

ORAL ULCERS AS A MANIFESTATION OF GASTROINTESTINAL DISEASES: A REVIEW

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ABSTRACT

Careful examination of the oral cavity may reveal findings indicative of an underlying systemic condition, and allow for early diagnosis and treatment. Examination should include evaluation for mucosal changes, periodontal inflammation and bleeding, and general condition of the teeth. The oral cavity changes may represent the first clinical manifestation of an underlying GI condition. Recognition and appropriate referral of a possible Gastro-Intestinal GI condition contribute to overall health and wellness in patients.

KEYWORDS: Gastrointestinal diseases; oral ulcers; celiac disease; crohn's disease; ulcerative colitis

INTRODUCTION

The oral cavity is a mirror that reflects and unravels many of the human body's internal secrets. Oral manifestations of systemic diseases are potential indicators of an array of conditions. Some of these manifestations are disease specific and help raise a high degree of suspicion for the alert clinician.^[1] Many times; the first sign of unnatural systemic health conditions reveal themselves in changes within the oral cavity.^[2] Ulcers are well circumscribed, often depressed lesions with an epithelial defect that is covered by a fibrin clot, causing a yellow white appearance.^[3] The term ulcer is used where there is damage to both the epithelium and lamina propria.^[4] Oral ulcers are one of the most common complaints of the oral mucosa. Oral ulcers are determined by the underlying systemic condition such as the

nature, site, duration and frequency. In addition, histopathological examination usually produces a definitive diagnosis for the majority of conditions described in this paper.^[3] Oral ulcers can be caused by a wide range of etiologic agents like mechanical, chemical, thermal or radiation induced trauma, viral infections like herpes simplex and herpes zoster, bacterial infections like acute necrotizing gingivitis and tuberculosis, fungal infections like histoplasmosis and mucomycosis, allergic conditions like stomatitis veneta and medicamentosa, neoplastic conditions like squamous cell carcinoma and malignant melanoma as well as systemic disorders of hematological, immunological or gastrointestinal origin.^[4] Oral ulcers may also arise from unknown etiologies like recurrent aphthous stomatitis, erythema multiforme, pemphigus, mucous membrane pemphigoid, erosive lichen planus and eosinophilic ulcers of oral mucosa.^[5] Many disease processes affecting the gastrointestinal (GI) tract may cause observable changes to the oral cavity. In fact, oral cavity changes may represent the first clinical manifestation of an underlying GI condition. Recognition and appropriate referral of a possible GI condition contribute to overall health and wellness in patients.^[2] This paper is an attempt to review the various gastrointestinal diseases that present as oral ulceration as its early manifestation.

METHOD

COLLECTION OF DATA

The collection of data for the review was done with the aid of the search engine Ebscohost. The basic search with the use of key words like oral ulceration, Celiac disease, Crohn's disease,

Ulcerative colitis and gastrointestinal disorders was done. The search resulted with 245 articles out of which 45 were relevant to the review. A total of 10 articles which were closely related to the review were selected as references.

CELIAC DISEASE

Celiac disease is also called as gluten sensitive enteropathy and previously called as nontropical sprue, idiopathic steatorrhea or primary malabsorption.^[6] It is caused due to permanent intolerance to gliadin the protein content of wheat. It is a lifelong inflammatory condition of the GIT tract that affects the small intestine in a genetically susceptible individuals. It is characterized by malabsorption due to morphological abnormalities in the small intestinal mucosa.^[7] Originally thought to be rare disorder, celiac disease is now recognized as one of the most common inherited diseases, with a world prevalence estimated at 1:266 people. Recent studies have revealed that celiac disease affects approximately 1% of the U.S. population (1:100 individuals) which is similar to data from European countries.^[8] Its prevalence is very variable from country to country and predominantly affects white individuals.^[9] Patients with celiac disease are usually short and 60% of children are below the third centile for age. Diarrhea and oral ulcers is the most common feature followed by lassitude, weight loss, myopathy, osteomalacia, severe anaemia are the other clinical features of celiac disease. Development of secondary sex characteristics is often late. Finger clubbing and koilonychia may be seen and oedema and asitis occur occasionally in severe cases due to hypoproteinemia.^[6] Oral signs and symptoms like delayed eruption of teeth, tooth enamel hypoplasia, oral mucosal ulcers, pain or burning of the tongue are of fundamental importance as diagnostic aids for this disease.^[9] These changes are reversible on the withdrawal of gluten from the diet.^[4] Superficial oral mucosal ulcers similar to recurrent aphthous stomatitis may be a feature of 1-5% patients with undiagnosed, untreated celiac disease.^[2]

