NARRATIVE REVIEW

Your Mouth is the Mirror of Health and Disease of the Gastrointestinal System: Oral Mucosal Manifestations of Gastrointestinal Disease

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Abstract

Introduction: Over the last few years, the importance placed on multi-disciplinary approach to patient care has been increasing. One such relationship is the between a dentist and medical practioner.

Methods: This narrative review examines the manifestations of gastrointestinal diseases in the oral mucosa. Understanding the interconnection between the oral cavity and gastrointestinal conditions can help with early diagnosis and can serve as an indicator of disease progression. The aim of this narrative review is to underscore the importance of recognising these suspicious oral mucosal signs and understand the bi-directional relationship between oral health and systemic well-being.

Results: The findings highlight the need to integrate oral examinations in patients at high risk of or with suspected or current gastrointestinal diseases. A holistic approach will help in better patient care and overall patient outcomes.

Discussion: There exists a gap in diagnostic approaches for oral manifestations of gastrointestinal diseases, which must be bridged to efficiently facilitate early diagnosis and treatment of these diseases. Understanding this interplay between oral health and systemic well-being will significantly improve patient care and outcomes, optimizing resource allocation for healthcare systems and promote disease prevention.

Keywords: Oral mucosa, Gastrointestinal disease, Inflammatory bowel disease, Coeliac disease, Gastro-oesophageal reflux disease, Helicobacter pylori, Hepatobiliary system

Introduction

The World Health Organization recognizes oral health as a "key indicator of overall health, well-being and quality of life"[1]. The oral cavity can be regarded as the mirror of systemic health and a gateway to the gastrointestinal tract. Several systemic diseases may have manifestations in the oral cavity and, vice-versa, oral diseases may affect systemic health[2]. Correlations between alterations in the oral cavity and systemic conditions have been widely reported, particularly gastrointestinal conditions[3]. The oral cavity and gastrointestinal tract share a common embryological origin; therefore, it is unsurprising that gastrointestinal diseases may have oral manifestations[4]. These signs or symptoms could manifest prior to or in the absence of gastrointestinal signs and may persist after the disease has resolved. They may occur alongside other systemic indications and could be a direct result of the disease itself or due to secondary effects such as ineffective nutrient assimilation by a compromised bowel[5]. Oral symptoms may not be sufficient to provide a definite diagnosis, although they may be useful in establishing required investigations and differential diagnoses. They may serve as an early warning sign, prompting a proactive approach to targeted diagnosis and treatment. Clinicians may establish a more informed and nuanced understanding of the patient's overall health, potentially uncovering subtle signs of gastrointestinal issues that might otherwise go unnoticed. For a healthcare system, early detection and intervention would assist in optimizing resource allocation and achieving greater cost-effectiveness. Awareness of these signs and links to gastrointestinal diseases would allow for public health interventions and preventative strategies to mitigate the risk of developing or exacerbating the below mentioned conditions.

A considerable number of gastrointestinal conditions of varied nature including, genetic, inflammatory, infectious, and metastatic may produce alterations in hard oral tissue and oral mucosa. These include inflammatory bowel diseases, coeliac disease, gastro-oesophageal reflux disease, and metastasis[3]. The oral mucosa includes lining mucosa (labial and buccal mucosa, soft palate), masticatory mucosa (gingiva, dorsal tongue surface, hard palate) and specialised mucosa (filiform papillae, fungiform papillae). This essay will discuss the oral mucosal manifestations of several gastrointestinal diseases and syndromes and explain

their histopathology, prevalence, and associations with disease progression.

