Celiac Disease and Nonceliac Gluten Sensitivity

Runa D. Watkins, MD*, Shamila Zawahir, MD

KEYWORDS

• Celiac disease • Gluten-free diet • Tissue transglutaminase • Autoimmune
• Children • Wheat allergy • Nonceliac gluten sensitivity

KEY POINTS

- Celiac disease is found in genetically susceptible individuals who carry the HLA DQ2 or DQ8 gene.
- Celiac serology testing is a good screening tool.
- The gold standard for diagnosis is still an upper endoscopy to acquire small bowel biopsies.
- Currently the only available treatment is gluten-free diet.
- NCGS can be considered in those without evidence of celiac disease and wheat allergy who have clinical improvement on a gluten-free diet.

INTRODUCTION

Celiac disease (CD) is an autoimmune enteropathy that causes damage to the small intestinal mucosa when gluten, found in wheat, barley, and rye, is ingested, which only occurs in genetically susceptible individuals. Innate gluten sensitivity, adaptive gluten sensitivity, and autoimmunity are essential in the development of CD.[1]

The prevalence of CD has been increasing worldwide, most likely because of greater awareness and better testing. Gluten has a high concentration of glutamine and proline residues referred to as prolamines, which are specifically found in wheat, barley, and rye. It is thought that under stressful situations, such as infection or surgery, the gliadin protein enters the lamina propria where it is deaminated by the enzyme tissue transglutaminase (tTG) and then it becomes attached to it to form a

Disclosure Statement: The authors have no commercial or financial disclosures.
Pediatric Gastroenterology & Nutrition, University of Maryland, 22 South Greene Street, N5W68, Baltimore, MD 21201, USA
* Corresponding author:
E-mail address: rwatkins@peds.umaryland.edu

Pediatr Clin N Am 64 (2017) 563–576
http://dx.doi.org/10.1016/j.pcl.2017.01.013 **pediatric.theclinics.com**

complex. This specific complex is then presented to the antigen-presenting cell resulting in secretion of proinflammatory mediators.[2] This process ultimately produces intestinal inflammation resulting in crypt hyperplasia and villous atrophy. CD should also be considered in certain populations with an increased prevalence of CD, such as those with selective IgA deficiency, first-degree relatives of patients with CD, autoimmune thyroiditis, type I diabetes, Down syndrome, Turner syndrome, and Williams syndrome.[3]

EPIDEMIOLOGY

CD occurs in genetically susceptible individuals, but the pattern of genetic inheritance is still somewhat obscure. The prevalence of CD is about 1% within the United States and Europe, and this may be even higher in certain Northern European countries.[4] It is now becoming a common disorder in North Africa, the Middle East, and India. However, the diagnostic rates are low in these regions because of low availability of diagnostic facilities and poor disease awareness.[5] It is thought that the increase in prevalence is also attributed to the adaptation of Western gluten-rich dietary patterns. Many new diagnoses are also being made through screening individuals who are at risk because of family history of CD.

SYMPTOMS

The range of symptoms present in CD is a wide spectrum. Individuals may have the classic symptoms of abdominal pain with diarrhea or constipation, neurologic manifestations, or be completely asymptomatic. Symptoms are described as typical, atypical, and latent. **Table 1** lists the specific symptoms according to their categories. The classic, or typical symptoms, usually emerge in the pediatric age and consist of diarrhea, abdominal pain, and weight loss, and poor growth. The atypical presentations include osteoporosis, dermatitis herpetiformis, peripheral neuropathy, short stature, delayed puberty, dental enamel hypoplasia, and anemia. A mild elevation of serum liver enzymes is well described as an initial presentation of CD in pediatric patients. Headaches, seizures, and psychiatric symptoms are also associated with CD.

The latent form of CD is defined as having a predisposing gene, normal biopsy findings, and weakly positive serologies.[6] It is thought that environmental factors affect the disease's clinical presentation, the time at presentation, and the characteristics of the disease.[7] Theories are now emerging in regards to infectious agents playing a role, at least on the timing of the presentation.[8]

Table 1
Signs and symptoms of celiac disease

Typical	Atypical	Latent
Diarrhea	Osteoporosis/fractures	Gene positive
Abdominal pain	Dermatitis herpetiformis	Weakly positive serologies
Bloating	Nonspecific transaminitis	Normal biopsies
Gassy	Fatigue	
Constipation	Anemia	
Alternating diarrhea and constipation	Migraines	
	Peripheral neuropathy	
Failure to thrive/weight loss	Dental enamel hypoplasia	
Vomiting	Short stature/delayed puberty	