Diagnostic Testing Algorithms for Celiac Disease

Presenter:

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Disclosures

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Utilization Message

• As you view this presentation, consider the following important points regarding testing:
  • How is the test going to be used in your practice?
  • When should the tests be used?
  • How will results impact patient management?
Introduction to Celiac Disease

- Chronic inflammatory disease targeting the small intestine
  - Associated with production of autoantibodies
  - Pro-inflammatory immune reaction within small intestine leads to damage and atrophy of intestinal villi

Clinical Manifestations of Celiac Disease

- Gastrointestinal
  - Diarrhea
  - Weight loss
  - Steatorrhea
  - Abdominal pain
  - Bloating
  - Constipation
  - Nausea

- Malabsorption
  - Fe-deficient anemia
  - B12 deficiency
  - Folate deficiency
  - Hypoproteinemia
  - Hypocalcemia

- Extra-GI
  - Ataxia
  - Infertility
  - Arthralgias
  - Dermatitis herpetiformis
  - Hyposplenism
  - Other autoimmune conditions
Factors Associated with Development of Celiac Disease

- Genetic component
  - Increased risk for family members
    - Prevalence of 10% in first-degree relatives
  - Known genetic association
    - HLA-DQ2
    - HLA-DQ8

- Environmental component
  - Ingestion of cereal grain proteins
    - Wheat
    - Barley
    - Rye
  - Collectively referred to as gluten

Diagnosis of Celiac Disease

- Initial diagnosis
  - Positive antibody serology
  - Intestinal biopsy with characteristics of villous atrophy

- Definitive diagnosis
  - Resolution of clinical symptoms after initiation of gluten-free diet
    - Generally accompanied by conversion to negative serology and reconstitution of intestinal villi
Diagnosis of Celiac Disease

• Serologic tests
  • Endomysial antibodies
  • Tissue transglutaminase antibodies
  • Gliadin antibodies
    • Unmodified gliadin antigen
    • Deamidated gliadin antigen

• Genetic tests
  • HLA-DQ2 and HLA-DQ8

• Serologic tests
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• Genetic tests
  • HLA-DQ2 and HLA-DQ8
Caveats of Serology Testing for Celiac Disease

- Selective IgA deficiency
  - Defined as absence of IgA in presence of normal IgG and IgM production
  - More common in patients with celiac disease compared to general population
  - IgA isotype for celiac-specific serologies more sensitive and specific compared to IgG isotype
- Effect of gluten-free diet
  - Downregulation of inflammatory immune response
  - Reduction in autoantibody production

Caveats of Genetic Testing for Celiac Disease

- HLA-DQ2
  - Present in 90% to 95% of patients with celiac disease
- HLA-DQ8
  - Present in 5% to 10% of patients with celiac disease
Caveats of Genetic Testing for Celiac Disease

- **HLA-DQ2**
  - Present in 90% to 95% of patients with celiac disease
- **HLA-DQ8**
  - Present in 5% to 10% of patients with celiac disease

Combined frequency of 30%-40% in most US and European populations

Negative for HLA-DQ2 and DQ8
Exclude celiac disease as a possible diagnosis
Caveats of Genetic Testing for Celiac Disease

- **HLA-DQ2**
  - Present in 90% to 95% of patients with celiac disease

- **HLA-DQ8**
  - Present in 5% to 10% of patients with celiac disease

Combined frequency of 30%-40% in most US and European populations

**Negative for HLA-DQ2 and DQ8**
Exclude celiac disease as a possible diagnosis

**Positive for HLA-DQ2 and/or DQ8**
Consistent with possible diagnosis of celiac disease

Test Performance and Utility

- **TTG and deamidated gliadin IgA**
  - Best combination of sensitivity and specificity

- **EMA IgA**
  - Excellent specificity
  - Analytical challenges

- **TTG and deamidated gliadin IgG**
  - Most appropriate in context of IgA deficiency

- **HLA-DQ2 and HLA-DQ8**
  - Useful as rule-out test
Laboratory Testing Algorithms

- Celiac Disease Serology Cascade
  - CDSP
  - Serologic testing only

- Celiac Disease Comprehensive Cascade for Patients on a Gluten-Free Diet
  - CDGF
  - Perform serology only for individuals with HLA-DQ2 and/or HLA-DQ8 alleles

- Celiac Disease Comprehensive Cascade
  - CDCOM
  - Serologic and genetic testing
HOT TOPIC / Diagnostic Testing Algorithms for Celiac Disease

Summary

• Laboratory diagnostic testing algorithms
  • Celiac Disease Serology Cascade (CDSP)
  • Celiac Disease Comprehensive Cascade (CDCOM)
  • Celiac Disease Comprehensive Cascade for Patients on a Gluten-Free Diet (CDGF)
• Individual test options
  • Most appropriate for monitoring patients on a gluten-free diet

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