Oral manifestations of gastrointestinal diseases in children. Part 4: Coeliac disease

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ABSTRACT

Alterations within the oral cavity can be the first sign of systemic diseases and may thus allow for an early diagnosis and treatment. In particular, being the oral cavity part of the gastrointestinal system, oral alterations can be an expression of a gastrointestinal disease. Dental enamel hypoplasia and aphthous ulcers have been found to be more common in children with coeliac disease compared with the general population and to regress after the patient is started on a gluten free-diet. A prompt recognition of systemic diseases through a careful examination of the oral cavity could allow the child to have appropriate investigations and to be treated in a timely fashion.

Keywords *Alterations of the oral cavity; Children; Coeliac disease; Gastrointestinal diseases.*

Coeliac disease

Coeliac disease (CD) is a common, chronic, multi-system disorder that may develop in genetically susceptible subjects that are exposed to gluten in their diet. While in 1950s the cumulative detected incidence of the disease in England and Wales was 1/8000, and in Scotland of 1/4000 [Davidson, 1950], today CD is one of the most common disorders worldwide. In fact twenty years ago Italy started a campaign based on serological screening of general population samples: the overall prevalence of CD (including known CD cases) was estimated to be 1 in 184 subjects in a pool sample of 17,201 healthy Italian students with most atypical cases remaining undiagnosed unless actively searched by serological screening [Catassi, 1996]. Subsequently a huge number of further studies showed that CD is one of the most common, lifelong disorders affecting mankind all over the world, with an estimated mean prevalence of 0.9% [Lionetti, 2014]. While symptoms related to malabsorption such as abdominal pain, diarrhoea and weight loss are well recognised, atypical non GI symptoms might be ignored [Hill ID, 2005; AGA Institutes, 2006]. Anaemia, extreme weakness, short stature, osteoporosis, menstrual irregularities and infertility, delayed growth and puberty are possible signs of CD. In addition, oral alterations have been recognised as related to this pathology: dental enamel defects, delayed eruption, recurrent aphthous stomatitis (RAS), cheilosis, oral lichen planus, atrophic glossitis and xerostomia have been described in CD [Rashid, 2011; Tack, 2010] (Fig. 1). Malabsorption of a variety of macro- and micronutrients or immune-mediated damage with stimulation of naïve lymphocytes by gluten in the oral cavity have been speculated as possible causes of the previously listed oral alterations [Pastore and Carroccio, 2008; Pastore and Campisi, 2008; Fraser, 1982] (Fig. 2).

Dental enamel defects are more common in patients with CD compared with the general population [Rashid, 2011]. The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition highlighted that presence of (specific) dental enamel defects as suggestive of CD [Hill JD, 2005]. Prevalence of dental defects in children with CD is estimated to

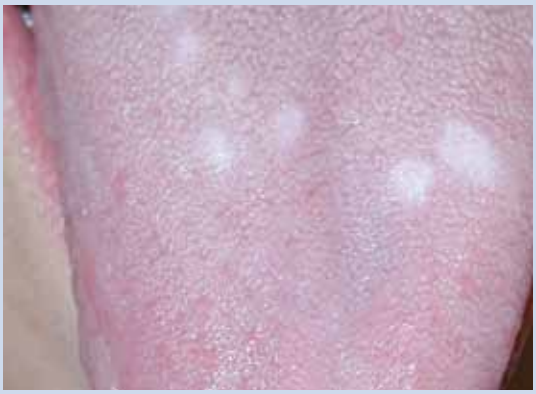

FIG. 1 Papular Oral Lichen Planus localised on the dorsum of the tongue.

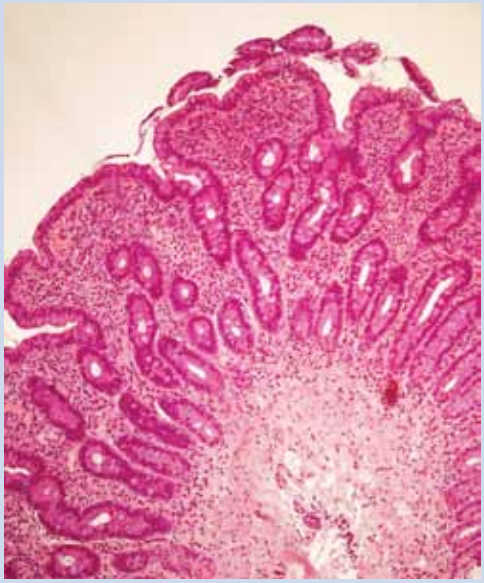

FIG. 2 Partial villous atrophy, crypt hyperplasia, and intra-ephithelial lymphocytosis in the duodenal biopsy of a child with 3b Oberhuber coeliac disease. Ematossilin Eosin original magnification.