CROHN'S DISEASE (CD)

CD is caused due to genetic factors i.e. mutation in the CARD15 (NOD2) gene on chromosome 16 have been found in about 1/3rd of patients with CD and are particularly associated with ileal disease, smoking, infection by mycobacterium

paratuberculosis and diet containing high intake of refined sugar and less fibres.^[6] There is a predilection for males and onset in youth.^[3] The prevalence rate is estimated to have between 20% and 50%.^[7] These patients were more likely to have anal and esophageal lesions like abdominal pain, diarrhea, obstructive symptoms, mass in right iliac fossa and extra intestinal features like acute arthritis eye complications like, conjunctivitis and uveitis.^[6] Oral ulcers arises in approximately 9% of patient with undiagnosed CD and can be the first and or only clinical features of this disorder.^[2] In inspection oral lesions are multifocal, linear, nodular, indurated tag like, polypoid or diffuse mucosal thickenings, with a predilection for occurring in the labial and buccal mucosa, mucobuccal folds, lips, gingival and retromolar areas respectively. In these lesions cobblestoning is seen in the posterior buccal mucosa and may be associated with succulent mucosal folds with normal epithelium. The lesions usually consist of mucosal colored papules that produce firm plaques on the buccal mucosa and palate. On palpation these oral lesions are characteristically firm, pink and painless to palpation unless there are ulcerations that may cause pain on touch, or when eating acidic, spicy or hot foods. These ulcers, which are typically persistent, linear and deep, may feel granular below the epithelium, reflecting the histological findings.^[10]

ULCERATIVE COLITIS (UC)

UC is a multi factorial disease caused by genetic factors, physiological factors like increase in intestinal permeability, immunological factors like increased interleukins 1, 6, 8 and environmental factors like smoking and due to presence sulphate of reducing bacteria.^[6] There is a male predilection in UC. The hallmark of UC is rectal bleeding and diarrhoea with urgency and crampy abdominal discomfort before defecation. Anorexia, fever, tachycardia, and abdominal tenderness is also seen in most of the patients.^[11] Ulcerative colitis can give rise to either aphthous ulcers or multiple pustules termed pyostomatitis vegetans. In this oral ulcer out breaks may occur at any age.^[11] The ulcers of Pyostomatitis vegetans arise on the upper and lower anterior vestibules, the soft palate and posterior hard palate. Pyostomatitis vegetans tends to arise in patients with undiagnosed or active ulcerative

colitis. Pyoderma gangrenosum, manifesting as a solitary, necrotic mucosal ulcer has rarely been reported in the mouth.^[2] Clinically, the lesions consist of scattered, clumped or linearly oriented pustules on an erythematous mucosa at multiple oral sites, with variable severity, but usually sparing the dorsum of the tongue. Long-standing lesions may become granular, polypoid or fissured, clinically.^[12]

