Review article

Celiac disease in children.

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Abstrac

Celiac disease (also known as celiac sprue, gluten-sensitive enteropathy, nontropical sprue) has been defined[7] as a chronic disorder with a characteristic but nonspecific small intestinal mucosal biopsy shows lesion that is associated with nutrient malabsorption.

Celiac disease is one of the most common chronic diseases in childhood, affecting 1%-2% of the population worldwide, although a substantial variation in prevalence has been reported in different region.[1] Celiac disease is characterized by chronic diarrhea, failure to thrive and abdominal distention usually observed within the first 1-2 years of life. At the older age, atypical features such as anemia, short stature, bone disease and liver failure may occur.[5] Since the symptoms of the disease are diverse, pediatricians must be able to recognize its varied clinical presentations. The prevalence of CD increases to more than 40% in patients presenting such typical symptoms as chronic diarrhea[6].

Key words : Celiac disease, Children

Introduction

Celiac disease is one of the most common chronic diseases in childhood, affecting 1%-2% of the population worldwide, although a substantial variation in prevalence has been reported in different region[1].

In 1888, Samuel Gee described the clinical features of childhood celiac disease[2]. After the Second World War, Dicke and colleagues from Holland noted that certain cereal grains, particularly wheat and rye, were harmful to children with celiac disease. Later studies showed that gliadin, the alcohol-soluble component of gluten, a water-insoluble protein from wheat, could cause impaired fat absorption in these patients[3]. Between 1954 and 1960, the intestinal histopathological features of celiac disease were described[4] based on per oral small intestinal biopsy, refining earlier descriptions based on surgical specimens. During the last 40 years, the clinical and pathological spectrum of celiac disease has become further appreciated, especially in recent studies that have implicated genetic, immunologic, and environmental factors in the etiology and pathogenesis of this most intriguing disorder.

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Since the symptoms of the disease are diverse, pediatricians must be able to recognize its varied clinical presentations.

The prevalence of CD increases to more than 40% in patients presenting such typical symptoms as chronic diarrhea[6]. Celiac disease (also known as celiac sprue, gluten-sensitive enteropathy, nontropical sprue) has been defined[7] as a chronic disorder with a characteristic but nonspecific small intestinal mucosal biopsy shows lesion that is associated with nutrient malabsorption.

Following removal of dietary wheat gliadins (the toxic alcohol-soluble gluten fractions) and equivalent dietary

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prolamines in barley, rye and oats, prompt improvement in clinical condition as well as the small intestinal biopsy appearance, along with improved nutrient absorption.

Etiopathogenesis

CD is a unique autoimmune disorder because both the environmental trigger (gluten) and the autoantigen (tissue Transglutaminase) are known and elimination of the environmental trigger (gluten) leads to a complete resolution of the disease. Genetic factors-increased incidence of HLA-B8 and HLA-DR3 and also HLADQ2 and HLADQ8 which facilitate the immune response against gluten proteins. Ingestion of gluten, the gliadin fraction of it results in activation of gliadin-reactive T cells in the intestine. These CELIAC DISEASE4 T cells are hypothesized to provide immunologic help to B cells to produce TG auto-antibodies. Concordance rates of 70% to 75% among monozygotic twins and 5% to 22% among first-degree relatives.

Clinical features

Celiac disease (CD) may occur without any symptoms; asymptomatic or minimally symptomatic celiac disease is probably the most common form of the disease, especially in older children and adults.

Currently[8] possible presentations of celiac disease are recognized, as follows :

- **Typical :** This presentation is primarily characterized by GI signs and symptoms.
- **Atypical :** GI signs and symptoms are minimal or absent, and various extra-intestinal manifestations are present.
- **Silent :** The small intestinal mucosa is damaged, and celiac disease autoimmunity can be detected with serology; however, no symptoms are present.
- **Potential :** Patients have a positive specific autoimmune serology and may or may not be symptomatic, but the mucosa morphology is normal. These individuals have genetic compatibility with celiac disease and full-blown celiac disease may develop at a later stage in some or all of these individuals.
- **Latent :** Individuals with normal mucosal morphology who "have had a gluten-dependent enteropathy at some point in their life." This subset of patients is the rarest of the group.

