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Celiac disease and the dental patient

by THEOLOGOS (TED) MALAHIAS, DDS

Celiac disease is the most under-diagnosed hereditary autoimmune disease in the U.S.[1] One percent of the population is affected.[2] The incidence of celiac disease has increased fivefold, from 1.3 per 100,000 in 1999 to 6.5 per 100,000 in 2008, with the highest rate of increase among those over 34 years of age.[3] Dentists are not universally aware of the oral presentation of celiac disease or of its varied clinical presentations. A review of the literature can be helpful to dentists and in turn benefit their patients.

The major environmental precipitant of celiac disease is gluten.[4] Gluten is the term for the storage protein of wheat. The gluten fraction most studied is gliadin. Barley and rye are closely related genetically to wheat, and their respective storage proteins also are considered toxic to celiac patients.[1]

The gliadin fraction promotes an inflammatory response, primarily in the upper intestine, characterized by infiltration of the lamina propria and the epithelium with chronic inflammatory cells and villous atrophy (see Figure 1).

In order to develop Celiac disease, the person must have HLA genes that encode for HLA-DQ2 or HLA-DQ8 proteins. Presence of these genes is not diagnostic for celiac disease, but absence of these genes can be used to rule out the diagnosis of celiac disease. Diagnosis of celiac disease in a patient also increases the probability that a first degree relative is at risk for celiac disease.[1]

Environmental factors can influence the emergence of celiac disease in a patient. Breast feeding has been found to be protective. Introduction of gluten in the diet before four months of age may increase the risk of celiac disease. Infection with rotavirus also may increase the risk of celiac disease.[1,4]

SYMPTOMS AND TERMINOLOGY

The classic clinical presentation of celiac disease had been considered to be abdominal distention, chronic diarrhea and failure to thrive. In the last 20 years, non-classical presentations have increased in frequency.[5] Included in these findings are iron deficiency anemia, constipation, osteopenia, osteoporosis, fatigue, irritable bowel syndrome, psychological disorders (e.g., depression), neurologic disorders (e.g., cerebellar ataxia), migraine, neuropathies, epilepsy, dermatitis herpetiformis, hypoprotinemia, hypocalcemia and elevated liver enzymes.[4,6,7]

Celiac disease occurs in those at increased risk, either because they are relatives of an individual with celiac disease, or they have an associated autoimmune disease. The associated autoimmune diseases include Type I diabetes mellitus, autoimmune thyroiditis, Sjögren's syndrome, Addison disease, idiopathic dilated cardiomyopathy, autoimmune myocarditis, primary biliary cirrhosis, autoimmune hepatitis and autoimmune cholangitis. Those with selective IgA deficiency also are at increased risk.[4,7,8,9,10] Patients with Down syndrome and Turner syndrome have an increased incidence of celiac disease.[4]

A positive intestinal biopsy is considered the gold standard in diagnosing celiac disease.[1]

Intestinal biopsy usually is performed after positive serological tests. The tests most often used are the tissue transglutaminase IgA and the deamidated gliadin peptide (IgA and IgG). Two other serological tests, which still are available, are IgA endomysial antibodies (which are expensive and require experience in interpretation) and IgG Transglutaminase (which is not routinely used and is only of value in IgA deficiency). Total IgA antibodies will help identify patients who are IgA deficient.[1]

This article is concerned with those patients who are diagnosed with celiac disease confirmed by intestinal biopsy; however, dentists will encounter patients who report "gluten intolerance" on their medical history. Experts quickly recognized that standardization of terminology was needed, and a consensus at the 2012 international celiac disease conference resulted in such definitions.[11] A listing of commonly used definitions follows:

- *Asymptomatic CD*: Is not accompanied by symptoms even in response to direct questioning at initial diagnosis.
- *Classical CD*: Presents with signs and symptoms of malabsorbtion, diarrhea, steatorrhea, weight loss and growth failure.
- *Non-Classical CD*: Presents without signs and symptoms of malabsorbtion.
- *Subclinical CD*: Below the threshold of clinical detection without signs or symptoms sufficient to trigger CD testing in routine practice.
- *Symptomatic CD*: Characterized by clinically evident gastrointestinal and/or extraintestinal symptoms attributable to

gluten intake.

