
Resources

- AGA Institute Medical Position Statement on the Diagnosis and Management of Celiac Disease

- American Gastroenterological Association (AGA) Institute Technical Review on the Diagnosis and Management of Celiac Disease

- National Institutes of Health Consensus Development Conference Statement on Celiac Disease, June 28–30, 2004
  - GASTROENTEROLOGY 2005;128:S1–S9
Definition

• Celiac disease is a life-long inflammatory condition of the gastrointestinal tract that affects the small intestine in genetically susceptible individuals.
  • Small bowel mucosal inflammation and villous atrophy which occur with exposure to the wheat protein gluten
• Older and less preferred terms
  • Nontropical sprue
  • Celiac sprue
Etiology

- An inappropriate T-cell–mediated immune response to ingested gluten that causes inflammatory injury to the small intestine in genetically predisposed persons.
Serological Testing

- These tests have increased our understanding of the prevalence of celiac disease.
- Test while on a diet containing gluten, ideally a significant amount of gluten.
- False negatives can result from testing patients who have already started a gluten-free diet.
- Antibodies remain elevated for 1 to 12 months.
IgA Antihuman Tissue Transglutaminase AB (tTG)

- Tissue transglutaminase is an intracellular enzyme.
- Released by inflammation
- Test Characteristics
  - Sensitivity of 90% to 96%
  - Specificity is greater than 95%
- Not positive in patients with IgA deficiency
IgA Endomysial Antibody Immunofluorescence (EMA)

- EMA and tTG appear to have equivalent diagnostic accuracy.
- tTG is the specific protein that is identified by the IgA-EMA.
- Technical issues with the test mean IgA tTG AB is used instead.
Antigliadin Antibody (AGA)

- No longer routinely recommended because of lower sensitivity and specificity
- Frequent false positives
- An older test
Patients with negative serologic testing and suggestive symptoms

- Possibilities
  - IgA deficiency
  - False negative test
    - Low-gluten diet at the time of testing
  - Not celiac disease
Prevalence of IgA Deficiency

• 1:500 to 1:700 individuals in the population
• Occurs in 2% to 5% of patients with Celiac disease
• Testing strategy for IgA deficient patients
  – IgG-tTG or IgG-EMA tests are available
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4. Empiric trial of a gluten free diet
5. EGD with small bowel biopsy
Prevalence of Celiac Disease

• More common than previously recognized
• Range of 0.5% to 1% in the United States
  • Includes symptomatic and asymptomatic individuals
  • Limited studies about prevalence in non-Caucasians
  • Appears to be more common in Northern Europe population
Question #2

The prevalence of celiac disease in the United States is currently thought to be approximately:

1. 10%
2. 1%
3. 0.1%
Question #6

Assuming the prevalence of celiac disease is 15%, and the sensitivity and specificity of the tTG are both 98%, the PPV will be:

1. 95%
2. 90%
3. 50%

Note: The question weights the prevalence and test characteristics in favor of a high PPV.
How is the diagnosis made?

• No one test can conclusively make or exclude the diagnosis.
  • There is a spectrum of celiac disease.
  • There is a range of laboratory and pathology findings.
  • Ideally, all testing should be done while the patients is on a gluten-containing diet.
• Serologic testing is the first step.
Small bowel biopsies

- Indicated in patients with positive celiac antibody testing
  - Except with biopsy-proven dermatitis herpetiformis
- Done by EGD
- Endoscopic appearance by itself is not enough to rule out the diagnosis.
Making the Diagnosis

- Presumptive diagnosis
  - Positive serologic tests and biopsy
- Definitive diagnosis
  - Symptoms resolve on a gluten-free diet
  - Repeat small bowel biopsy to document normalization on a gluten-free diet is no longer recommended to establish the diagnosis.
- When diagnosis is uncertain
  - Consider obtaining HLA haplotypes
  - Over 97% of patients with celiac disease have the DQ2 and/or DQ8 marker
  - High negative predictive value
    - If the patient is negative for DQ2 and DQ8, it is very unlikely that they have celiac disease.
Question #4

She might have celiac disease but is not following a strict gluten-free diet.

- True
- False
Question #5

The initial tTG could have been a false positive, and she might not have celiac disease.

• True
• False
Question #3

What do you do next?

1. Recommend a gluten-free diet
2. Recommend EGD with small bowel biopsies
Question 7

How long should she be on a gluten-containing diet before having an EGD?

1. She hasn't been on the gluten-free diet long enough to effect the biopsies. You can do the EGD and SB biopsies now.
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Question 8

• Some patients can take years before having a relapse after resuming a gluten-containing diet.

• True
  • False
Screening

- First-degree relatives of patients with celiac disease are at higher risk for biopsy-confirmed celiac disease than those in the general population.
  - Prevalence of 10%.
- There are no current recommendations to screen the general population for celiac disease.
- First-degree relatives should be screened only if they have suggestive symptoms.
Question 9

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- True
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Question 10

Her children's pediatrician reports that your patient is insisting that her children be tested. He tells you that they are asymptomatic. He wants to know the best first test to order.

You suggest:
1. Tissue transglutaminase (tTG) IgA
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Question #3

What do you do next?

1. Recommend a gluten-free diet
2. Recommend EGD with small bowel biopsies
Treatment

- Six key elements to management
  - Consultation with a skilled dietitian
  - Education about the disease
  - Lifelong adherence to a gluten-free diet
  - Identification and treatment of nutritional deficiencies
  - Access to an advocacy group
  - Continuous long-term follow-up by a multidisciplinary team
Treatment (cont.)

• Needs to be life long
• Gluten-free diet
  • Wheat, rye, and barley
  • Oats
    • Data about tolerance is unclear
    • Most commercially available oat products are contaminated with wheat gluten.
    • Recommendation is to avoid oats
  • Beer
    • Gluten-free beer is available
      • Made with rice, sorghum, buckwheat, and corn
Screening

- Specific diseases (a partial list)
  - Type 1 diabetes mellitus
    - Especially individuals with gastrointestinal (GI) symptoms
    - Benefits of screening individuals without GI symptoms is unclear
  - Autoimmune thyroid and hepatobiliary disorders
    - Primary biliary cirrhosis
  - Down and Turner syndromes