Inflammatory bowel disease

Inflammatory Bowel diseases (IBD) comprise Crohn's disease and ulcerative colitis. Inflammatory bowel diseases affect the intestinal tract and may have extra-intestinal involvement, such as in the oral cavity. Particularly in IBD, these manifestations may assist in the diagnosis and monitoring of disease progression or exacerbations. Manifestations of oral signs in inflammatory bowel disease show a male predominance and are more common in children[6]. Studies indicate that the oral cavity is a useful source of diagnostic material in paediatric population with suspected IBD, particularly in Crohn's disease. This suggests the need for routine examination of oral cavity and dental health in children and increased awareness of disease-specific manifestations amongst physicians[7]. Additionally, oral lesions are more common in Crohn's disease compared to ulcerative colitis[6]. This is of particular significance since in up to 60% of patients with Crohn's disease oral lesions may be the primary presenting sign[8]. IBD patients, when compared to matched controls, have significantly increased prevalence of periodontitis, caries, and non-specific oral lesions[9]. Patients with ulcerative colitis are 27% and Crohn's patients are 89% more likely to seek more comprehensive and expensive dental treatment compared to controls[9]. A survey suggested only 12.5% of patients remembered being counselled by their physicians on the link between IBD and oral lesions and only 10% received treatment for them[9]. Evidence suggests the higher prevalence of oral health problems and higher need for dental treatment in IBD patients is partly due to the nature of their systemic disease. As such, the need for a multi-disciplinary approach in IBD is essential to ensure optimal dental and oral health in patients and to allow for early diagnosis and treatment, particularly in paediatric population.

Crohn's disease

Crohn's disease is a chronic inflammatory condition characterised by non-caseating granulomas in the gastrointestinal tract, commonly the terminal ileum and colon[6]. The prevalence of oral lesions in Crohn's disease patients is higher with perianal and proximal gastrointestinal tract involvement[6]. They may be the primary presenting signs preceding gastrointestinal symptoms in up to 60% of Crohn's patients[6]. Generally, patients with active Crohn's have been reported to have a higher degree of oral lesions, although the type of lesion has no association with intestinal disease activity. Oral lesions can be specific or non-specific depending on the presence of granulomas on histopathology. Diffuse labial, gingival and mucosal swelling and fissuring are specific signs of Crohn's disease[10]. A distinctive feature that may appear is cheilitis granulomatosa which is a manifestation of orofacial granulomatosis[11]. Particularly in children, this granulomatous inflammation of the lips or buccal mucosa may be indicative of underlying disease. A systematic review determined 40% of children with orofacial granulomatosis had concurrent intestinal Crohn's[12]. On histology, it is characterised by noncaseating giant cell granulomas and epithelioid histiocytes[13]. Given the appropriate clinical background, the microscopic presence of granulomas is considered diagnostic of oral Crohn's disease[17]. In adults, cheilitis granulomatosa can occur as a part of Melkersson-Rosenthal syndrome, a rare presentation of orofacial granulomatosis, which includes facial palsy and fissured tongue[6]. Additionally, a combination of deep, transverse, and longitudinal ulcers separating portions of the mucosa may create a cobblestone appearance in the oral mucosa[10]. This is usually seen in the posterior buccal mucosa and causes pain, especially during speaking or eating[14]. White reticular mucosal tags in the labial and buccal vestibules and retromolar regions are also specific to Crohn's disease[14]. Cobblestoning and mucosal tags are considered pathognomonic for Crohn's disease, although are not necessarily concurrent with intestinal disease activity[10]. Persistent and deep linear ulcerations with hyperplastic margins may also be found in the buccal sulci[10]. Oral Crohn's disease may also manifest with mucoginigivitis, i.e. hyperplastic and granular gingiva[10]. Non-specific oral lesions include aphthous stomatitis and angular cheilitis[10]. Aphthous stomatitis is one of the more prevalent lesions among Crohn's patients reported in up to 27% of patients[10]. The correlation of recurrent aphthous ulcers with disease activity has not been established although during active disease lesions can be more severe[10].

