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REVIEW ARTICLE

Clinical manifestations of gastrointestinal diseases in the oral cavity

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Abstract *Aim:* In this review, several gastrointestinal diseases that dentists may encounter in practice are highlighted and discussed.

Materials and methods: Using MEDLINE (PubMed), a comprehensive review of gastrointestinal diseases and their oral cavity manifestations was performed.

Results: Many gastrointestinal diseases present with oral symptoms that are detectable by dentists and dental hygienists. Often, oral manifestations of the disease may appear before systemic signs and symptoms. Managing patients with these conditions requires dentists to adjust their treatment and/or involve other health professionals.

Conclusion: Care must be taken when providing periodontal therapy or dental implants to patients suffering gastrointestinal diseases who are at high risk of bleeding, infection, or malnutrition, for example. Also, pharmacological therapy for these patients may need to be customized.

Contents

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1. Introduction

In contemporary dental practice, a significant number of patients seeking treatment are medically compromised. In addition, oral health care providers are increasingly involved with often-stressful surgical procedures that can require challenging postoperative care. Proper knowledge of patient health conditions is a cornerstone of optimal medical care. Thorough medical history and clinical examination usually alert clinicians to the need for further investigation and/or referral, especially since a patient may not be aware of certain health issues. In fact, in some cases, oral findings may precede systemic manifestations.

Table 1 Gastrointestinal diseases and their oral manifestations.

Gastrointestinal diseases	Oral findings
Gastroesophageal Reflux Disease	Erosion of dental hard tissues
Peptic ulcers and *Helicobacter pylori*	*H. pylori* in the oral cavity may be a source of re-infection
Ulcerative colitis	Pyostomatitis vegetans (PV); aphthous stomatitis; hairy leukoplakia
Crohn's disease	Corrugated, cobblestone appearance of the buccal and labial mucosa; linear ulceration; PV; labial swelling; persistent aphthous ulcers
Disease of the hepatobiliary system	Yellowish discoloration of mucosa
Celiac disease	Dental enamel defects; oral ulcers
Familial adenomatous polyposis	Osteomas; odontomas; supernumerary teeth, impacted permanent teeth; fibrous tumors; skin pigmentation; epidermoid cysts
Cowden's syndrome	Papillomatous lesions; maxillary and mandibular hypoplasia; enlarged and fissured tongue; hypodontia; severe dental caries; periodontitis
Plummer-Vinson syndrome	Oral burning sensation; glossitis
Peutz-Jeghers syndrome	Oral labial and facial melanotic macules

The gateway to the gastrointestinal (GI) tract is the oral cavity, which shares a common embryogenic origin with the GI tract. Thus, it is not surprising that many GI disorders have detectable oral manifestations (Wray, 1998).

This review aims to highlight several GI diseases relevant to dental health professionals. In the following sections, selected GI diseases will be discussed (Table 1).

2. Gastroesophageal reflux disease

Gastroesophageal reflux disease (GERD) is among the most common GI disorders, affecting between 10 and 20% of the Western population (Tantbirojn, et al., 2012). In Saudi Arabia, the prevalence of GERD has been found to be 28.7% (Alsuwat, et al., 2018). GERD is caused by failure of the barrier between the esophagus and stomach, resulting in backflow of stomach content to the esophagus (Malfertheiner and Hallerback, 2005). Heartburn, dysphasia, and chronic cough are common symptoms (Malfertheiner and Hallerback, 2005, Kamal and Vaezi, 2010). Chronic tissue injury due to GERD can cause Barrett's esophagus, in which the squamous epithelium of the esophagus is replaced with metaplastic columnar epithelium (Velanovich, 2012). An increased risk of adenocarcinoma has been associated with Barrett's esophagus (Milind and Attwood, 2012, Velanovich, 2012).

Treatment of GERD involves lifestyle modifications, control of gastric acid secretion with medication (e.g., proton pump inhibitors and histamine H_2-receptor antagonists), or in severe cases, by corrective anti-reflux surgery (Nwokediuko, 2012).

