Celiac Disease and Gluten Sensitivity

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KEYWORDS

• Celiac disease • Gluten sensitivity • Iron deficiency • Malabsorption
• Gluten-free diet • Gluten challenge • FODMAPs • Irritable bowel syndrome

KEY POINTS

- Use anti–tissue transglutaminase IgA as the single initial diagnostic test for celiac disease in most patients.
- Upper endoscopic evaluation with histologic analysis of the small bowel is a necessary step when celiac disease is suspected, even if serologies are negative.
- Evaluation of celiac disease should be undertaken in patients on a gluten-containing diet; consider a gluten challenge for those who have already eliminated gluten.
- Treatment of celiac disease requires strict adherence to a gluten-free diet, which can eliminate symptoms and reverse histologic and serologic changes.
- For patients with gluten sensitivity and no evidence of celiac disease, consider first advising general nutritional improvements followed by gluten-free or low FODMAP diet with involvement of a trained dietitian.

CELIAC DISEASE

Definition

Celiac disease (CD) is defined as an autoimmune-mediated enteropathy triggered by dietary gluten (storage proteins of wheat, barley, and rye) in genetically predisposed individuals.[1]

Epidemiology

The prevalence of CD in Western populations is estimated at 1%,[2] with worldwide prevalence ranging from 8 to 200 per 100,000 for those with clinical disease.[3] The overall prevalence of CD is on the rise[4] and is estimated to affect more than 2 million people in the United States.[5]

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Risk Factors and Associated Conditions

CD is linked to HLA-DQ heterodimers DQ2 and DQ8, the presence of which confer the most important risk factor for development of CD.[1] History of CD in a first-degree relative is associated with increased risk of disease, as is history of an affected second-degree relative to a lesser extent.[6] Certain conditions have been closely associated with CD, including type 1 diabetes,[7,8] dermatitis herpetiformis,[9] Down syndrome,[10] and selective IgA deficiency.[11] Other possible associations include severe food allergies,[12] psoriasis,[13] Turner syndrome,[14] Williams syndrome,[15] Sjögren syndrome,[16] and rheumatoid arthritis.[17]

Numerous studies have attempted to identify risk factors in children, raising concerns about pediatric viral enteropathy infections and changes to the gut bacterial flora as potential exposures favoring the development of CD in children,[18] but this remains an area of further study. Gluten consumption during pregnancy, breastfeeding duration, or timing of the introduction of gluten, however, do not appear to increase risk of development of CD among offspring.[19–21]

Complications and Prognosis

CD has well-recognized nutritional complications, such as iron-deficiency anemia, various micronutrient deficiencies, and reduced bone mineral density.[1,22] Reproductive and obstetric complications are also possible with CD including infertility,[1,23] increased risk of spontaneous abortion and intrauterine growth restriction,[1,24] and increased risk of preterm- and stillbirths.[1,25] Children with CD may have developmental limitations, such as short stature or failure to thrive.[1,22]

CD carries an increased risk of all-cause mortality and risk of malignancies including small-bowel adenocarcinoma, esophageal cancer, B-cell and T-cell non-Hodgkin lymphomas, and intestinal T-cell lymphomas. Importantly, the risk of complications and mortality are reduced by adherence to a gluten-free diet.[1,22]

Pathophysiology

CD arises from immune dysregulation triggered by the gliadin component of gluten in individuals with genetic predisposition. This leads to inflammation and, over time, small intestinal villous atrophy and crypt hyperplasia in the small bowel (**Fig. 1**) followed ultimately by malabsorption.[26,27]

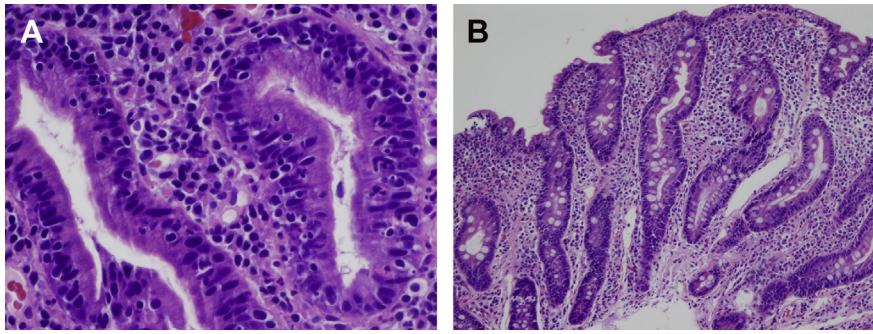

Fig. 1. Histologic changes of the small bowel associated with celiac disease. Histologic images from duodenal biopsies showing (*A*) intraepithelial lymphocytes and (*B*) villous blunting (atrophy) (original magnification × XXX) hematoxylin and eosin (H&E) stain, 400 × (*A*) and 100× (*B*).