An overview on oral manifestations of gastrointestinal diseases

C. Mantegazza*, F. Angiero**, R. Crippa***, M. Paglia****, G.V. Zuccotti**

* Department of Pediatrics, University of Milan, Children’s Hospital “Vittore Buzzi”, Milan, Italy
** Department of Pediatrics, University of Milan, ASST-FbF-Sacco, Milan, Italy
***Department of Surgical sciences and Integrated Diagnostics, University of Genova, Genoa, Italy
****Department of Pediatric Dentistry, Italian Stomatological Institute (ISI), Milan, Italy

KEYWORDS

Alterations of the oral cavity, Celiac disease, Crohn’s disease, Gastro-esophageal reflux disease, Gastrointestinal diseases, Ulcerative colitis.

ABSTRACT

Aim: The oral cavity is part of the gastrointestinal system and as such the presence of alterations in this district can be the first sign of both systemic and gastrointestinal diseases. As such alterations are very common, especially in children, it is important for the dentist to distinguish when they are the expression of a gastrointestinal condition. The aim of this review is to provide the dental practitioner with useful data for the diagnosis, treatment and management of the most common conditions, such as Crohn’s disease, ulcerative colitis, gastro-esophageal reflux disease, and celiac disease.

Results: One of the most common oral alterations is tooth erosion, with enamel loss and an increased risk of dental caries, which have been reported in children and adolescents with gastro-esophageal reflux. Dental enamel hypoplasia and aphthous ulcers have been found to be more common in children with celiac disease than in the general population. Another very common oral alteration is gingivitis, which is reported to affect 9-95% of children in Europe and in North America and more than 60% of adolescents [Italian Ministry of Health, Guidelines 2013]. Pyostomatitis vegetans can be a sign of ulcerative colitis and Crohn’s disease, the latter has also been related to diffuse mucosal swelling, cobblestone mucosa, localized muco-gingivitis, deep linear ulceration, fibrous tissue tags, polyps, nodules, and aphthous-like ulcers.

Conclusion: A prompt recognition of systemic and gastrointestinal diseases through a careful examination of the oral cavity could be the first step of further investigations that may lead to an early diagnosis and timely treatment.

Introduction

Correlations between alterations in the oral cavity and systemic conditions have been widely reported (Chi, 2010; Majorana, 2010) and during the oral examination it is also possible to detect signs and symptoms of systemic diseases, such as mucocutaneous, immunologic disorders, hormone diseases, haematological conditions, systemic infections, and nutritional problems (US Department of Health, 2000). In particular, alterations in the oral cavity, as it is part of the gastrointestinal (GI) system, may reveal a GI disease, such as celiac disease, gastroesophageal reflux disease or inflammatory bowel disease.

Oral manifestations include dental enamel defects, dental caries and aphthous ulcers which have been reported to occur in subjects with celiac disease and to regress with a gluten-free diet [Pastore, 2008]. Tooth erosion can be a consequence of gastroesophageal reflux disease [Tolia, 1997; Bishop, 1994; Schroeder, 1995], and the latter can be diagnosed in 25–83% of patients with caries, many of whom are children [Smith, 2015]. It is worthwhile mentioning that in recent years an increase in tooth erosion has been highlighted (Mulic et al., 2013); in Europe its prevalence has been reported to be higher than 50% in young adults (age 18-35 years) (Bartlett et al., 2013).

Other oral manifestations common in Crohn’s disease include geographic tongue, ulcers, stomatitis and periodontal disease [Bishop, 1972; Stankler, 1972; Van Dyke, 1986]. Moreover, oral alterations can be detected in up to one-third of pediatric patients with ulcerative colitis and are usually nonspecific [Katsanos, 2015].

The spectrum of oral lesions is wide, especially in
children, and therefore it is important for the dentist to understand which are most commonly associated with GI diseases as well as their approach and management, in order to make a correct differential diagnosis and provide adequate treatment. The role of the dentist is very important in these situations, as symptoms are often unrecognized or overlooked by gastroenterologists (Harty et al., 2005) and in many cases diagnosis is made when a specialist in oral medicine or dentistry is involved (Pittock et al., 2001; Campbell et al., 2011; Lankarani et al., 2013).

The aim of this article is to review the literature on oral lesions associated with GI diseases, in order to provide useful data for the diagnosis, treatment and management of the most common conditions, such as Crohn’s disease, ulcerative colitis, gastro-esophageal reflux disease, and celiac disease.

Crohn’s disease
Since the mid-1970s the Incidence of Crohn’s disease (CrD), a chronic relapsing inflammatory condition, has increased in Western countries (Hoede and Mourn, 2012), with a prevalence varying from less than 10 to about 150 per 100,000 inhabitants in European countries (Yapp et al., 2000; Gheorghie et al., 2004). CrD has a complex aetiology and its pathogenesis is still uncertain (Crippa et al. 2016).