Dental erosion, a significant oral finding in patient with GERD, affects the palatal surfaces of the maxillary anterior teeth and the occlusal and lingual surfaces of the mandibular incisors (Greenwood and Meechan, 2003, Chi, et al., 2010, Firouzei, et al., 2011, Marsicano, et al., 2013, Alnasser, et al., 2019). Additional oral manifestations may include xerostomia, burning sensation, halitosis, palatal erythema, and temporomandibular disorders (Chi, et al., 2010, Yoshikawa, et al., 2012, Marsicano, et al., 2013, Li, et al., 2019). Furthermore, patients affected with GERD may feel uncomfortable while in the fully supine position in the dental chair, which must be considered during dental visits (Greenwood and Meechan, 2003).

3. Peptic ulcers and *Helicobacter pylori*

Peptic ulcers can be classified as either gastric or duodenal. *Helicobacter pylori (H. pylori)*, a Gram-negative spiral microorganism, is the main etiologic factor in peptic ulcers while non-steroidal anti-inflammatory drugs (NSAIDs) are the main etiologic factor for *H. pylori*-negative ulcers (McColl, 2010).

In the United States, the prevalence of peptic ulcers is estimated to be about 8.4%, while in Saudi Arabia the prevalence of peptic ulcers is almost 22%, of which 16.2% were found to be gastric ulcers (Albaqawi et al., 2017). Peptic ulcers are associated with older age, smoking, and alcohol consumption (Garrow and Delegge, 2010). Most patients with peptic ulcers may complain of abdominal pain, primarily of epigastric origin. Other symptoms included indigestion, regurgitation, chest pain, nausea, vomiting, and appetite loss (Albaqawi et al., 2017; Barkun and Leontiadis, 2010). If left untreated, the sequelae of both kinds of peptic ulcers can include severe erosion, leading to perforation and serious hemorrhage (Najm, 2011). Moreover, gastric ulcers carry the risk of malignant transformation (Najm, 2011).

H. pylori are linked not only to peptic ulcers but also to a wide range of pathologies, including gastric cancers (Czesnikiewicz-Guzik, et al., 2005, McColl, 2010). *H. pylori* is considered by the World Health Organization to be a class I (or definite) human carcinogen (International Agency for Research on Cancer., 1994). *H. pylori* colonize at least 50% of the world's human gastric mucosa, a prevalence that is even higher in developing countries (Czesnikiewicz-Guzik, et al., 2005, McColl, 2010).

The oral cavity is a potential extra-gastric reservoir for *H. pylori* (Dowsett and Kowolik, 2003, Anand, et al., 2006, Gebara, et al., 2006). *H. pylori* has been isolated from the saliva, tongue, and supra- and sub-gingival plaque (Riggio and Lennon, 1999, Avcu, et al., 2001, Bago, et al., 2011). Moreover, *H. pylori* were found to co-aggregate with *Fusobacterium* species during dental plaque biofilm formation (Andersen, et al., 1998). *H. pylori* were also isolated in greater quantities in the plaque biofilm of individuals with *peri*-implantitis (Persson and Renvert, 2013).

Several investigators have reported a positive relationship between the presence of oral *H. pylori* and *H. pylori* in the stomach (Dowsett and Kowolik, 2003, Eskandari, et al., 2010, Silva, et al., 2010, Agarwal and Jithendra, 2012). In contrast, other authors were unable to demonstrate this association, and some questioned whether *H. pylori* inhabit the oral cavity, arguing that its presence is transient and unrelated to oral status (Asikainen, et al., 1994, Hardo, et al., 1995, Martinez-Gomis, et al., 2006, Al-Ahmad, et al., 2012).