Ulcerative colitis

Ulcerative colitis is characterised by non-granulomatous inflammation limited to the mucosa of the rectum and colon[6]. Pyostomatitis vegetans is an oral lesion highly associated with ulcerative colitis and is a specific marker of active disease or exacerbations[16]. It is most commonly found in the buccal gingiva, labial gingiva, and buccal mucosa. Pyostomatitis vegetans are white-yellow pustules with an erythematous and oedematous mucosal base. The pustules may rupture and coalesce to form snail-track ulcers[10]. It is also seen in Crohn's patients although it is non-specific[10]. Histologic features include intraepithelial and subepithelial microabscesses with eosinophil and neutrophil infiltrates[15]. Hyperkeratosis and acanthosis can be present as well[15]. Pyostomatitis vegetans tends to resolve itself with adequate control of underlying inflammatory bowel disease[16]. Non-specific lesions include aphthous ulceration, angular stomatitis, and superficial haemorrhagic ulcers. Some reports of ulcerative colitis suggest 4.3% of patients presented with non-specific lesions during active flare-ups suggesting a correlation with disease activity[6]. Hairy leukoplakia and halitosis (bad breath) have been associated with the long-term use of corticosteroids and immunosuppressive agents in the treatment of ulcerative colitis and Crohn's disease[15].

Coeliac disease

Coeliac disease or gluten-sensitive enteropathy is an autoimmune condition associated with villous atrophy[10].

Several oral signs and symptoms have been recorded in patients with coeliac disease. Dental enamel defects, specifically enamel hypoplasia and delayed tooth eruption are common oral manifestations[3]. Oral mucosal manifestations such as atrophic glossitis are observed secondary to anaemia and hematinic deficiencies such as iron, B12 and folate[17]. Atrophic glossitis is the atrophy of the filiform papillae of the tongue, causing a smooth, glossy, and red appearance which may be patchy or involve the entire dorsum of the tongue[17]. Active coeliac disease is associated with dysfunction of salivary glands and decreased salivary flow rates, which may present as glossopyrosis and xerostomia post-gluten exposure3. Some studies have associated recurrent aphthous-like ulcers due to hematinic deficiencies with Coeliac disease. Cheng et al. (2010) observed aphthous ulcers were more common in untreated patients with coeliac disease compared to control (42.4% vs. 23.2%)[18]. These may manifest as single or multiple recurrent ulcers with erythematous halo and a yellow or grey floor3. However, there is a lack of consensus in literature supporting the relationship between aphthous ulcers and coeliac disease[18]. Rarely, dermatitis herpetiformis, a dermatological manifestation of coeliac disease may present as oral erythematous-purpuric macules, vesicles, erosions and ulcers, which can affect the alveolar ridge, buccal mucosa and tongue[10]. Additionally, a study examined the detection of anti-endomysial and anti-tissue transglutaminase autoantibodies in cheek biopsies from patients with coeliac disease, suggesting oral mucosal involvement in the disease[19].

Considering that 50% of patients with coeliac disease do not exhibit digestive symptoms at the time of diagnosis, it is essential for physicians to be aware of possible indicating oral signs of coeliac disease[10]. Although, the evidence for cheek biopsies for the diagnosis of coeliac disease is insufficient, oral lesions could still be useful in raising suspicion for asymptomatic coeliac disease.

Gastro-oesophageal reflux disease

Gastro-oesophageal reflux disease involves the regurgitation of gastric contents into the oesophagus due to the weakening of the lower oesophageal sphincter causing recurrent symptoms such as heartburn[20]. Dental erosion is the most common extra-oesophageal manifestation, commonly affecting the lingual or palatal surface of anterior teeth[10]. Damage may vary from loss of enamel to exposure of dentin[10]. Enamel erosion is directly proportional to the contact time with gastric acid[17]. Assessing the extent of enamel loss may allow gastroenterologists to approximate the frequency and duration of the disease.