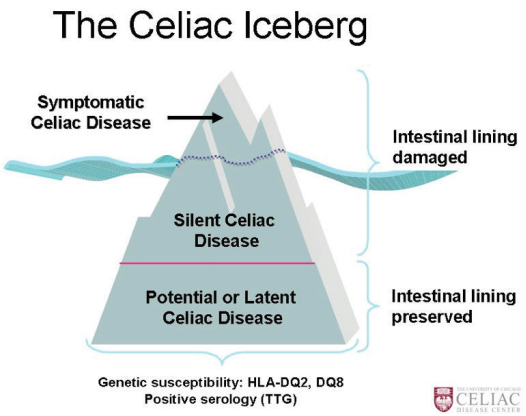

Fig : 1 the celiac Iceberg

Typical presentation

Numerous studies demonstrate that children with CD frequently have gastrointestinal (GI) symptoms such as chronic recurrent diarrhea, anorexia, abdominal pain, vomiting, constipation and abdominal distension, with failure to thrive (FTT), weight loss . However, there is little information currently available about the precise prevalence of CD in children with these specific types of GI symptoms. GI symptoms that characteristically appear at age 9-24 months[5]. Symptoms begin at various times after the introduction of foods that contain gluten. The variability in the age of symptom onset possibly depends on the amount of gluten in the diet and other environmental factors, such as duration of breast feeding.

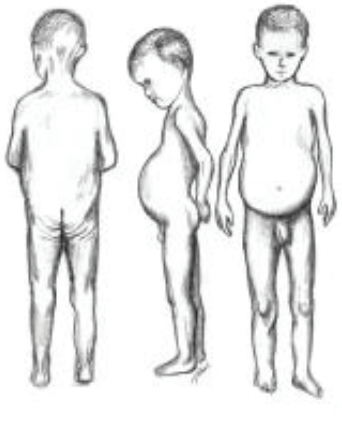

Fig : 2 Bloating of the abdomen is a relatively common finding, potbelly and muscle wasting in a child with celiac disease.

Examination findings depend on extent of celiac disease.

- Dry mucosal membranes with vomiting or diarrhea

indicate the degree of dehydration.

- Oral aphthae are more frequent than in normal population.
- Dental enamel hypoplasia is a highly specific but relatively uncommon finding.
- Bloating of the abdomen and muscle wasting are relatively common finding.
- Muscle wasting is an obvious finding and is part of the malnutrition that ensues because of the mal-absorptive condition.

Atypical presentation

An increasing number of patients are being diagnosed without typical GI manifestations at older ages. A reasonable assumption is that approximately 70% of patients with newly diagnosed celiac disease do not present with the typical major GI symptoms. Once again, a relationship between the age of onset and the type of presentation is noted in infants and toddlers where GI symptoms and failure to thrive predominate,[9] whereas, during childhood, minor GI symptoms, inadequate rate of weight and height gain, and delayed puberty tend to be more common. In teenagers and young adults, anemia is the most common form of presentation[10,11,12] Later may present with neurological disease[13] and osteoporosis[14].

Extra-intestinal manifestations of celiac disease.

Dermatitis herpetiformis15, dental enamel hypoplasia[16], aphthous ulcers, delayed tooth eruption, iron-deficiency anemia, short stature and delayed puberty, chronic hepatitis and hyper-transaminasemia, arthritis and arthralgia, osteopenia[17,18] and osteoporosis, neurological problems, psychiatric disorders.

Associated non gastrointestinal diseases

Celiac disease is also known to be strongly associated with numerous disorders, specifically with autoimmune conditions and genetic syndromes.

Down syndrome, Williams's syndrome, Turner syndrome, with autoimmune disorders like type 1 diabetes mellitus[19], thyroiditis[20,21].

Turner's syndrome, alopecia, selective IgA deficiency, Those who have first degree relatives with celiac relatives have their own chance of CD is more.

For whom screening needed:

Testing for CD should be offered to the following groups :

Group A - with symptoms like CD : Children and adolescents with the otherwise unexplained symptoms and signs of chronic or intermittent diarrhea, failure to thrive, weight loss, stunted growth, delayed puberty, amenorrhea, iron-deficiency anemia, nausea or vomiting, chronic abdominal pain, abdominal cramping or distension, chronic constipation.

Group B - asymptomatic with other presentations : Asymptomatic children and with an increased risk for CD such as type 1 diabetes mellitus (T1DM), Down syndrome, autoimmune thyroid disease, Turner syndrome, Williams syndrome, selective immunoglobulin A (IgA) deficiency, autoimmune liver disease, and affected with CD in first-degree relatives . Atypical with minimal intestinal or extraintestinal presentations like chronic fatigue, recurrent aphthous stomatitis, dermatitis herpetiformis–like rash, fracture with minor traumas, osteopenia, osteoporosis and abnormal liver biochemistry.

