The Other Inflammatory Bowel Diseases: Celiac Disease and Microscopic Colitis

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CELIAC DISEASE IS AN INFLAMMATORY BOWEL DISEASE

Celiac disease is considered to be under-diagnosed.

Why?
WHAT ARE WE DEALING WITH?

- Celiac/celiacs
- Celiac disease
- Coeliac disease
- Sprue
- Celiac sprue
- Non-tropical sprue
- Spruce/screw
PREVALENCE OF CELIAC DISEASE

- Common, affects ~1% of the population
- Evidence from serologic screening studies
  - UK adults (Gut, 2003) 1/100
  - UK children (BMJ, 2004) 1/100
  - Finland children (NEJM, 2003) 1/99
  - Turkey children (J Clin Gastroenterol, 2005) 1/115
  - Turkey adults (J Clin Gastroenterol, 2005) 1/99
  - North Africa children (Lancet, 1999) 1/18
  - USA adults & children (Arch Int Med, 2003) 1/133

Increasing Prevalence of Celiac Disease

Positive: +TTG, +EMA

INCREASING PREVALENCE OF CELIAC DISEASE

- Finland 2.4% elderly
- Sweden 3% children aged 12
- United States 0.2% 1950s
  ~1% 2008

RATE OF CELIAC DISEASE DIAGNOSIS (CIGNA 2000 – 2003)

N = 10,000,000

WHY IS CELIAC DISEASE UNDERDIAGNOSED?

- Rate of diagnosis is low, varies country to country
- Finland 70%, Australia, Ireland, Italy 20-30%
- USA ~1%

WHY

- Shift to silent form (due to breast feeding?)
- Failure of physician recognition, healthcare system
- Lack of pharmaceutical industry involvement
PATHOGENESIS OF CELIAC DISEASE

GENETIC FACTORS
- HLA D02/8
- Unidentified genes

EPITHELIUM
- Innate immune response
- LAMINA PROPRIA
- Adaptive immune response

LAMINA PROPRIA
- Intraepithelial lymphocytosis
- Villous atrophy

ENVIRONMENTAL FACTORS
- Breast feeding
- Cesarean section
- Timing of gluten ingestion
- Infections
- Other factors??

GLUTEN
- Toxic peptides

ENVIRONMENTAL FACTORS – THE SWEDISH EPIDEMIC

ENVIRONMENTAL FACTORS
- Celiac disease in childhood
  - Breast feeding
  - Timing of gluten introduction
  - Cesarean section
  - GI infections
- Adult celiac disease
  - Can occur at any age
The “old” CD epidemiology

- A rare disorder typical of infancy
- Malabsorption
- Ricketts
- Growth failure
**MODE OF PRESENTATION**
**DIAGNOSIS AFTER 1993**
*N*=170


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**PEDIATRIC CELIAC DISEASE (CHONY)**
Modes of Presentation
*N*=224 (2000-2008)

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**DOES IT MATTER?**

**MORTALITY RISK OF CELIAC DISEASE**

- Undiagnosed celiac disease
- Diagnosed celiac disease
WAFB COHORT

50-year Old Sera

- The sera was collected from 1948-1954 in 8916 healthy persons*
  (Warren Airforce Base Cohort - WAFB)

<table>
<thead>
<tr>
<th>Age (mean ± SD)</th>
<th>20.5 ± 2.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>MALE 99%</td>
</tr>
<tr>
<td>Race</td>
<td>WHITE 89.1%</td>
</tr>
<tr>
<td></td>
<td>African American 10.5%</td>
</tr>
<tr>
<td></td>
<td>Others 0.4%</td>
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</tbody>
</table>

* Denny FW, et al. Prevention...streptococcic infection: JAMA 1950

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Survival

- Survival (%)
  - Mortality
  - Positives (36%)
  - Negatives (74%)

Time since serum draw (years)

Rubio-Tapia et al., DDW 2008 @Mayo Clinic

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RISKS OF UNDIAGNOSED CELIAC DISEASE

- SIGNIFICANT MORTALITY RATE WITH UNDIAGNOSED CELIAC DISEASE
- WHAT IS THE RISK IN DIAGNOSED CELIAC DISEASE?
STANDARDIZED MORTALITY RATES

SWEDEN

CD
Inflam
Gluten Sen

1.39
1.72
1.28
1.77
2.41

N. IRELAND

JAMA, 2009

WJG, 2007

DIAGNOSIS OF CELIAC DISEASE

Clinical Suspicion

Positive Serologies

BIOPSY

Endoscopy for any Reason

BIOPSY

- WHEN: Celiac disease + serologies
  weight loss, diarrhea, iron deficiency
  routine biopsies?
- WHERE: jejunum = duodenum = bulb
- TYPE OF FORCEPS
  regular = jumbo
- NUMBER OF BIOPSIES
  4-6 pieces (+2 from the bulb)

Rostom, Gastro, 2006
QUALITY ISSUES IN THE DIAGNOSIS OF CELIAC DISEASE

THE GASTROENTEROLOGIST

- Analyzed the results of biopsy specimens of 132,352 patients (Caris, Dallas, TX)
- States (n=43)
- Providers (n= 1243)
- Determined degree of adherence to the guidelines and the result of adherence