Oral mucosal lesions may result from direct acid or acidic vapour contact[21]. There is a lack of data establishing the effect of gastro-oesophageal reflux disease on the oral mucosa. However, a case-control study found palatal and uvula mucosal erythema to be a significant clinical sign of gastric-oesophageal reflux disease, manifesting in 21.5% of patients in the study[22]. Additionally, xerostomia, halitosis and oral burning sensations were reported in 54.5%, 49.2% and 43.2% of patients in the study respectively[22]. Furthermore, Silva et.al (2001) found microscopic alterations in the palatal mucosa of gastric-oesophageal reflux disease patients[23]. Upon morphometric analysis of the palatal epithelium, epithelial atrophy and increased fibroblasts were detected. The results of a cross-sectional study indicated that aphthous ulceration, gingivitis and angular cheilitis are correlated with gastric-oesophageal reflux disease and dental erosion[24]. They found 60% of participants to have soft-tissue aphthoid lesions i.e. ulcerative lesions on the buccal mucosa, soft/hard palate mucosa, tongue and uvula[24]. There is no consensus as to whether these lesions are directly related to gastric-oesophageal reflux disease as several studies have failed to find statistically significant differences between symptomatic and control groups[24].

Compared to diseases such as inflammatory bowel disease and coeliac disease, evidence supporting the significance of oral lesions in gastro-oesophageal reflux disease is lacking. However, acknowledging the link between gastro-oesophageal reflux disease and dental erosion is essential as it may be associated with debilitating dentition and complex restorative therapy for patients in the long term[21]. In a survey of gastroenterologists, only 42% strongly agreed that such an association existed in adults[21]. Failure to diagnose early signs of erosion can result in significant damage to dentition and the masticatory system, therefore, promoting awareness of this association has become imperative.

Gastritis, Peptic Ulcer Disease and Helicobacter Pylori

Helicobacter pylori (H. pylori) infection is one of the leading causes of chronic gastritis and peptic ulcer disease, including gastric and duodenal ulcers[25]. Studies have determined that the oral cavity may serve as an extra-gastric reservoir for H.pylori[25]. H.pylori has been isolated from the saliva, tongue, and supra-gingival and subgingival plaque[26]. This can be attributed to the low concentrations of antibiotics that reach oral fluids, dental plaque and periodontal pocket[25]. Recent studies show patients with chronic gastritis have a higher prevalence of H.pylori in the dental plaque than in the stomach, suggesting the role of the oral reservoir as a source of infection and re-infection[27]. Wang et. Al (2014) concluded the successful eradication of gastric H. pylori bears a significant relationship to oral infection from H. pylori[28]. Therefore, poor dentition and oral hygiene may be contributing factors in a patient with H.pylori-associated disease. Antibiotics are the first-line protocol to combat H.pylori associated peptic ulcer disease and gastritis[25]. Even though, gastric eradication is successful, reinfection is still possible due to the poor penetrance of antibiotics in the oral cavity and dental biofilm[25]. Gastroenterologists must consider this aspect of recurrence and highlight the importance of good dental hygiene in patients with a history of H.pylori associated gastric disease.

The oral presence of H.pylori has been associated

with recurrent aphthous stomatitis, glossitis, halitosis, gingivitis and dental caries[25]. Birek et. Al (2007) postulated a relationship between H.pylori and recurrent aphthous ulcers, as 71.9% of recurrent aphthous ulcer samples tested had H.pylori deoxyribonucleic acid (DNA)[29]. They suggested H. pylori may be a cofactor in the pathogenesis of recurrent aphthous ulcers, especially in people sensitised through gastric colonisation and mucosal attachment[30]. H.pylori-associated chronic atrophic gastritis and autoimmune chronic gastritis can lead to iron deficiency anaemia and pernicious anaemia, caused by vitamin B12 malabsorption. In severe cases, this can manifest as atrophic glossitis and persistent aphthous-like ulcers that are responsive to replacement therapy[10]. Peptic ulcer disease may manifest in the oral cavity as an erythematous tongue with a slimy yellowish coating and congestion and dilatation of sublingual veins[10].