Treating peptic ulcers is focused on eradicating *H. pylori* (McColl, 2010). The most common therapy consists of a combination of three drugs: a proton-pump inhibitor, clarithromycin, and amoxicillin (metronidazole in cases of penicillin allergy) (McColl, 2010). While H. pylori may be eradicated with this regimen, the possibility of recurrence remains a treatment challenge (McColl, 2010). A *meta*-analysis concluded that the presence of *H. pylori* in the oral cavity may be a source of re-infection (Zou and Li, 2011). Furthermore, Lou et al. found that patients suffering from chronic atrophic gastritis caused by H. pylori had significant periodontal attachment loss (Luo, et al., 2019). Antibiotic therapy alone is not sufficient to eradicate H. pylori from the dental plaque since it is protected by the plaque biofilm environment (Gebara, et al., 2006). However, periodontal treatment as an adjunct to eradication therapy has been shown to reduce gastric *H. pylori* recurrence in patients with *H. pylori*-induced gastric diseases (Zaric, et al., 2009, Bouziane, et al., 2012, Jia, et al., 2012).

4. Inflammatory bowel disease

Inflammatory bowel disease (IBD) consists mainly of ulcerative colitis (UC) and Crohn's disease (CD). UC is a condition of unknown etiology that targets the large intestines, with a reported prevalence of 238 per 100,000 people (Kappelman, et al., 2007). In the Arab population, the incidence has been reported to be 22 in 100,000 (Alharbi, et al., 2014). However, the prevalence of UC in Saudi Arabia is still unknown (Alharbi, et al., 2014). The main symptoms of UC are abdominal pain, diarrhea, and lower GI bleeding (Ford et al., 2013). Several extra-intestinal manifestations have been reported in the literature (Greenwood and Meechan, 2003). CD may affect any part of the GI tract (Harikishan, et al., 2012). The main symptoms of CD include diarrhea, abdominal pain, and fever (Baumgart and Sandborn, 2012).

The incidence of CD in Saudi Arabia has been increasing in recent years, which necessitates the importance of early diagnosis and management (Al-Bawardy, 2017). The oral signs of CD are uncommon but may precede or appear concomitantly with intestinal lesions (Daley and Armstrong, 2007). These indicators are non-specific and may be caused either by the disease itself or nutritional deficiencies associated with it (Carey, et al., 2012). Manifestations may appear as linear pustules on erythematous mucosa, which is a rare condition known as Pyostomatitis vegetans (PV) (Chaudhry, et al., 1999, Lourenco, et al., 2010, Lopez-Jornet, et al., 2012). Other oral manifestations may include aphthous stomatitis or hairy leukoplakia (Fluckiger et al., 1994, Daley and Armstrong, 2007).

In CD, up to 30% of patients may have oral lesions that may precede another lesion (Daley and Armstrong, 2007). In fact, in some patients, the oral cavity is the sole location of the disease (oral CD). It is not yet clear whether patients with oral CD will ultimately develop intestinal lesions (Harikishan, et al., 2012).

Oral lesions usually present as a corrugated, 'cobblestone' appearance of the buccal and labial mucosa, linear ulceration, PV, labial swelling, and persistent aphthous ulcers (Daley and Armstrong, 2007, Lourenco, et al., 2010, Harikishan, et al., 2012). Microscopically, the lesions typically appear as non-specific chronic inflammation but may also appear as non-caseating granulomas in cases of long-standing lesions; thus, CD can also be considered a granulomatous disorder (Zbar, et al., 2012).

IBD is similar to periodontitis in many respects since evidence has implicated commensal bacteria, genetic susceptibility, and smoking in the etiology of both conditions (Sanz, et al., 2011). However, the evidence demonstrating an association between IBD and periodontitis is limited (Brito, et al., 2008, Stein, et al., 2010).

Some precautions must be taken when planning oral surgical treatment for patients with IBD. These patients, especially

CD patients, may suffer from delayed wound healing after surgical procedures compared to systemically healthy patients (Scammell and Keighley, 1986, Andersen et al., 2003). Furthermore, lower GI bleeding may result in anemia; therefore, blood analysis should be ordered, mainly if surgical treatment is intended. Another vital point is that an IBD patient may be treated with steroids and/or drugs with immune-suppressive effects. Communication with the patient's physician therefore is crucial. Also, pain control after surgical treatment can be challenging since NSAIDs could be contraindicated.

