Clinical Presentation of Celiac Disease in the Pediatric Population

ALESSIO FASANO
Mucosal Biology Research Center and Center for Celiac Research, University of Maryland, School of Medicine, Baltimore, Maryland

Celiac disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten-containing grains (including wheat, rye, and barley) in genetically susceptible individuals. CD is associated with HLA molecules DQ2 (90%–95%) and DQ8 (5%–10%), and in the continued presence of gluten the disease is self-perpetuating. CD is one of the most common lifelong disorders worldwide and is characterized by a variety of clinical presentations. These include the typical malabsorption syndrome (classic symptoms) and a spectrum of symptoms potentially affecting any organ or body system (nonclassic symptoms). Because CD often is atypical or even clinically silent, many cases go undiagnosed and are exposed to the risk of long-term complications. There is growing interest in the social aspects of CD because the burden of illness related to this condition is doubtless higher than previously thought.

Celiac disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. Gluten is a protein component in wheat, a staple food for most populations in the world, and other cereals (rye and barley). The major CD-predisposing genes are located in the HLA region, namely the HLA-DQ2 and/or DQ8 genotypes found in at least 98% of patients. CD is one of the most common lifelong disorders in Europe and in the United States. This condition can manifest with a previously unsuspected range of clinical presentations, including the typical malabsorption syndrome (chronic diarrhea, weight loss, abdominal distention) and a spectrum of symptoms potentially affecting any organ or body system (Table 1). Because CD often is atypical or even clinically silent, many patients remain undiagnosed and are exposed to the risk of long-term complications, such as osteoporosis, infertility, or cancer.[1] The burden of illness related to CD is doubtless higher than previously thought[2] and there is growing interest in the social dimensions of this condition. Although CD can present at any age, including the elderly, typical cases often manifest in early childhood. In 1888, Samuel Gee,[3] having drawn attention to the disorder in a lecture delivered on October 5, 1887, at the Hospital for Sick Children in London, produced his classic paper, *On the Coeliac Affection*. Dr. Gee described celiac disease as follows: "There is a kind of chronic indigestion which is met with in persons of all ages, yet is especially apt to affect children between one and five years old . . . Signs of the disease are yielded by the faeces; being loose, not formed, but not watery; more bulky than the food taken would seem to account for . . ." Remarkably, he already hypothesized that foodstuffs could be the trigger of the disease: "The causes of the disease are obscure. Children who suffer from it are not all weak in constitution. Errors in diet may perhaps be a cause, but what error? Why, out of a family of children all brought up in much the same way, should one alone suffer? To regulate the food is the main part of treatment . . . The allowance of farinaceous food must be small; highly starchy food, rice, sago, corn-flour are unfit." Despite his great clinical acumen, Gee[3] was not able to make the final link between gluten ingestion and celiac disease because he concluded: "Malted food is better, also rusks or bread cut thin and well toasted on both sides."

Clinical Presentations of CD in Children

The clinical spectrum of CD in children is wide (Tables 1 and 2, Figure 1).[1,4–9]

CD With Classic Symptoms

This form is characterized by gastrointestinal manifestations starting between 6 and 24 months of age, after the introduction of gluten in the diet. Infants and young children typically present with impaired growth, chronic diarrhea, abdominal distention, muscle wasting and hypotonia, poor appetite, and unhappy behavior (Table 1). Within weeks to months of starting to ingest gluten,

Abbreviations used in this paper: CD, celiac disease; GFD, gluten-free diet.

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Table 1. Clinical Manifestation of CD in Pediatrics

Manifestations secondary to untreated CD	Associated diseases (or secondary to untreated CD?)	Genetic-associated diseases
CD with classic symptoms	Autoimmune diseases	Down syndrome
Abdominal distension	Type 1 diabetes	Turner syndrome
Anorexia	Thyroiditis	Williams syndrome
Chronic or recurrent diarrhea	Sjogren's syndrome	IgA deficiency
Failure to thrive or weight loss	Neurologic and psychologic disturbances	
Irritability	Ataxia	
Muscle wasting	Autism	
Celiac crisis (rare)	Depression	
CD with nonclassic symptoms	Epilepsy with intracranial calcifications	
Arthritis	IgA nephropathy	
Aphthous stomatitis	Osteopenia/osteoporosis	
Constipation		
Dental enamel defects		
Dermatitis herpetiformis		
Hepatitis		
Iron-deficient anemia		
Pubertal delay		
Recurrent abdominal pain		
Short stature		
Vomiting		

weight gain velocity decreases and, finally, weight loss can be observed. A celiac crisis, characterized by explosive watery diarrhea, marked abdominal distension, dehydration, electrolyte imbalance, hypotension, and lethargy, was described more commonly at the beginning of this century, but it is now observed rarely. Despite a wide variability between countries, typical CD still represents a common presentation in the pediatric age group.

CD With Nonclassic Symptoms

Currently, there is a general trend of delayed onset of symptomatic CD involving older children (5–7 years old). These children tend to experience unusual intestinal complaints (eg, recurrent abdominal pain, nausea, vomiting, bloating, and constipation) or extraintestinal manifestations (eg, short stature, pubertal delay, iron deficiency, dental enamel defects, abnormalities in liver function tests) (Table 1). Dermatitis herpetiformis, a blistering skin disease, at present is regarded as a variant of CD rarely affecting the pediatric population.

Table 2. Histologic and Clinical Manifestations of CD in Pediatrics

Clinical form	Histologic and clinical manifestations
CD with classic symptoms	Fully expressed enteropathy Intestinal symptoms
CD with nonclassic symptoms	Fully expressed enteropathy Extraintestinal manifestations
Silent	Fully expressed enteropathy Minimal complaints or symptom-free (occasionally discovered by serologic screening)
Potential	Minimal changes enteropathy or normal small intestinal mucosa Sometimes symptomatic

Silent CD

CD is defined as silent when typical gluten-sensitive enteropathy is found in a patient who apparently is healthy. Large numbers of silent cases of CD have been reported in at-risk groups (such as patients with insulin-dependent diabetes and first-degree relatives) and in general population samples enrolled in screening programs. An in-depth clinical examination shows that many of these silent cases are indeed affected with a low-grade illness often associated with decreased psychophysical well being.

Potential CD

A potential form of CD is diagnosed in patients who have anti-endomysium antibodies (AEA) and/or anti-human tissue transglutaminase antibodies, the typical HLA-predisposing genotype (DQ2 or DQ8), but a normal or minimally abnormal mucosal architecture (increased intraepithelial count) at the intestinal biopsy examination. These patients are at risk for developing a typical CD enteropathy later in life.

Untreated CD is associated with a list of diseases and complications (Table 1).[1]

Associated Conditions

An increasing number of studies have shown that many CD-associated problems, which originally were described mostly in adults, can indeed be observed in