- *Refractory CD*: Consists of persistent or recurrent malabsorptive symptoms and signs with villous atrophy despite a strict gluten-free diet for more than 12 months.
- *Potential CD*: Relates to people with normal small intestinal mucosa who are at increased risk of developing celiac disease as indicated by positive celiac disease serology.
- *CD autoimmunity*: Relates to increased tTG or EMA on at least two occasions when the status of the biopsy is not known. If the biopsy is positive, then this is celiac disease; if the biopsy is negative, then this is potential CD.
- *Genetically at risk of CD*: Family members of patients with CD that test positive for HLADQ2 and/or DQ8 are genetically at risk of CD.
- *Gluten-related disorders*: All conditions related to gluten, such as gluten ataxia, dermatitis herpetiformis, non-celiac gluten sensitivity, wheat allergy and celiac disease.
- *Non-celiac gluten sensitivity*: Relates to one or more of a variety of immunological, morphological or symptomatic manifestations that are precipitated by the ingestion of gluten in people for whom celiac disease has been excluded.

ORAL MANIFESTATIONS OF CELIAC DISEASE

Patients who have celiac disease at an early age (7 years or younger) may have the enamel formation of their permanent teeth affected. Multiple studies have confirmed this association [12],[13],[14],[15], but other studies have failed to do so[16]; the discrepancy may be due to the presence of a different HLA genotype in the particular populations examined.[13] Clinical signs include bilateral, symmetrical and chronologic white or yellow opacities, with or without horizontal lines or grooves. Enamel is without glaze and enamel structural defects may be present. These lesions must be present in all four quadrants.[12],[13],[17] Lesions mainly affect the permanent incisors and molars; however deciduous canines and second molars can exhibit enamel defects.[13] Enamel defects have been classified from grade 0 to grade IV with increasing structural defects and discoloration as the grade increases (see Table 1).

The cause of the dental enamel defects is unknown. Possibilities include hypocalcemia caused by malabsorbtion, a gluten-induced immunological process that occurs in patients between ages of 6 months up to 7 years, which damages the enamel-producing organ.[14] Dental enamel defects are not exclusive to celiac disease. Excessive fluoride intake infections such as rubella, genetic conditions such as Amelogenisis imperfecta, or antibiotic use also can result in enamel defects. Local trauma or infection in a deciduous tooth may cause an enamel defect in the underlying permanent tooth but this is a localized insult, unlike celiac and other systemic conditions which would affect teeth in all arches chronologically.

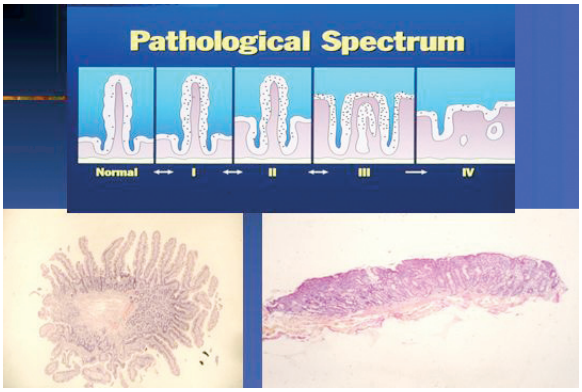
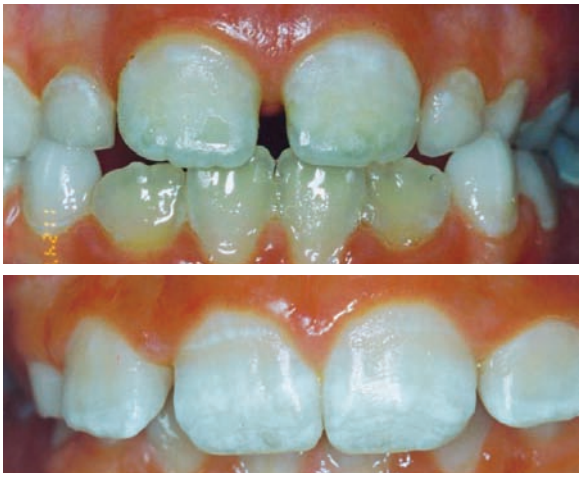


FIGURE 1 Normal villi progressing to atrophic villi demonstrating Marsh class I through IV inflammatory response with infiltration of lamina propria with chronic inflammatory cells.