5. Disease of the hepatobiliary system

Jaundice results from increased bilirubin in the circulatory system, which accumulates in tissues and causes yellowish discoloration of mucosa and skin (Daley and Armstrong, 2007). Proper referral and consultation are importance to determine the cause of jaundice. If the jaundice is caused by liver damage, cirrhosis may have developed.

Bleeding tendency and pharmacological therapy used are vital points that should be evaluated in treating hepatic patients. The liver metabolizes many drugs that dentists routinely prescribe; therefore, adjusting the dose and/or changing the medication may be necessary. Furthermore, clinicians should carefully evaluate the patient's history of alcohol use since it may have caused hepatitis or cirrhosis (Daley and Armstrong, 2007).

6. Celiac disease

Celiac disease (CeD) is an autoimmune inflammatory disease. CeD involves the small intestine and is triggered by the ingestion of the protein gluten in genetically predisposed individuals; thus, CeD is also called gluten-sensitive enteropathy (Schuppan, et al., 2009). The estimated prevalence of CeD is about 1% of the world's population (Pastore, et al., 2008a). While CeD does not primarily affect children and young adults, it can appear at any age (Vilppula, et al., 2009). In Saudi Arabia, the prevalence of CeD was found to range from 1 to 2.7% based on the test used (Al Hatlani, 2015, Al-Mendalawi, 2016). Typical symptoms of CeD include abdominal pain, diarrhea, malabsorption, and weight loss (Gujral, et al., 2012). Atypical symptoms of CeD include some extra-intestinal manifestations, such as abnormal liver function, anemia, osteoporosis, neurological problems, and dental problems (Pastore, et al., 2008a, Pastore, et al., 2008b, Gujral, et al., 2012). Currently, the only effective treatment available for CeD is adopting a gluten-free diet (Stoven, et al., 2012).

Several oral symptoms have been reported in CeD patients, including dental enamel defects (Pastore, et al., 2008b, Cheng, et al., 2010, Ouda, et al., 2010) and oral ulcers (Cheng, et al., 2010, Ouda, et al., 2010, Baccaglini, et al., 2011). Even though an association between recurrent aphthous ulcers and CeD has been reported, CeD screening is not routinely recommended for patients with aphthous ulcers (Pastore, et al., 2008b, Yasar, et al., 2012). However, the clinician should suspect CeD when oral ulcers are associated with anemia or anemia-related symptoms (Cekin et al., 2012; Pastore et al., 2008b; Zoumpoulakis et al., 2019).

7. Familial adenomatous polyposis

Familial adenomatous polyposis (FAP) is an inherited autosomal-dominant condition that causes widespread adenomas of the colon and rectum, with an elevated risk of malignant transformation (Ramaglia, et al., 2007, Shaik, et al., 2015). If a patient with FAP is left untreated, colorectal cancer will likely develop by the age of 35–40 years (Galiatsatos and Foulkes, 2006, Ramaglia, et al., 2007). FAP is an uncommon disorder, with an incidence of approximately 2 per million and a prevalence of around 40 per million, with no gender predilection (Varesco, 2004). Clinical features in the orofacial area include osteomas, odontomas, supernumerary teeth, impacted permanent teeth, fibrous tumors, skin pigmentation, and epidermoid cysts (Sondergaard et al., 1987, Carl and Sullivan, 1989, Wijn, et al., 2007, Lee, et al., 2009). Ten percent of FAP patients can be categorized as having Gardner syndrome, in which the presence of osteomas is considered a diagnostic feature (Ramaglia, et al., 2007). Osteomas are more common in the mandible and usually appear as enostoses (Wijn, et al., 2007). Exostoses may occur in about one-third of FAP patients with osteomas (Wijn, et al., 2007). Most osteomas are asymptomatic, and patients may seek treatment for esthetic reasons.

Since osteomas can be detected both clinically and radiographically before the appearance of other symptoms, oral surgeons and dental practitioners may play a crucial role in the early detection of FAP (Panjwani, et al., 2011).