Differential diagnosis of the flat lesion of celiac sprue

Nonspecific lesions

Soya protein (and/or milk protein) lesion, tropical sprue, stasis and bacterial overgrowth, lesions of the Third World (including kwashiorkor), nutrient deficiency (folic acid, vitamin B12, and zinc), immunodeficiency syndromes (AIDS, graft vs. host disease), infectious agents with parasites like Giardia, Cryptosporidium, microsporia, Isospora belli, Strongyloides, hookworm, Schistosoma, Capillaria, Virus like Cytomegalovirus. Fungal infection with Candida, Histoplasma. Mycobacterial like Mycobacterium-avium intracellulare and congenital microvillus inclusion disease and also unclassified sprue.

Specific lesions

Collagenous sprue, whipple's disease, eosinophilic gastroenteritis, intestinal lymphoma, immuno-proliferative small intestinal disease.

Laboratory Studies

Serology

- IgA tissue transglutaminase (tTGA) as the first choice test. IgA endomysial antibodies (EMA) test is indicated if the result of the tTGA test is equivocal.
- Check for IgA deficiency if the serology is negative
- IgG tTGA and/or IgG EMA serological tests are indicated for people with confirmed IgA deficiency .
- Antigladine antibody (AGA) IgA and AGA IgG tests are no longer recommended as initial testing because of low sensitivity and specificity for celiac disease.

Biopsy

- When the serum tTG is elevated small intestinal biopsy is recommended.
- It is currently recommended that confirmation of the diagnosis of CD requires an intestinal biopsy in all cases.
- Even if serological tests for CD are negative, a small intestinal biopsy may be useful in symptomatic children (particularly when they are 0 to 2 years old) with chronic diarrhea, FTT, a positive family history of CD.

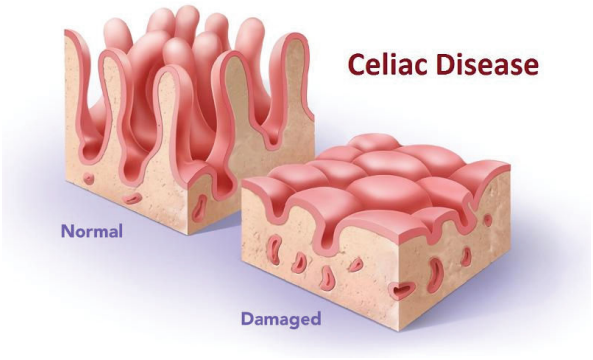

Fig: 3 Villus atrophy in celiac disease

Long Term Complications of celiac disease

Anemia and failure to thrive are common complications in children. Delayed diagnosis can leads to delayed puberty and dental problems. Osteoporosis and increased risk of fracture, unfavorable pregnancy outcomes and a modest increased risk of intestinal malignancy like intestinal B cell and T-cell lymphoma[22], gastrointestinal lymphoma[23] also occur in adult life.

Treatment

The only treatment currently available for CD is strict adherence to a GFD (Gluten Free Diet) for life. Avoid gluten which is found in wheat, rye and barley lifelong. The clinical response to gluten withdrawal occurs rapidly, usually within the first month. Normalization of the small intestinal mucosal lesion may require longer periods. There is evidence that diagnosed but untreated CD is associated with a significant increase in morbidity and mortality. Prolonged adherence to a GFD may reduce this risk for both morbidity and mortality to the levels found in the general population. For these reasons prompt diagnosis and treatment with a GFD as early as possible is desirable.

There is Iron deficiency along with there is deficiency of folate, vitamin B-12, vitamins ADEK, thiamine, niacin, calcium, beta-carotene, zinc, essential fatty acid deficiency, should be replaced as needed. There is also temporary lactose intolerance due to deficiency of lactase enzyme managed with lactose free milk.

Follow up

Periodic visits for assessment of symptoms, growth, physical examination and adherence to the gluten-free diet. Measurement of TTG 6 months after treatment with a gluten-free diet is begun, and then approximately once a year if the patient has no symptoms. Measurement of TTG at any time after starting a gluten-free diet if the patient has persistent or recurring symptoms

Conclusions

Many children with celiac disease show an atypical clinical presentation. The understanding of presentations of celiac disease may prevent delayed diagnosis. Celiac disease should be specially investigated in patients with recurrent iron deficiency anemia, short stature as because approximately half of the patients with CD might present with atypical manifestations and also children with autoimmune disorders. Delays in diagnosis of CD may predispose patients to complications such as reduced bone mineral density, autoimmune disorders and even malignancies.

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