Celiac disease

ESPGHAN goes Africa Course
Cape Town 29 September-6 October 2015
Celiac disease
Jan Taminiau Academic Medical Center Amsterdam Netherlands
Symptoms in Celiac Disease
(Classical presentation)

Diarrhea
Distended abdomen
Vomiting
Anorexia
Irritability
Weight loss
Failure to thrive
Height and Weight from birth to 19 months in Celiac patient
Arrow moment of start of wheat cereals
Symptoms caused by small intestinal villous atrophy

Celiac Crisis
Epithelial mucosa consists of rapid transit of crypt cells, which can go in an acute secretory state and cause acute diarrhea and dehydration
Intestinal villous cell damage in celiac disease
Loss of absorptive surface leads to malabsorption and malnutrition

- Normal villi
- Absent villi
- Increased inter epithelial lymphocytes
- Crypt hyperplasia
Child with Celiac disease put on a Gluten free diet
Complete recovery of intestinal villi, malabsorption and symptoms

After gluten free diet
Stunting despite adequate gluten free diet
Persistent villous atrophy
Girl from India

Symptoms

Diarrhoea
Steatorrhoea
Short stature/growth failure
Unexplained weight loss
Did not impove on gluten free diet
Celiac disease is a small intestinal mucosal injury

- Small bowel villous atrophy
- Nutrient malabsorption
- Genetically susceptibility
- Gluten (wheat, gliadin) ingestion
- Gluten intolerance
Distant related but cause no disease
Celiac disease is a multifactorial disease

Caused by interactions between genes and environmental factors
When a child looks like his father it is because of the genes

When a child looks like the neighbor it is the environment
Genes and environment

Environment: gluten from wheat, rye, barley and oats
Gluten is a mixture of proteins

Genes involved: HLA-DQ2 en HLA-DQ8

What is the function of HLA???????????
Alleles common 20-25% population

The more your DQ molecules are DQ2
the more chance you have to get CD
Foreign protein specific T cell response in the small bowel
Foreign protein specific T cell response in the small bowel
Foreign protein specific T cell response in the small bowel
Foreign protein specific T cell response in the small bowel
Foreign protein specific T cell response in the small bowel

White blood cell

Protein fragment

Cell

HLA

Bacteria or virus
Foreign protein specific T cell response in the small bowel

White blood cell attacks infected cell: Inflammation
Coeliac disease

Gluten fragment

White blood cell

HLA

Cell

Gluten proteins
Celiac disease

Gluten specific T cell response in the small bowel

Gluten does not fit in HLA-DQ2/DQ8
Celiac disease

Gluten specific T cell response in the small bowel

TransGlutaminase alters gluten

White blood cell

Gluten fragment

HLA-DQ2/8

Cell

Gluten proteins
Celiac disease
Gluten specific T cell response in the small bowel
TransGlutaminase alters gluten

White blood cell
Glutenfragment
HLA-DQ2/8
Cell
Gluten proteins
Celiac disease
Gluten specific T cell response in the small bowel
And therefore it suddenly fits into HLA-DQ2 and HLA-DQ8
Elevated IgA Tissue transglutaminase (TTG)

Elevated IgA-TTG highly specific in celiac Disease
Only blood withdrawal needed
Now we can screen all possible symptoms for Celiac Disease
Might change the incidence/prevalence
With high titers small bowel biopsy might not be mandatory for diagnosis

Disease expression is variable
Family screening 5-10% have celiac disease as well
Celiac Associated illnesses
Consider screening with IgA TTG

<table>
<thead>
<tr>
<th>Illness</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis herpetiformis</td>
<td>30 - 50</td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>8 - 15</td>
</tr>
<tr>
<td>Turner syndrome</td>
<td>5 - 7</td>
</tr>
<tr>
<td>Diabetes mellitus type I</td>
<td>2 - 8</td>
</tr>
<tr>
<td>Autoimmune thyroiditis</td>
<td>3</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>IgA deficiency</td>
<td>2</td>
</tr>
</tbody>
</table>
Serological screening for celiac disease
By IgA tissue trans glutaminase

**False negative**
Undetected 10-15% of celiacs by IgA TTG screening
Including 2% IgA deficient (Celiac patients)

**False positive**
Autoimmune disease
Liver disease
Inflammatory bowel disease
Normal controls
Epidemiology

World wide prevalence

Prevalence 1:100-200

Sahrawi people (Western Sahara, Mauretania) 1: 18
Italy 1: 95
Sweden 1: 100
Netherlands 1: 200
Germany 1: 500

Increase in gluten in Swedish infant diet increased incidence
Decrease in gluten in Swedish diet decreased incidence
Sahrawi people (Western Sahara, Mauretania)
Is Celiac disease possible in Africa
Study in African American children with DM type 1

METHODS:
IgA and IgG Anti-gliadin antibodies, IgA tissue transglutaminase and HLA typing was measured in blood collected
34 children with type1 diabetes mellitus
Patients with positive anti-tissue transglutaminase antibody underwent small intestinal biopsy

RESULTS:
17 patients had elevated IgG AGA
None showed elevated IgA AGA
One patient had elevated IgA and anti tTG levels, and a normal small intestinal biopsy
28 patients had HLA DQ2 or DQ8 present.
Is Celiac disease possible in Africa
Celiac registry in USA