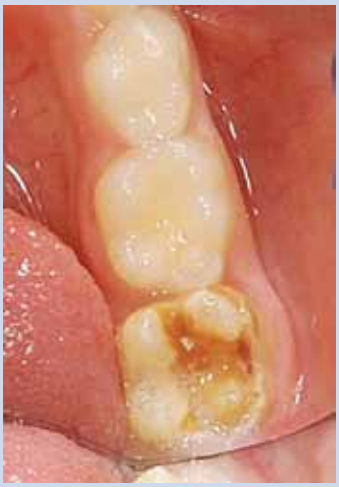

FIG. 3 Enamel hypoplasia and hypomineralisation of the lower right first molar.

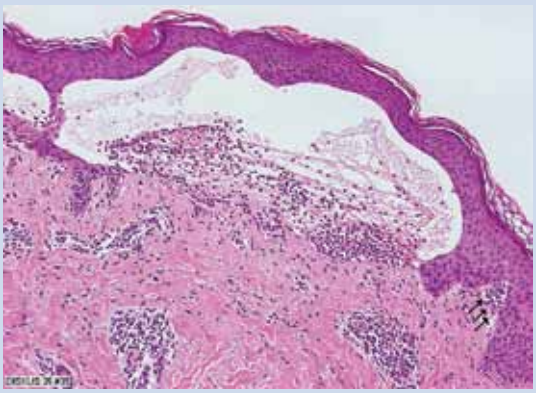

FIG. 4 Herpetiformis dermatitis: bollous derma-epidermal separation with an infiltrate of eosinophils.

be 5.8% to 13.3% (mean 9.6%) in patients with deciduous teeth and 9.5% to 95.9% (mean 51.1%) in those with mixed or permanent dentition [Pastore and Carroccio, 2008]. Children affected by CD before 7 years of age may develop dental enamel abnormalities of their permanent dentition such as hypoplasia and hypomineralisation. These alterations appear symmetrically and chronologically in all 4 quadrants, with more defects in the maxillary and mandibular incisors and molars that often show intact cusps [Rashid, 2011] (Fig. 3). Aine et al. developed a classification of the localised enamel defects in CD such as pitting, grooving and sometimes complete loss of enamel.

Teeth development is also delayed or slowed down in coeliac children. Campisi et al. [2008] and Condò et al. observed a significantly increased occurrence of delayed eruption in children with CD in comparison with healthy children. Moreover the introduction of a gluten-free diet has beneficial effects on skeletal development and dental age in children with CD [Condo, 2011].

RAS is a frequent oral alteration characterised by repeated episodes of single or multiple ulcers of the oral mucosa, that can be round or ovoid with an erythematous halo and a yellow or gray floor. Despite being the most common oral ulcerative disease, affecting 10%–20% of the general population, RAS is even more frequent in children affected by systemic diseases such as CD [Regezi, 2008; Trandafir, 2014]. In a large survey conducted in Canada in children with biopsy-proven CD (< 16 years of age), 16% reported recurrent oral ulcers [Cranney, 2007]. Sedghizadeh et al. demonstrated that 41% of the patients with CD had a history of RAS compared to 27% of the healthy controls, nevertheless this difference was not statistically significant. However it should be said that RAS can be a sign of other systemic diseases such as immunodeficiency, oral infections, Crohn's disease, nutritional deficiencies and malabsorption [Regezi, 2008; Trandafir, 2014].

Association between CD and caries is controversial in children. While Condò et al. [2011] observed a more frequent occurrence of caries in patients with this disease, other authors have shown that a better control over the diet, with the use of a smaller number of snacks as well as a better oral cavity hygiene [Shetyer, 2013] may prevent the development of dental erosions in CD [Farmakis, 2005]. On the other hand, Acar et al. report on a smaller level of cariogenic bacteria in the saliva of patients with CD (Streptococcus mutans, Lactobacillus). The topic is still a matter of debate.

Finally few more oral alterations have been described in CD: oral lichen planus, whose aetiology is unknown [Trandafir, 2014]; atrophic glossitis, a condition characterised by red, smooth, shiny tongue caused by vitamin B12 deficiency [Trandafir, 2014]; xerostomia due to salivary gland dysfunction with diminished salivary flow that develops after gluten exposure [Lähteenoja, 1998; Shetyer, 2013; Ertekin, 2005]; angular cheilitis

due to malabsorption [Rashid, 2011].

Until 2012, positivity for anti-transglutaminase and/or anti-endomysium antibodies associated with characteristic histological findings based on multiple biopsies of duodenum were required to diagnose CD [Benkebil, 2013]. Currently an algorithm which can be found In the European paediatric guidelines permits to avoid biopsy in those children with typical clinical symptoms, >10-fold anti-transglutaminase antibody titer with positive anti-endomysium antibodies and a genotype compatible with CD development [Husby, 2012].

As far as treatment is concerned, gluten-free diet remains in 2015 the only treatment available and effective for CD [Husby, 2012].

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