Diseases of the hepatobiliary system

Chronic cirrhotic liver disease

Oral manifestations of cirrhotic liver disease include jaundice and prolonged bleeding[25]. Excess bilirubin in the blood results in its accumulation in the oral mucosa[25]. Patients with jaundice have a diffuse, uniform, yellow discolouration of all mucosal surfaces[31]. Bilirubin has a high affinity for elastin, therefore mobile oral tissues with higher elastin particularly the lingual frenum and soft palate are more severely affected[17]. Examination of these regions may provide useful diagnostic clues in patients with darker skin or physiologic conjunctival pigmentation and to clinically assess the extent of jaundice[17]. Due to thrombocytopenia and deficiency in coagulation factors, additional oral manifestations may include petechiae on the palate and gingival bleeding[32]. Spider angioma or spider naevus is a vascular lesion caused by abnormal dilation of central arterioles with radiating thin-walled vessels[33]. They are characteristic of chronic liver disease with a specificity of 95% and may manifest in the mucosa of the oral cavity[33]. Patients with severe liver disease, as classified by B/C on Child-Pugh scale, are more frequently prone to oral candidiasis, due to overuse of antibiotics and immunosuppressants[34]. In paediatric populations with hyperbilirubinemia, biliverdin may deposit in teeth during calcification causing a permanent pigmentation of teeth[34]. Studies have suggested that the prevalence of oral lesions such as angular cheilitis, strawberry-looking lips with erosions, smooth and atrophic tongue, and petechiae are statistically significant in children with liver diseases[35]. Some cases of congenital hepatic disease such as biliary atresia have presented with pigmentation of the gingiva, gingivitis and green-staining of the teeth[36].

Hepatitis C infection

One of the leading causes of chronic liver disease is Hepatitis C (HCV) infection. There is some evidence of a relationship between HCV and oral lichen planus. Oral lichen planus is a T-cell-mediated chronic inflammatory disease of the oral mucosa, characterised by white papules and plaques with a reticulated appearance[37]. The evidence varies by region, wherein epidemiological data suggests that lichen planus may be significantly associated with HCV infection, mainly in Southern Europe and Japan[38]. Oral lichen planus typically has a bilateral distribution and most commonly appears on the buccal mucosa, tongue, gingiva, and possibly labial mucosa and lower lip[39]. Studies determined that patients with lichen planus are reported to have a 5 times higher risk for HCV seropositivity[31]. The mechanism is assumed to involve cell-mediated cytotoxicity induced by HCV[31]. The prevalence of general liver disease in patients presenting with lichen planus ranges between 0.1 to 35% with the erosive variant of lichen planus being predominant[40].

Metastatic disease

Metastasis of primary tumours to the oral and maxillofacial region is rare, representing only 1% of all oral cancer[41]. Oral cavity metastasis typically involves the mandible, with only 16% affecting the oral soft tissues, most commonly the gingiva and tongue[42]. Although rare, several cases involving colorectal adenocarcinoma metastasis in the oral cavity have been observed in the mandible and oral mucosa. In a literature review conducted by Lanca et al. (2023), in 22% of patients, the metastasis to the oral cavity was identified before the primary colorectal adenocarcinoma[43]. Mucosal manifestations reported include gingival overgrowths and tongue mass[44]. Gingival metastases resemble a hyperplastic or reactive lesion, such as pyogenic granuloma, peripheral giant cell granuloma, or fibrous epulis[43]. Other soft tissue manifestations are submucosal masses and ulceration. Lesions on the gingiva have been associated with chronic inflammation that attracts malignant cells. Malignant cells may be entrapped by the rich capillary network of chronically inflamed gingiva. Oral pain and mandible and maxillary masses were reported in hard tissue metastasis[45,46]. It has been hypothesised that metastasis to the mandible and maxilla involves the Baston Plexus[43]. Increased pressure in the abdomen can lead to haematogenous dissemination of malignancy in the vertebral venous plexus, affecting the oral hard tissue[43]. According to Maria et al. (2021), cases of gastrointestinal stromal tumour metastasis to the buccal soft tissues and mandible have also been reported[47]. The malignant form of oral acanthosis nigricans has been reported as a rare marker of intestinal malignancy, especially gastric adenocarcinoma[48]. These lesions present as hyperpigmented areas and are characterised by papillomatosis of the lips, palate, gingiva, and tongue[49]. Histologic features of oral acanthosis nigricans include true acanthosis, epithelial papillary hyperplasia and hyperkeratosis[50]. Distant metastasis of primary gastrointestinal tumours to oral mucosal and hard tissue is extremely rare and is considered a poor prognostic sign.

Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant genetic disorder characterised by benign hamartomatous polyps in the gastrointestinal tract, mainly the small

intestine[17]. Another characteristic manifestation is oral mucosal melanotic macules[17]. Intraorally, the lesions are usually flat, painless, brown-pigmented patches of the buccal mucosa, tongue, or labial mucosa[17]. These are found in 95% of patients with Peutz-Jeghers syndrome and usually become pronounced in childhood[51]. It often precedes gastrointestinal symptoms and is an essential clinical sign of the disorder. Pigmentation may fade after puberty but often persists in the buccal mucosa[52]. Upon histology, prominent basal layer melanin hyperpigmentation is observed without an increase in melanocytes[17]. Mucocutaneous pigmentation is a key diagnostic factor for Peutz-Jeghers syndrome. Unlike other gastrointestinal conditions, the oral-mucosal manifestation is a part of the disease diagnostic criteria, whereas other manifestations as in inflammatory bowel disease are suggestive or prognostic as in metastatic disease.

Plummer-Vinson Syndrome

Plummer-Vinson syndrome is a rare disorder characterised by the triad - microcytic hypochromic anaemia, dysphagia, and oesophageal webs. The most common oral mucosal manifestation is atrophic glossitis[53]. It serves as a suggestive factor of disease and should promote further testing into suspected Plummer-Vinson Syndrome. Others include angular cheilitis, burning mouth syndrome, erythematous mucositis, oral candidiasis, pale oral mucosa and recurrent aphthous stomatitis[53]. These oral manifestations can be attributed to iron deficiency anaemia. Plummer-Vinson syndrome predisposes a patient to develop squamous cell carcinoma of the upper gastrointestinal tract, especially the pharynx and proximal oesophagus[54]. A typical clinical picture would be that of a middle-aged woman with weight loss, symptoms of anaemia, oesophageal webs on endoscopy, glossitis, angular cheilitis and koilonychia[54].

Conclusion

Our mouth is the mirror of systemic health and disease of the gastrointestinal system. The presence or extent of oral manifestations allows for monitoring of disease severity and prognosis. The response of oral tissue may also reflect the success of the management of gastrointestinal disease. Although the frequency of oral manifestations is variable and non-specific, these alterations may precede the underlying disease and therefore can facilitate an opportune diagnosis and encourage vigilance. For some disease, these oral lesions may serve as a key diagnostic factor, aiding in raising suspicion and further testing.

In patients with suspicious oral alterations such as those discussed in this essay and suspected gastrointestinal disease, a multidisciplinary approach of general practitioners, dieticians, gastroenterologists, dentists are essential to improve patient care, disease management and outcome. Integrating a clinical examination of the whole oral cavity into a gastrointestinal examination can promote early diagnosis. The importance of oral hygiene and lifestyle modifications such as tobacco and smoking cessation is essential in these cases to promote gastrointestinal and systemic well-being[15]. For a healthcare system, integrating this step in a gastrointestinal examination, may in the long run optimise resource allocation and cost-effectiveness, by promoting early diagnosis and treatment. By encouraging further research into the oral signs of these diseases, public health interventions and prevention strategies may also be successfully put into place. ◄

Declarations

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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