Coeliac Disease: Diagnosis and clinical features

Australasian Gastrointestinal Pathology Society AGM
28 Oct 2016

Dr. Hooi Ee
Gastroenterologist,
Sir Charles Gairdner Hospital

Coeliac disease

- Greek: *koiliakos* = of the belly
- = gluten enteropathy, nontropical sprue

Abnormal immune response to gluten in wheat, rye, barley

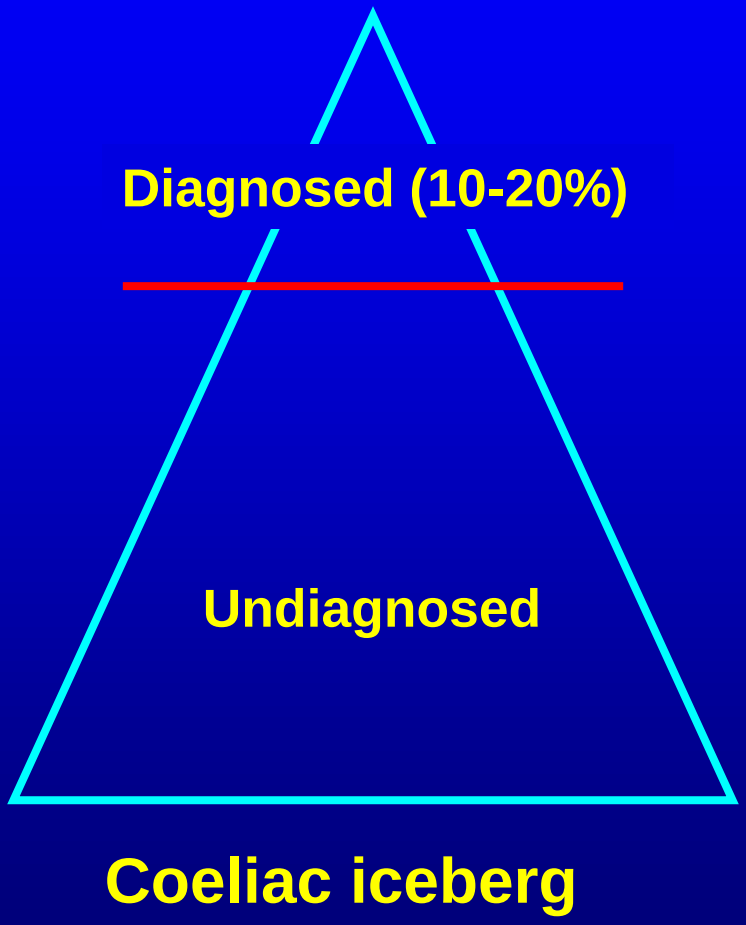
↓

Small intestinal inflammation, crypt hyperplasia, villous atrophy

↓

Malabsorption

Epidemiology



- 0.5-1% prevalence in Western populations
- Increasingly recognised in northern India, Middle East, North Africa
- 80-90% remain undiagnosed
- Usually present in 20-30s
- Uncommon in:
  - Chinese
  - Japanese
  - sub-Saharan Africans

Pathogenesis

Genetics

HLA DQ2, DQ8

Other loci

Gluten

t-TransGlutaminase

Cross links glutamine-rich proteins

Deamidates glutamine

Enhances gluten binding to DQ2/DQ8

Gliadin reactive T cells

Other immune, extrinsic factors

Intraepithelial lymphocytes

Crypt hyperplasia

Villous atrophy

Clinical groups

- Classic
  - GI symptoms, malabsorption, histology, resolution with GFD
- Atypical (largest group)
  - No GI symptoms
  - Iron deficiency, osteoporosis, short stature, infertility
- Silent
  - Asymptomatic, incidentally discovered
- Latent
  - Yet to develop (e.g. +ve serology, inconclusive histology)
  - Diagnosed, normalised on GFD, now gluten tolerant