It is important to note that tooth extraction in patients with FAP may be difficult because of increased bone density and narrowing of the periodontal ligament space due to hypercementosis (Galiatsatos and Foulkes, 2006). It is also important to note that NSAIDs may be used as part of the medical management of FAP (Wijn, et al., 2007), which should be taken into consideration during dental management (Septer, et al., 2018).

8. Cowden's syndrome

Cowden's syndrome (CS), also known as multiple hamartoma or neoplasia syndrome or multiple hamartoma syndrome, is a rare hereditary autosomal-dominant disorder characterized by the development of hamartomatous papules and nodules of the skin and oral mucosa and polyposis of the gastrointestinal tract, as well as an increased risk of developing thyroid, breast, and endometrial cancers (Porter, et al., 1996, Ha, 2013). The estimated prevalence of CS is about 1 in 200,000 (Ha, 2013). In addition, females are affected slightly more than males (Segura Saint-Gerons, et al., 2006).

Mucocutaneous abnormalities are prevalent among CS patients, typically trichilemmomas, papules, or nodules on the face, neck, hands, and forearms, and keratoses on the palms and soles (Swart, et al., 1985, Porter, et al., 1996).

The most common oral manifestation includes papillomatous lesions that affect various parts of the oral mucosa, including the tongue, the gingiva, the palate, and the buccal and labial mucosa (Chaudhry, et al., 2000). Other manifestations may include maxillary and mandibular hypoplasia, an enlarged and fissured tongue, hypodontia, severe dental caries, and periodontitis (Swart, et al., 1985, Chaudhry, et al., 2000, Blanco and Keochgerian, 2006).

Dental practitioners may play an essential role in screening for CS, since the skin and mucosal lesions are common around the oral area (Swart, et al., 1985, Mignogna, et al., 1995). Proper referral may facilitate the early diagnosis of CD as well as breast, thyroid, and endometrial malignancies that are associated with CS (Swart, et al., 1985, Stanich, et al., 2011). Since orofacial signs are common among individuals with CS, these signs be properly eliminated from the differential diagnosis of any papillomatous lesion affecting the oral cavity (Chaudhry, et al., 2000, Mignogna, et al., 2000).

9. Plummer-Vinson syndrome

Plummer-Vinson syndrome is an extremely rare disorder that is associated with anemia. (Novacek, 2006) Patients usually complain of dysphasia, an oral burning sensation, or glossitis (Novacek, 2006, Mitma and Frisancho, 2012). Oral manifestations and considerations are mainly related to anemia (Kim, et al., 2005). These patients must be carefully managed due to the high risk of esophageal and pharyngeal carcinomas (Novacek, 2006, Karthikeyan, et al., 2017).

10. Peutz-Jeghers syndrome

Peutz-Jeghers Syndrome (PJS), a rare condition affecting about 1 in 200,000 individuals, is characterized by the development of intestinal polyps. PJD is an inherited autosomal dominant condition (Higham, et al., 2010), but in about a third of the cases, the disease is a new mutation (Pereira, et al., 2005). One of the characteristic features of PJD is the development of oral labial and facial melanotic macules. Recognition of these pigmentations by dental health providers could lead to the early diagnosis and management of the disease. However, oral surgical treatment may be complicated by the presence of anemia, malnutrition, and bleeding tendencies (Higham, et al., 2010). Thus, before surgical treatment, medical consultation and lab work are required.

11. Conclusion

In this review, several GI diseases that dentists may encounter in practice were highlighted. Concerns for managing these patients are focused on bleeding, infection, malnutrition, and pharmacology. Furthermore, modification of pain management protocols may be needed.

Authors contribution

MSA conceived and designed, conducted the literature review search, provided the materials, and collected and organized data. AAA and KHZ organized the data, wrote the initial and final draft of article. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Disclaimer

The authors have read and approved the manuscript and the requirement of authorship have been met and that the manuscript represent honest work. The authors also report no conflict of interests.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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