Lesions within the oral cavity can represent an initial and primary manifestation of CrD (Daley, 2007; Hussey, 2011; Boirivant, 2012) or may occur concurrently, or follow the onset of GI involvement (Kalmar, 2000); however oral lesions without gastrointestinal involvement are rarely reported in the literature (Zbar, 2012; Fatah zadeh, 2009; Chi, 2010; Daley, 2007). These lesions may be a consequence of low serum levels of micronutrients and macronutrients secondary to malabsorption (Jacobs, 1968) or to local immune reactions to oral antigens typical of CrD (Lehner, 1972; Basu, 1976).

Oral CrD can be detected in the buccal mucosa, lips, tongue, hard and soft palate, salivary glands, gingiva and teeth with alterations that can either be typical and pathognomonic, in most cases associated with or highly suspicious for inflammatory bowel disease, or nonspecific (Katsanos, 2015).

The prevalence of Oral CrD is about 20%, but it has been reported as high as 50% (Laube et al., 2017; Pittock et al., 2001; Rowland et al., 2010; Lankarani et al., 2013) especially in the younger age groups, as these subjects seem to have a lower age of manifestation with respect to the average CrD population (Mahid et al., 2008).

In up to 5-15% of subjects affected by CrD a typical acute oral manifestation, defined orofacial CrD, may arise and show as recurrent or persistent lip swelling, cobblestone of the oral mucosa, stomatitis, mucogingivitis, deep linear or serpiginous ulcerations surrounded by epithelial hyperplasia, tissue tags or polyps, often related to Candida-associated angular cheilitis (Boirivant, 2012; Fatahzadeh, 2009; Katsanos, 2015; Tilakaratne, 2008; Kolho, 2011; Wies enfeld, 1985; Van der Waal, 2002). Macroscopic and histological characteristics of this manifestation are similar to those found in the gastrointestinal tract (Stankler, 1972) and can be associated with pain on touch or on eating acidic or spicy foods, impairment of oral function, eating, speaking, and psychosocial stress (Plauth, 1991). Characteristic oral alterations of CrD include orofacial CrD, granulomatous cheilitis and pyostomatitis vegetans.

Diagnosis can be very difficult, since orofacial CrD is indistinguishable from orofacial granulomatosis, which can be detected in several conditions (such as sarcoidosis, Miescher’s cheilitis granulomatosa, Melkerson-Rosenthal syndrome, foreign body granuloma, rosacea, and various granulomatous infectious diseases) (Wies enfeld, 1985; Bogenrieder, 2003). Up to 40-50% of young patients with orofacial granulomatosis might develop CrD and it may be noticed even years after the first appearance of oral symptoms (Rowland, 2010).

Harty et al. [2005] reported that granulomatous inflammation was present in 100% of biopsies collected in their study, thus underscoring that oral mucosa represents an easily accessible site for harvesting diagnostic material.

Granulomatous cheilitis is a sub-acute uncommon granulomatous inflammation involving the lip area [Allen, 1990] and is described as an initial sudden swelling of the lips, mainly the lower one, which resolves within hours or days, but is followed by permanent edema and lumpy swelling [Friedrich, 1990; Alawi, 2005]. This condition can also be a sign of other diseases such as allergy, sarcoidosis, Melkerson-Rosenthal syndrome, relapsing herpes simplex, relapsing erysipelas, cancers and genetic disorders [Katsanos, 2015].

Pyostomatitis vegetans is a rare manifestation showing thickened and erythematous oral mucosa covered with pustules and superficial erosions with a ‘snail tracks’ pattern. It has been associated in 75% of cases with inflammatory bowel disease [Ayangco, 2002; Lankarani, 2013; Delaporte, 1998] and can also be an expression of autoimmune pemphigoid diseases and infections [Hansen, 1983].

Other oral lesions suggestive of CrD are cobblestoning, mucogingivitis, gingival hypertrophy, lip swelling with vertical fissures, midline lip fissuring, deep linear ulcers of the buccal and labial mucosa and indurated tag-like lesions [Greenstein, 1976; Lisciandrano, 1996; Field, 1989; Colella, 1971; Lourenço, 2010].
CrD has also been related to non-specific lesions such as recurrent aphthous stomatitis (RAS), dry mouth, salivary duct fistula, recurrent buccal infections, persisting buccal space, aseptic abscesses, pustular ulcerations, erythema, swelling and cobblestoning of the gingiva, mandibular osteomyelitis [Correl, 1981; Delaporte, 1998; Gargiulo, 1989; Ciantar, 2007].

As for diagnostic examinations, Van der Waal et al. [2002] do not recommend routine investigation of the gastrointestinal tract in patients with a negative history of gastrointestinal conditions, whereas Plauth et al. [1991] recommend exhaustive and repeated investigations for CrD in cases of orofacial granulomatosis even when no gastrointestinal symptoms are present; endoscopy is recommended in patients with bowel symptoms or/and highly specific types of oral lesions [Katsanos, 2015]. Periodical screening of fecal calprotectin, a surrogate marker for mucosal inflammation (e.g. in CrD), is also suggested [Roseth, 1999; Sipponen, 2008].

