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Celiac Disease

AT WAR WITH WHEAT

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Slide 2

Objective

- 1. Recognize Signs, Symptoms and Concomitant Conditions
- 2. Identify Appropriate Work Up
- 3. Discuss why some patients feel limited improvement from Gluten Free Diet

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Slide 3

Classic Signs and Symptoms

- Post-prandial Pain
- Gas/ Bloat
- Constipation
- Diarrhea
- Wt Loss
- Dermatitis Herpetiformis
- Iron Def Anemia
- Transaminases
- Aphthous Ulcers
- Nausea/ Vomiting
- Infertility
- IUGR
- Short Stature
- Pubertal Delay
- Osteoporosis
Nebulous Signs and Symptoms

- Fatigue
- Alopecia
- Ataxia
- Peripheral Neuropathy
- Seizure D/O
- Migraine
- Mood D/O
- Tooth Decay
- Arthralgias
- Myalgias
- Sleep d/o
- Vasculitis
- Cardiomyopathy
- Vit D Deficiency

Historical Points

- Turkey, 250 A.D. Aretaeus “Koliakos” – Greek for “Suffering in the Bowels”
- (1956, Francis Adams) Latin “Coeliacas”
- Dr. Sam Gee (UK), 1888 - First to make Association With Diet, “Gees disease”
- Dr. Willem Dicke (UK), 1952 confirmed diet as treatment “Sprue”

Pathogenesis

- Genetic Auto Immune Illness – T cell (Cell Mediated) and B cell response (Humoral)
- Majority associated with HLA-DQ2 and HLA-DQ-8 expression – Same as many DM-1, Trisomy 21
- Non-HLA cases exists – Negate HLA DQ-2/8 testing
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Major Players
- Gliadin
- Wheat Protein
- Endomysium
  - Connective Tissue in Smooth muscle
- Tissue Transglutaminase
  - Deamination protein—Kinase
  - AUTO-ANTIGEN

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Pathogenesis
1. Environmental Irritant
   - Gliadin from wheat
2. Secretion of deamination proteins from endomysium
   - Tissue Transglutaminase
3. Antigen Presenting Cells
4. T Cell Response ----WBCs!
5. B Cell Response ----Antibody Formation
Innate Response

- Antigliadin Antibody – IgG, IgA
  - 2-33%
- Anti-Endomysium Antibody – IgG, IgA
  - 100% Pathoneumonic
- Tissue Transglutaminase – IgG, IgA
  - 80%
Inaccuracy in Serological Testing

- Timing of diagnosis
  - Before enough auto-antigen accumulates
- Dose dependent
- Latency
- Sample error—20%

Epidemiology

**CELIAC ICEBERG**

- Pre-2000 Occurrence—“1:10,000”
- Northern European-Celtic 2001 n=13,145 children
  - Overall 1:133
  - (+) Family Hx in second degree relative 1:39
  - (+) Family history in first degree relative 1:20
- USA Random screened Blood Donors > 18yo
  - 1:250 (n=10,000)

Epidemiological studies

**2000-2001**

- Italy, 6-15yo, n=17,201
  - 1:184
- Blood Donors > 18yo
  - Sweden (n=3866) 1:250
  - Finland (n=3564) 1:99
  - Italy (n=3188) 1:96
  - India and Punjabi State (n=2780) 1:310
- WORLD WIDE 1% or 40 million
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Case 1

- 22yo Female with post prandial, generalized abdominal pain, diarrhea and weight loss over the last 6-8 months. No family history of Sprue. Benign exam.

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Making the Diagnosis

- CBC, Sed or CRP, total IgG, total IgA, TTG IgG, TTG IgA
  - Selective IgA or IgG deficiencies
    - 33% have Selective IgA Deficiency
    - Atopic pts have elevated Antibodies
    - Captures 80%
    - False (-) and False (+)
- Equivocal or elevated warrants EGD +/- C-Scope

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Case 1

- Hgb = 10.8,
- Hct = 31.7
- MCV = 77
- Sed/CRP WNL
- Total IgA WNL
- TTG IgA 9.2 (normal < 4)
  - Strong Positive would be > 100
Endoscopic Findings
- Duodenopathy
- Duodenal Villous Blunting or “Scalloping”
- Duodentitis
- Esophageal erythema

Scalloping of the Duodenum

Typical Mosaic Duodenum
Pathology Findings

- Intraepithelial Lymphocytosis
  - False (+) with increase NSAID
- Crypt hyperplasia
  - Also seen in Crohn's
- Villous atrophy or blunting
  - Can be secondary to other enteropathies or malnutrition

Pathology Considerations

IE Lymphocytosis without Villous Atrophy
- NSAIDS
- Latency
- Partially Treated
- Sampling Error
- LYMPHOMA
Villous Atrophy and Crypt Hyperplasia

Formal Diagnosis of Celiac Disease
1. Patient with Symptoms of Malabsorption
2. Villious Atrophy on EGD/Path
3. Resolution with Gluten Free Diet

Treatment
• Gluten Free Diet (Wheat, Barley, Rye, Oats)
  - With the help of a well trained Dietitian
  - www.csaceliac.org
• Calcium and Vitamin D
• Refractory cases
  - Budesonide
  - Prednisone
  - Mesalamine
  - Purine Analogs
Concomitant Conditions

- Collagenous Sprue
- Collagenous Colitis
- IBD (10x > risk)
- Lymphoma (EATL)
- Small Bowel bacterial Overgrowth
- IBS
- Anorexia/Bulimia Nervosa
- Dermatitis Herpetiformis
- DM1
- Thyroiditis
- PBC/AIH/PSC
- Trisomy 21
- IgA Deficiency
- Osteoporosis and Rickets
- Pancreatitis
- Glossitis

Case 2

- 37yo female G1P1 referred from Dermatology with unusual rash
  - Vesicular rash
  - Crosses Midline
  - Neck and Extensor surface of Extremities
  - Conceived with IVF
  - Surg Hx - C-sect at 36 weeks for IUGR
  - NO GI SYMPTOMS !!!
Case 2
- Punch Biopsy with Dermatology reveals DERMATITIS HERPETIFORMIS (DH)
- DH = Celiac Disease, no need for GI work up
- Instruction with Diet and use of appropriate topical agents provided

CASE 3
- 62 yo male with 12 year H/O Celiac Disease
  - 1 year of chronic, intermittent post-prandial diarrhea. No abdominal pain
  - Weight stable
  - Sometimes “cheats with diet”
  - No anemia, TSH wnl
  - TTG IgA moderately elevated
- We re-work diet and f/u in 1 month

Case 3
- NO IMPROVEMENT WITH DIET
  - TTG IgA improved but still symptomatic
- DDX:
  - Refractory Sprue
  - Collagenous Sprue
  - Collagenous Colitis
  - IBD
  - Lymphoma
- DDx:
  - Radiation Sprue
  - Collagenous Sprue
  - Collagenous Colitis
  - IBD
  - Lymphoma
Case 3

- Bidirectional Endoscopic Evaluation
  - EGD normal
  - Biopsy: IEL, 10-15/100 HPF
- Colonoscopy
  - Colon endoscopically normal
  - Solitary area of Linear Erosion in the Terminal Ileum
  - Biopsy reveals chronic and active Ileitis with erosion and crypt architecture erosions - CROHNS

Summary

- Celiac Disease is a Genetic Autoimmune illness
- Incidence of Celiac Disease is Higher than we think
- Confirmation of Disease requires EGD
- Treated with GFD
  - If no improvement, rethink diagnosis
- Concomitant Disease is COMMON