TABLE 1: Classification of Systemic and Chronologic Enamel Defects

Classification	Enamel Defect
Grade 0	No Defect
Grade I	Defect in color of enamel consisting of single or multiple cream, yellow or brown opacities (marks), and loss of normal enamel glaze
Grade II	Slight structural defects consisting of a rough surface with horizontal grooves or shallow pits; light opacities and color changes also may be found; part or the entire surface of enamel is without glaze
Grade III	Obvious structural defects with part, or the entire surface, of enamel rough and filled with deep horizontal grooves, which vary in width or have large vertical pits; large opacities of different colors or linear discoloration may be present in combination
Grade IV	Severe structural defects; shape of the tooth is changed; tips of cusps are sharp-pointed and/or incisal edges are unevenly thinned and rough; thinning of the enamel material is easily detectable and the lesion may be strongly discolored

Adapted from Aine, L. "Dental enamel defects and dental maturity in children and adolescents with coeliac disease," Proc. Finn. Dent. Soc., 82(4): 227-229; 1986.



IMAGES 1 & 2 Grade II Dental Enamel Defects.

OTHER ORAL MANIFESTATIONS

Celiac patients have a significantly higher rate of oral aphthous ulceration than non-celiac patients. The rate of occurrence decreases when patients begin a gluten-free diet.[17],[18] Eruption of adult teeth also is delayed when celiac disease is present.[15] Delay in dental age in children with celiac disease may be considered as a reliable indicator of somatic growth and also of biologic age.[19] Celiac disease also may alter the pattern of craniofacial growth. This was demonstrated in a study by Ciacci which showed that Caucasoid Mediterranean adult celiac individuals tend to have a peculiar aspect of the face characterized by a larger forehead when compared to general population controls.[20]

Assessed by a scanning electron microscope, hypoplastic enamel defects of a group of celiac children the first published in literature, demonstrates that the enamel hypoplasia of deciduous and permanent teeth in celiac disease is highly hypomineralized with shorter prisms, more irregularly distributed and less interprismatic substance than observed in the non-celiac enamel hypoplasia.[21]

Celiac disease patients on a gluten-free diet still experience common symptoms of the disease, such as oral soreness, burning sensations or xerostomia. The tongue

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is most often affected.[9] Biopsy of the bucal mucosa of gluten-free diet treated patients shows that T-cells were clearly more present in the lamina propria than in that of healthy controls.[9] Celiac patients who have taken a gluten-free diet for five years or more do not have an increased risk of developing cancer over all sites when compared with the general population. The risk increased in those taking a reduced-gluten or normal diet. This population has an excess of cancers of the mouth, pharynx and esophagus.[22]

Celiac disease patients following a strict gluten-free diet secrete lower relative amounts of amylase, IgA, and IgM into paraffin-stimulated whole saliva than do healthy controls. No difference in salivary flow rate was noted in celiac disease patients versus controls.[23]

TREATMENT OF PATIENTS WITH CELIAC DISEASE

The current treatment of celiac disease consists only of adherence to a gluten-free diet. Potential therapies being considered are genetically modified wheat, immunizations, permeability blockers, oral peptidases, blocking tissue transglutaminase (tTG), designer drugs and cytokine blockers.

Celiac patients are wary of what they ingest and thus are very concerned about the ingredients of products used in oral hygiene care and dental treatment. Manufacturers have been alerted to this concern and have realized that by labeling products that are gluten free, and by producing gluten-free alternative formulations for other products, they can accommodate consumers and thus encourage sales.

The first step for dentists toward successful treatment of celiac patients is to demonstrate an understanding of the disease. Second, dentists should have gluten-free prophy paste and fluoride, both of which are now available from multiple manufacturers and dental suppliers. A query of dental manufacturers revealed that gluten is not usually found in impression materials, cements or restorative materials. However, manufacturers cannot always immediately confirm that their products are gluten free, due to outsourcing of ingredients and the possibility of cross-contamination in the manufacturing process.

The dentist can make a valuable contribution toward recognizing patients who may be undiagnosed celiac. Dental enamel defects observed through oral examination, as well as a family history of celiac disease or the presence of other autoimmune conditions that are highly associated with celiac disease (e.g., juvenile diabetes, dermatitis herpetiformis or autoimmune thyroditis), may prompt the dentist to advise the patient to seek further medical evaluation. *f*

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