Oral CrD treatment may include steroid therapy [Hussey, 2011; Harikishan, 2012], tumor necrosis factor-alpha-antagonist agent infliximab (administered [Peitsch, 2007; Hussey, 2011; Harikishan, 2012], tumor necrosis factor-alpha-antagonist agent infliximab (administered promising results in chronic granulomatous cheilitis and in a case of orofacial CrD and lip swelling not responsive to any other treatment) [Peitsch, 2007; Sipponen, 2008].

Ulcerative colitis

Ulcerative colitis (UC) is considered with CrD the most common type of inflammatory bowel disease, with the highest incidence in subjects aged between 15 and 25 years and a second, smaller peak between 55 and 65 years (Mantegazza et al., 2016a).

Like CrD, also UC is immunologically based [Lourenço, 2010], UC and CrD also share some clinical manifestations, such as mucosal ulcers (Seo, 1992), pyostomatitis vegetans (Alstead, 1991; Calobrisi, 1995), diffuse pustules (O’Laughlin, 1978) and lichen planus (Alstead, 1991; Davies, 1984). In addition, some medications used for the treatment of GI diseases are sometimes responsible for oral side effects (Parvinen, 1984; Sreebny, 1986).

Again, pyostomatitis vegetans manifests as multiple miliairy white or yellow pustules that can merge in snail-trail ulcers, with an erythematous and edematous mucosal base involving mostly the labial gingiva and the labial and buccal mucosa. It is can be diagnosed when a combination of clinical features of inflammatory bowel disease, peripheral eosinophilia, histological findings, and negative culture of the exudate are present [Mijandrusi-Sinci, 2010]. Average age at diagnosis is usually about 34 years.

Other non-specific oral manifestations in UC are oral aphthae (5-10% of patients), glossitis, cheilitis, stomatitis, lichen planus, mucosal ulcers, diffuse pustules, and non-specific gingivitis [Folashade, 2008; Lekovi, 2011; Krebs, 2011].

Diagnosis of UC is based on the presence of bloody diarrhea with negative stool cultures and diffuse continuous mucosal inflammation involving the rectum and extending to a point more proximal in the colon at the endoscopic evaluation [Kugathasan, 2003; Bentsen, 2002]. Treatment includes oral steroids [Thrash, 2013]. However, a dental evaluation can be useful during the investigation of patients with suspected UC (Elahi, 2012).

Gastro-esophageal reflux disease

Gastro-esophageal reflux is the physiologic movement of gastric content into the esophagus and oropharynx occurring through the relaxation of the lower esophageal sphincter; it can become pathologic [Colletti, 2003] when repeated regurgitation, nausea, heartburn, coughing, laryngitis, asthma, or pneumonia occur and is therefore defined Gastro-esophageal reflux disease (GERD). It can also be accompanied by secondary complications such as esophagitis, hemorrhage, stricture, Barrett’s esophagus, and adenocarcinoma [Vakil, 2006].

A strong association between GERD and DE has been reported (Pace, 2008). The 2009 NASPGHAN and ESPGHAN guidelines on reflux in children report that oral manifestations have also been described in GERD, and in particular its correlation with dental erosions [Vandenplas, 2009; Pindborg, 1970]; in fact, their prevalence in children with GERD has been reported as high as 83.3% [Dahshan et al., 2010], though in the literature different figures are reported.

It is worthwhile mentioning that in GERD subjects tooth erosion mainly involves the mixed dentition and starts from the posterior area, in particular facial, occlusal, and lingual surfaces [Dahshan et al., 2010]. In these situations, administration of proton pump inhibitors has proven to be effective [Wilder-Smith et al., 2009].

GERD may also be the cause of changes in soft tissues and salivary flow [Silva, 2001]; Di Fede et al. [2008] reported a significant association of GERD with oral acid/burning sensation, xerostomia, subjective halitosis and soft/hard palate and uvula mucosal erythema.

Celiac disease

Celiac disease (CD) is an autoimmune condition that may develop as a consequence of the consumption of gluten [Barker and Liu, 2008] in genetically susceptible subjects. Its incidence has increased over the last decades, and presently it is one of the most common, lifelong disorders worldwide (Mantegazza...
oral mucosal lesions, especially in children, are important clues to diagnose systemic diseases of which they may be the primary presenting sign, preceding gastrointestinal symptoms. One of the first steps to diagnosis of GI diseases begins with a clinical dental examination of the whole oral cavity and a detailed medical history (Mantegazza et al., 2016c); therefore, dentists are encouraged to inquire about symptoms associated to these disorders and family history of GI diseases that represent potential etiological factors associated with oral disease. As the presence of suspicious oral alterations requires interdisciplinary cooperation, communication between gastroenterologists and dentists is mandatory for the success of the treatment.

**References**


