Celiac Disease and Autoimmune Diseases

I. David Shocket, MD
Medstar Washington Hospital Center
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Outline

• Introduction
• Autoimmune features of CD
• CD and Autoimmune Diseases
• Malignancy in CD
• Screening in SD
Let food be thy medicine
and medicine be thy food

-Hippocrates
Autoimmune Disease

A disease state arising from an abnormal immune response of the body to substances and tissues that are normally present in the body.
Introduction

• CD is an autoimmune enteropathy caused by gluten in genetically predisposed individuals
• Immune activation results in intestinal damage and a wide range of clinical manifestations
• Previously, CD thought to be limited to GI tract
• 50% adults present with extra-intestinal signs and symptoms
CD and AD

• High prevalence of AD in CD and first degree relatives
• AD in CD up to 15%
• Early diagnosis of CD and family history of autoimmunity are risk factors for other AD
• GFD has a protective effect
CD and AD

• Genetic susceptibility
• Similar environmental triggers
• Loss of intestinal barrier secondary to dysfunction of intercellular tight junctions with increased intestinal permeability
Autoimmune Features of CD

- Highly disease specific IgA and IgG autoantibodies to TTG with gluten exposure
- Small intestinal intraepithelial lymphocytes mediate cytotoxicity of enterocytes
- Early diagnosis and treatment can revert the autoimmune process and prevent complications
Conditions Suggesting CD

- Symptomatic malabsorption
- Diarrhea with weight loss
- Chronic diarrhea with or without abdominal pain
- Chronic iron deficiency anemia
- Metabolic bone disease and premature osteoporosis
- Postprandial bloating and gaseousness
- Unexplained weight loss
- Abnormal elevated liver enzymes
- Incidental discovery of villous atrophy endoscopically or histologically
- Dermatitis herpetiformis
- Peripheral neuropathy
- Oral aphthous ulcers
- Growth failure
- Discolored teeth or developmentally synchronous enamel loss
- Thyroid disease
- Irritable bowel syndrome
- Down’s and Turner’s syndromes
Less Common Presentations of CD

- Pulmonary hemosiderosis
- Unexplained male or female infertility
- Dyspepsia
- Amenorrhea
- Chronic fatigue
- Apparent malabsorption of thyroid replacement medication
- Epilepsy or ataxia
- Constipation
- Recurrent abdominal pain
CD and Autoimmune Diseases

2 Theories

• Linkage disequilibrium between the genes responsible for CD and associated AD (inherited together more often than would be expected by chance)

• Untreated celiac disease leads to onset of other autoimmune disorders
• Genetic predisposition
• Exposure to the triggering antigen
• Loss of the protective function of mucosal barriers that interface with the environment (GI and lung mucosa).
Celiac Disease and Associated Autoimmune Disorders

- Liver diseases
- Endocrine diseases
- Dermatologic diseases
- Neurologic diseases
- Rheumatologic/connective tissue diseases
- Cardiac diseases
- Others
CD and AI Endocrine Diseases

- Diabetes mellitus
- Autoimmune thyroid disease
- Addison’s disease
  - Prevalence of CD 5 to 12%
  - No response to GFD
CD and Thyroid Disease

• Prevalence of CD in autoimmune thyroid disease (Graves and Hashimoto’s) 2 to 7%

• CD
  – Signs of autoimmune thyroid disease up to 26%
  – Thyroid dysfunction up to 10%
  – 3-fold risk of thyroid disease compared to controls
  – Reports of normalized thyroid function after 1 yr GFD

• Increased prevalence of CD, autoimmune thyroid disease, and T1D
CD and Type I Diabetes

- Diagnosis often simultaneous or CD subsequent to diabetes in majority
- Share similar HLA and non-HLA genetic loci
- Prevalance of CD in T1D 4% (2% to 11%)
- Risk highest with onset in childhood (<4 yrs) and correlates with longer diabetes duration
- CD associated with risk of T1D before age 20
CD and Type 1 Diabetes

- 2nd peak of T1D at age 45
- Screen children and adults with T1D for CD
- Share HLA genotypes
- 90% TID have either DQ2 or DQ8 vs. 40%
Role of GFD in CD and T1D