NUMBER OF SPECIMENS OF SMALL BOWEL BIOPSIES
DIAGNOSIS COMPARED TO NUMBER OF BIOPSY SPECIMENS

ADHERENCE ACCORDING TO INDICATION

EFFECT OF ADHERENCE TO THE GUIDELINES

- Adherence to guidelines was low
- Increased from 2006 (33.8%) to 2009 (37.2%)
- With all indications adherence was associated with greater rate of celiac disease diagnosis
- The probability of a new diagnosis of CD was significantly increased when ≥4 specimens were submitted (1.8% vs. 0.7%, p<0.0001).
QUALITY ISSUES IN THE DIAGNOSIS OF CELIAC DISEASE

THE PATHOLOGIST

- We reviewed 102 biopsies taken at “St Elsewheres”

RESULTS

- Change in diagnosis in 25%
- 11% more diagnosed with CD and 9% were considered normal
- Infrequent use of Marsh classification

Degree of agreement

- very good agreement (k=0.888, p< 0.0001) university hospitals
- moderate with community hospitals (k=0.465, p< 0.0001) and commercial labs (k=0.419, p< 0.0001).

CAUSES OF POOR RESPONSE TO GLUTEN-FREE DIET

- Wrong diagnosis
- Gluten ingestion*
- Lactose intolerance*
- Pancreatic insufficiency*
- Microscopic colitis*
- Bacterial overgrowth*
- Other food intolerances (fructose, milk, soy)
- Collagenous colitis

* common

THERAPY OF POORLY RESPONSIVE CD

- Check diagnosis (HLA, serologies, bx)
- Check diet
- Consider bacterial overgrowth, pancreatic insufficiency
- Trial of pancreatic supplements, antibiotics
- ? microscopic colitis
- EGD with T cell studies ?refractory CD
MICROSCOPIC COLITIS

- Lymphocytic + collagenous colitis
- Incidence approaches that of UC
- The course is chronic relapsing and benign
- No increased risk of colorectal cancer
- The natural history of the condition is unknown
- Concomitant autoimmune diseases are common: thyroid disorders, celiac disease, diabetes mellitus, rheumatoid arthritis, asthma/allergy

Nyhtin et al Systematic review: microscopic colitis APT 2006

MICROSCOPIC COLITIS ON CELIAC DISEASE

- 44 of 1009 patients had MC
  - Lymphocytic colitis: 33
  - Collagenous colitis: 11
- All cases were diagnosed >1990
- These 44 represented 5.1% of the cohort

Green CGH 2009

MICROSCOPIC COLITIS IN CELIAC DISEASE

<table>
<thead>
<tr>
<th>INITIAL DIAGNOSIS</th>
<th>%</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Celiac disease</td>
<td>64</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Simultaneous</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Microscopic colitis</td>
<td>11</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>LOCATION OF COLITIS</th>
<th>%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left sided</td>
<td>20</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Right sided</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Pancolitis</td>
<td>64</td>
<td></td>
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### SIR FOR MC IN CELIAC DISEASE COMPARED WITH GENERAL POPULATION

<table>
<thead>
<tr>
<th>Condition</th>
<th>SIR</th>
<th>CI (95%)</th>
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<tbody>
<tr>
<td>Collagenous colitis</td>
<td>21.2</td>
<td>2.7–39.8</td>
</tr>
<tr>
<td>Lymphocytic colitis</td>
<td>53.7</td>
<td>30.2–77.3</td>
</tr>
<tr>
<td>Microscopic colitis</td>
<td>45.5</td>
<td>27.7–63.3</td>
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COMPAORED TO OMSTEAD CO. Gut 2007; 56:504-508

### THERAPY OF MICROSCOPIC COLITIS

- Bismuth*
- Mesalamine
- Steroids – budesonide*, prednisone
- Immunomodulatory drugs
  - AZA, cyclosporine
  
  *clinical trials+

- 63% of the cohort (n=44) required steroids (prednisone or budesonide) and/or immunosuppressants during the course of their illness.

### COURSE OF PATIENTS WITH Rx

<table>
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<tr>
<th>Response</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Good response, GFD alone</td>
<td>5%</td>
</tr>
<tr>
<td>Good response, single course of therapy</td>
<td>27%</td>
</tr>
<tr>
<td>Good response, maintenance therapy</td>
<td>32%</td>
</tr>
<tr>
<td>Poor response, GFD alone</td>
<td>7%</td>
</tr>
<tr>
<td>Poor response, maintenance therapy</td>
<td>16%</td>
</tr>
<tr>
<td>Status unknown</td>
<td>14%</td>
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FOLLOW UP – CD+MC

• Those with persistent diarrhea 30% improvement on repeat duodenal biopsy vs 80% for those without diarrhea (P = .05).
• Persistent diarrhea associated with both persistent VA in 70% and colitis in 80%
• Those in whom the diarrhea resolved VA in 20%, but persistent colitis in 50%, suggesting that the improvement in the villous atrophy may be responsible for the clinical improvement
• Colitis may persist despite resolution of diarrhea

FUTURE

• More diagnosed
• Greater awareness
• Increased services
• NON-DIETARY THERAPIES
  glutenases*
  zonulin blockers - larazotide*
  DQ2 blockers
  tTG blockers
  hookworm*, vaccines*
*IN CLINICAL STUDIES