GI symptoms

- Bloating, distension
- Abdominal pain
- Flatulence, wind
- Lactose intolerance
- Diarrhoea, altered bowel habits
- Reflux
- Weight loss

Non-GI symptoms

- Iron deficiency +/- anaemia
- Osteoporosis, osteomalacia
- Vitamin D and calcium deficiency
- Infertility
- Rheumatic disorders
- Hyposplenism
- Neuropsychiatric manifestations
  - Peripheral neuropathy, ataxia
  - Migraine, seizures
  - Depression, anxiety

Associations

- Dermatitis herpetiformis: 10%
- Eosinophilic oesophagitis: SIR =16.0
- Type 1 diabetes mellitus: 5-10%
- Lymphocytic colitis: 3-5%
- Auto-immune thyroid disease
- Immune liver diseases (AIH, PBC, PSC)
- IgA deficiency
- Down syndrome

Genetics

- **Concordance:**
  - **10% of 1^{o} relatives**
  - **30% of HLA identical siblings**
  - **70% of MZ twins**

- **HLA DQ2: 95% of CD, 30% of popn**
- **HLA DQ8: 5% of CD**
- **DQ2 (-) and DQ8 (-) excludes CD, 99% NPV**

Serology

- IgA anti-tissue Transglutaminase Ab
  - Commonly referred to as TTG
  - Sensitivity 90%, specificity 95% (high titre)
- Useful to exclude coeliac in low risk
  - E.g., irritable bowel syndrome, osteoporosis, infertility
- Useful to monitor response

Diagnosis

- Histology
  - Necessary for diagnosis
  - “Gold” standard
    - Patchy, non-definitive
    - Duodenal bulb biopsy now recommended
- Serology
  - Confirmatory
- Resolution with GFD
  - Not absolutely necessary

Histological differentials

- NSAID enteropathy
- H. pylori duodenitis
- Post-gastroenteritis, viral infections
- Angiotensin receptor blockers (-sartans)
- Crohn
- CVID, other immunodeficiencies

- Giardiasis
- Lymphoma
- Bacterial overgrowth
- GVHD
- TB
- Cow's milk, soy protein intolerance
- Eosinophilic gastroenteritis
- Tropical sprue
- Z-E
- Autoimmune enteropathy
- Whipple

Diagnostic difficulties

- On gluten free diet
  - 3g/d (2 slices bread) for 4 weeks
- Elevated TTG, normal histology
  - ? False positive
  - Latent/potential coeliac
  - Ultra short coeliac disease
  - Repeat in 1-2 years
- IgA deficiency (2-3% of CD)
  - Biopsy if clinical suspicion

Management

- Gluten-free diet, strict, lifelong
- Education
- Dietitian review
- Identify nutritional deficiencies
- Access to an advocacy group
- Multidisciplinary long-term follow-up

GFD for asymptomatic?

- Reduce micronutrient deficiency
- Decrease malignant potential
- Reduce low birth weight, pre-term
- Reduce autoimmune diseases

Non-responsive coeliac

- Usually sub-optimal compliance
- Other diagnoses:
  - Microscopic colitis, pancreatic insufficiency, lactose intolerance, irritable bowel syndrome
- Refractory coeliac disease: 5%
  - Type I: normal intra-epithelial lymphocytes
  - Type II: aberrant IEL clone
    - 50% progression to ulcerative jejunoileitis, lymphoma
    - High mortality

Malignancy

Risk not as high as previously thought

Strict compliance may reduce risk

- **Intestinal T-cell lymphoma (5X risk)**
- **Other GI (2x risk):**
  - **oropharyngeal**
  - **oesophageal squamous**
  - **small intestinal**
  - **colorectal**
  - **hepatocellular**
- **Reduced risk:**
  - **Breast (0.35)**
  - **Lung (0.34)**

Summary

- Coeliac disease is common
- Large undiagnosed group
- Classical presentation is uncommon
- Definitive diagnosis requires histology
- Strict gluten exclusion is mainstay of therapy
- Serious complications are rare