- GFD prevents growth failure in children
- GFD leads to better metabolic control?
- GFD prevents vascular complications of T1D
- GFD prevents bone loss
CD and AI Liver Diseases

• Primary biliary cirrhosis
  – Prevalence of CD 3-7%
  – PBC in CD 3%, 3x-20x increased risk of PBC

• Autoimmune hepatitis
  – AH and CD achieve higher treatment-free sustained remission, ?role of GFD

• Primary sclerosing cholangitis
  – Prevalence of CD 3%
  – 4x increased risk of PSC in CD, GFD no difference
CD and Dermatological Diseases

- Dermatitis herpetiformis
- Alopecia areata – association, variable response to GFD
- Vitiligo - controversial
- Dermatomyositis
Dermatitis Herpetiformis

- First described by Duhring in 1884
- Small bowel changes noted by Marks in 1966
- HLA predisposition, environmental trigger, dysregulation of the immune system
- Presence of active small bowel inflammation
- Circulating IgA (anti-tTG) binds to the skin
- Deposition of IgA at dermis leads to skin lesions
CD and AI Neurological Diseases

• Gluten ataxia
  – Sporadic ataxia triggered by gluten, antigliadin antibodies +/- enteropathy
  – 36% idiopathic sporadic ataxia
  – 72% HLA –DQ2; 13% GI symptoms

• Peripheral neuropathies
  – Gluten sensitivity may be the cause in 34%
  – Prevalence of biopsy-proven CD 9%
  – Presence of HLA types associated with CD 80%
CD and AI Rheumatologic Diseases

- Rheumatoid arthritis
- JRA
- Sjogren’s syndrome
- Systemic lupus erythematosus
CD and AI Cardiac Diseases

- Dilated cardiomyopathy
  - Prevalence of CD up to 5.7% in DCM
- Autoimmune pericarditis
  - No clearcut relationship
CD and Other AI Diseases

- Psoriasis
- Sarcoidosis
- Immune thrombocytopenic purpura
- Pancreatitis
- Microscopic colitis
  - CD in up to 15%, screen for CD in microscopic colitis
- Enteropathy-associated T-cell lymphoma
Malignancy in Celiac Disease

• Mortality risk increased slightly
• Highest shortly after diagnosis and in those with active malabsorption and enteropathy
• Implies beneficial effect of GFD
• NHL – 2 to 3 fold increase
• Small intestinal adenocarcinoma 10x risk
• EATL – half diagnosed simultaneously with CD
Enteropathy-Associated T-cell Lymphoma

- Rare complication (<1% lymphomas), poor prognosis
- 60-80% of RCD2 within 5 years
- Presents with typical symptoms of CD (pain, diarrhea, weight loss)
- Median age 60, M=F
- May also occur in pts without CD
- 25% multifocal, usually prox small bowel (jejunum)
# Monitoring in Celiac Disease

<table>
<thead>
<tr>
<th>Clinical Evaluation</th>
<th>Annually or if symptomatic</th>
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<tbody>
<tr>
<td>Serology</td>
<td>Every 3-6 months until normal, then every 1-2 yrs</td>
</tr>
<tr>
<td>Nutritional evaluation</td>
<td>Every 3-6 months until normal, then every 1-2 yrs</td>
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<tr>
<td>Bone density</td>
<td>Once within first 2 yrs</td>
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<tr>
<td>Liver enzymes</td>
<td>At diagnosis, then 1-2 yrs</td>
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<tr>
<td>Thyroid function tests</td>
<td>At diagnosis, then 1-2 yrs</td>
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<tr>
<td>Duodenal biopsy</td>
<td>Consider 1-2 yrs after diagnosis</td>
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<tr>
<td>Cancer screening</td>
<td>Same as general population</td>
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</tbody>
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Summary

• Response to GFD variable
• Cause and effect between CD, gluten, and AD not proven, often anecdotal
• Pre-existing conditions leading to AD
  – Genetic susceptibility
  – Antigen must be presented to the mucosal immune system
  – Loss of protective functions of the mucosal barriers