Coeliac disease

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Abstract

The incidence of coeliac disease remains high in the UK. This review describes the pathophysiology and presentation of children with coeliac disease. We discuss the new diagnostic process, which is now guided by the presence or absence of symptoms. New guidelines allow a secure diagnosis to be made in some children with the use of serological testing and genotyping, in place of duodenal biopsy.

A lifelong gluten free diet remains the only treatment for coeliac disease. The best practice for the dietary and medical management of a gluten free diet is summarised and the importance of regular follow-up is discussed. This ensures long-term adherence and reduces the likelihood of associated complications. A supervised gluten challenge may be considered in some children, at the appropriate age, with a previous insecure diagnosis.

Keywords childhood; coeliac; gluten

What is coeliac disease?

Coeliac disease is an immune-mediated systemic disorder, which is triggered by dietary gluten in genetically susceptible individuals. It is characterised by the presence of HLA-DQ2 or HLA-DQ8 genetic haplotypes, gluten-dependent signs and symptoms, coeliac-specific antibodies and enteropathy.

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Gluten is a mixture of proteins found in wheat, and is composed of gliadins and glutenins. Other grains like barley and rye, composed respectively by hordeins and secalins, can also be responsible for the enteropathy in coeliac disease. Of all the proteins that can result in coeliac disease, gliadins are the most immunogenic.

Who gets coeliac disease?

Coeliac disease is one of the most common chronic diseases in childhood, affecting about 1% of the UK population. Coeliac disease is still significantly under-diagnosed in the UK, with only 10%–20% of this figure having a confirmed diagnosis.

Coeliac disease was originally thought to be largely confined to Northern Europe and Australasia and be uncommon in North America and the Middle East. However it is now recognised to be equally common in all these countries. It is still thought to be rare in the Far East and Sub-Saharan Africa. There are a number of associated conditions (see Table 1).

There is evidence of an increasing incidence of both classic and non-classic presentations in UK children. Improved awareness of the heterogeneity of coeliac disease may directly influence the recorded incidence, as greater numbers will be diagnosed because of a lower threshold to test. Although the incidence of paediatric coeliac disease is increasing globally, it is uncertain whether this is attributed to improved identification or signifies a true rise.

Pathophysiology

The pathogenesis of coeliac disease is complex and involves both genetic and environmental factors. Genetics is important: there is a high concordance in monozygotic twins (between 70 and 86%) and the HLA haplotype of DQ2/DQ8 is the principal genetic factor described. It is important to remember that genetic predisposition does not mean the individual will certainly develop the disease. In the Caucasian population, between 30 and 35% will be carriers of these markers, but only 2–5% will go on to develop coeliac disease. In patients with coeliac disease, 95% have HLA-DQ2 and 5–10% will carry HLA-DQ8.

This variation in disease expression in children with similar known genotype highlights the undoubted importance of environment. There is some evidence that the timing of gluten introduction in to the weaning diet (early – before 17 weeks, and late – after 30 weeks), caesarean section delivery, absence of breastfeeding, infections and pro-immune genetic background are factors which may contribute to the onset of coeliac disease.

Conditions associated with coeliac disease

- Type 1 diabetes mellitus
- Down's syndrome
- Williams' syndrome
- Turner's syndrome
- Autoimmune liver disease
- Autoimmune thyroiditis

Table 1

How do children with coeliac disease present?

Only a small number of children present with the typical signs and symptoms of malabsorption (diarrhoea, faltering growth, pallor and fatigue), known as classic coeliac disease. A child may present with symptoms confined to the gastrointestinal tract or increasingly, symptoms with no association with the gastrointestinal tract (non-classic coeliac disease, see Table 2). Children may also be asymptomatic at diagnosis, and these patients are usually identified through the targeted screening of high risk groups.

Potential coeliac disease

This is defined as positive coeliac serology alongside normal intestinal biopsies. Although a diagnosis cannot be made, these children may progress to coeliac disease in the future and should be monitored.

Non-coeliac gluten sensitivity

This occurs in those who have had a diagnosis of coeliac disease excluded, but whereby there is a clear adverse response associated with gluten ingestion. Non-IgE mediated food allergy is a potential cause.

Differential diagnosis

The classic diagnosis of coeliac disease overlaps with the diagnosis of villous atrophy from other causes, as it is one of the principal findings in the duodenal biopsies of these patients. The main differential diagnoses of villous atrophy are listed in Table 3.

How are children diagnosed with coeliac disease?

The process for diagnosing coeliac disease in children has recently changed according to new guidelines from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN 2012). At present, it is important to identify whether the child is symptomatic or asymptomatic. The child must remain on a gluten-containing diet for at least 4–6 weeks prior to and during the diagnostic process.

Symptomatic children

Symptomatic children should have blood tests for tissue transglutamase (tTG-IgA) and total IgA. If tTG-IgA is more than ten times the upper limit of normal for assay, the likelihood of villous atrophy is very high. In these circumstances a diagnosis may now be made using further blood tests alone avoiding duodenal biopsy. A diagnosis of coeliac disease can be confirmed if additional blood tests reveals a further high tTG-IgA, positive anti-endomysial antibodies (EMA) and positive HLA-DQ2/8 haplotype. Children with a positive tTG-IgA less than ten times the upper limit of normal should proceed to duodenal biopsy to confirm diagnosis.

Coeliac disease is highly unlikely in children with a negative tTG-IgA and normal total IgA. Those with IgA deficiency should have further blood testing for tTG-IgG and/or EMA, but there should be a low threshold for biopsy given these tests are less specific.

Asymptomatic children

Asymptomatic children with a raised tTG-IgA should initially be tested for HLA-DQ2/8 haplotype and if negative, coeliac disease is highly unlikely and they need no further testing. Those who are asymptomatic and HLA-DQ2/8 haplotype positive should only have the diagnosis of coeliac disease made on duodenal biopsy, even if the tTG-IgA is more than ten times the upper limit of normal.

Duodenal biopsies

Before proceeding to biopsy, it is important to ensure the child has remained on a gluten-containing diet. During an endoscopy, four duodenal biopsies are taken from D2 or lower, and one to

Signs and symptoms of coeliac disease

Gastrointestinal tract	Non-gastrointestinal tract
• Recurrent abdominal pain	• Faltering growth
• Abdominal distension	• Idiopathic short stature
• Diarrhoea (persistent or intermittent)	• Dermatitis herpetiformis (pruritic vesicular rash)
• Persistent nausea and vomiting	• Recurrent aphthous stomatitis (mouth ulcers)
• Chronic constipation	• Delayed puberty/menarche
• Flatulence	• Dental enamel defects
• Anorexia	• Rickets/osteomalacia
	• Osteoporosis/pathological fractures
	• Iron deficiency anaemia unresponsive to treatment
	• Prolonged fatigue
	• Weakness
	• Unexplained liver disease

Table 2

Differential diagnoses/causes of villous atrophy

- Coeliac disease
- Food protein hypersensitivity (particularly cow's milk and/or soya proteins)
- Eosinophilic gastroenteritis
- Hypogammaglobulinemia
- Whipple diseases
- Abetalipoproteinaemia (Bassen-Kornzweig syndrome)
- Intestinal lymphoma
- Crohn's disease
- Infectious diseases (e.g. tuberculosis, giardiasis, parasitic infestations, infectious enteritis)
- Small bowel bacterial overgrowth
- Severe malnutrition
- Small bowel ischaemia
- Radiotherapy
- Autoimmune enteropathy
- Cytotoxic drugs

Table 3