1.3% of 700 proven Celiacs in the USA were from African origin

Symptoms:
- diarrhea
- abdominal pain
- anemia
- growth failure

HLA DQ 2 positive in tested patients

Associated diseases in 30%
- Rheumatoid arthritis
- DM type 1
- Dermatitis herpetiformis
- Microscopic Colitis
- Systemic lupus erythematosus (SLE)
Is celiac disease possible in Africa

Celiac disease is 1:100 in Arabic world including the Magreb
In other parts of Africa incidence depends on genetic mixture with Arabic descent
Sudan, Ethiopia, Somalia celiac disease is frequent although people have not Arabic features
In India in same population more Celiac Disease compared identical families in Africa from India, eat typical Indian diet, less bread
In the Punjab prevalence has risen to 1: 310 related to bread consumption
Bushmen have Arabic genetic influences
Around and North of Jos (Nigeria) Celiac disease is frequent, Arabic genetic influences
In Burkina Faso like Japan DQ2/DQ8 is almost absent: Very small chance for Celiac Disease
Sahrawi people (Western Sahara, Mauritania)
Celiac Disease Incidence 1:18
Celiac disease reported in children in Rwanda, Nigeria, Sudan, Ethiopia, Somalia, Kenya, South Africa
When should you consider the diagnosis of Celiac Disease
Gut-nutrition related symptoms
More in young children

Exposure to wheat

**Common presentations**

- Diarrhoea
- Steatorrhoea
- Short stature/growth failure
- Unexplained weight loss
- Bloating
- Postprandial abdominal pain
- Constipation
- Vomiting (especially nocturnal)
- Dyspepsia/GERD

**Less common**

- Iron deficiency anemia
- B12 deficiency
- Bleeding from Vitamin K deficiency
- Pica (due to deficiencies)

**Rare presentations**

- Acute abdominal pain
- Intussusception
- Intestinal lymphoma
- Ulcerative jejunal ileitis
- Perforation
Non-gut-nutrition related symptoms
More frequent in older children and adults
Exposure to wheat

**Skin**
- Itching skin rash
- Dermatitis herpetiformis

**Mouth**
- Aphthous ulceration
- Dental enamel defects

**Other**
- Chronic fatigue
- Unexplained infertility
- Poorly-controlled type I diabetes
- Non-Hodgkins lymphoma

**Neurologic syndromes**
- Ataxia
- Peripheral neuropathy
- Seizure disorders
- Mononeuritis multiplex
- Premature dementia/cognitive impairment

**Bone disorders**
- Osteomalacia
- Premature osteoporosis
- Arthralgias
Dermatitis herpetiformis adult disease
Skin and Gut (like Celiac)
How to make a Diagnosis of Celiac Disease

Symptoms start after wheat introduction
Possible gastrointestinal malabsorption-malnutrition

IgA-Tissue transglutaminase (IgA-TTG)

If not available

Faecal fat increased

Small bowel biopsy
Prevalence in your country

Possibility to find Celiacs

Diabetes Mellitus type 1
5% incidence of Celiac Disease
Collect DM1 in children in your country
Test blood for IgA TTG

Is performed in adults in several countries in Africa
## Who to screen for Celiac Disease Symptoms?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac Disease</td>
<td></td>
</tr>
<tr>
<td>Symptoms “celiac like”</td>
<td>?</td>
</tr>
<tr>
<td>Family members</td>
<td>5-10</td>
</tr>
<tr>
<td>Diabetes Mellitus type 1</td>
<td>5 (2-8)</td>
</tr>
<tr>
<td>Down Syndrome</td>
<td>8-15</td>
</tr>
<tr>
<td>Turner syndrome</td>
<td>5-7</td>
</tr>
<tr>
<td>Infertility</td>
<td>?</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>very rare</td>
</tr>
</tbody>
</table>
Prevalence of Celiac Disease in African Children
Prevalence of Celiac Disease in African Children

Might be a publication from your group

Biafra Nigeria 1970
Pathology and clinical symptoms are highly variable
Even small quantities of wheat can cause Celiac Disease
Mild symptoms in Celiac Disease
Should we treat?

Possible complications

Short adult stature
Pregnancy outcome is normal
Intestinal lymphoma is vary rare

Mild symptoms interfere with life performance

Recommendation is to treat all Celiac patients
Pathology and clinical symptoms are highly variable

<table>
<thead>
<tr>
<th>Few, if any GI, symptoms</th>
<th>Marked GI symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>tired, no energy</td>
<td>diarrhea</td>
</tr>
<tr>
<td>irritable, depressed</td>
<td>bulky, pale, foul stools</td>
</tr>
<tr>
<td>menstrual disturbance</td>
<td>distention, lots of gas</td>
</tr>
<tr>
<td>weakness, infertility</td>
<td>cramps, weight loss</td>
</tr>
<tr>
<td>growth disturbance</td>
<td>loss of appetite or</td>
</tr>
<tr>
<td>neurologic complaints</td>
<td>voracious appetite</td>
</tr>
</tbody>
</table>

older children  younger children
# Celiac Disease and Pregnancy

<table>
<thead>
<tr>
<th></th>
<th>undiagnosed celiacs n=51</th>
<th>known celiacs n=12</th>
<th>non celiacs n=4997</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (WK)</td>
<td>39</td>
<td>40</td>
<td>38</td>
</tr>
<tr>
<td>Spontaneous abortion (%)</td>
<td>11</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>Anemia (%)</td>
<td>35</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2800</td>
<td>3500</td>
<td>3220</td>
</tr>
</tbody>
</table>

Greco