DISCUSSION

Celiac disease is caused due to permanent intolerance to gliadin (the protein content of wheat) whereas Crohn's disease is a genetic condition occurring due to mutation in the CARD15 (NOD2 gene). UC is also caused by genetic factors but it is also associated with other factors like physiological factors (i.e. due to increase in intestinal permeability) immunological factors (due to increased interleukins 1, 6, 8) and environmental factors (due to smoking and due to presence of sulphate reducing bacteria).^[6] Celiac disease affects white individuals^[8] while CD and UC have predilection for males. Celiac disease and CD have a predilection for younger age while in UC oral outbreaks may occur at any age.^[2] Celiac disease contains wide variety of clinical features like diarrhoea, recurrent aphthous stomatitis (RAS), lassitude, weight loss, myopathy, osteomalacia, anaemia, clubbing, koilonychia, oedema and asitis, whereas in CD patients they mostly have GIT associated clinical features like abdominal pain, diarrhoea, obstructive symptoms, mass in right iliac fossa. UC also has mainly GIT findings but they are different than CD which are rectal bleeding and diarrhoea, urgency and crampy abdominal discomfort before defecation.^[3] Oral findings in all three diseases are mainly oral ulceration. But there is difference in features of ulcers also. In celiac disease, ulcers are mainly like RAS. They are superficial oral mucosal ulcers and may be feature of 1-5% patients with undiagnosed, untreated celiac disease. In celiac disease other associated oral findings are delayed eruption, enamel hypoplasia and pain or burning of the tongue. In CD oral ulcers arise in approx 9% of patient who are undiagnosed and can be the first and only clinical feature.^[1] Oral lesions are multifocal, linear, nodular, indurated tag like, polypoid or diffuse mucosal thickenings. Lesions have predilection

towards labial and buccal mucosa, mucobuccal folds, lips, gingiva and retromolar areas. As lesions progress cobblestoning is seen in the posterior buccal mucosa which is associated with succulent mucosal folds.^[11] Lesions are firm, pink and painless to palpation unless there is ulceration which may cause pain. UC can give rise either RAS like ulcers or pyostomatitis vegetans.^[10] Lesions are mainly seen in upper and lower anterior vestibule, soft palate and posterior hard palate. Pyostomatitis vegetans tends to arise in patient with undiagnosed or active UC. Clinically lesions are scattered clumped or linearly oriented pustules on erythematous mucosa at multiple oral sites with variable severity but sparing dorsum of tongue.^[12] To confirm the diagnosis of all three diseases biopsy of intestine is a gold standard. But before that to come to a conclusive diagnosis other investigations are also there. In celiac disease hematological examination for anemia, elevated titers of IgG, IgM and IgA, antibody to gliadin can be done followed by bone densitometry, CT scan and MRI. For CD stool examination should be done to exclude known pathogens followed by small bowel enema, CT scan, MRI, colonoscopy and sigmoidoscopy. In UC investigation are same as CD except of barium enema.^[6] The first and foremost goal of treatment should be treating the GI disorders. That should be done by a gastroenterologist. Management of oral ulcers and other oral findings is the duty of the oral diagnostician. As the underlying GI disorders gets treated the severity of oral ulcers decreases but patient still may complain of burning and pain in ulcers. In celiac disease RAS is mainly given symptomatic treatment by giving topical analgesics and sometimes topical antiseptic is given to treat localized infection.^[8] Oral lesions of Crohn's disease are typically persistent, remit and relapse over years. Their response to systemic therapy is highly variable and unpredictable. Oral lesion may require topical corticosteroids or even intralesional injections of same. General measures like well balanced diet with high fibre is advised.^[11] Pyostomatitis vegetans of UC is generally treated with topical steroid therapy but in many cases systemic treatment with or without azathioprine or sulfamethoxy pyridazine is required.^[10] Apart from this some studies have reported a strong association of GERD in the

Table 1 Oral ulcers and other oral manifestations of gastrointestinal diseases

Gastrointestinal disorder	Oral manifestations
Bulimia nervosa	Necrotizing sialometaplasia, Superficial oral ulcers
Post-cricoid webbing	Dental erosion, Bilateral parotid enlargement
Gastro-oesophageal reflux disease	Chronic mucocutaneous candidosis
Gluten-sensitive enteropathy	Dental erosion, burning mucosal sensation, mucosal erythema of palatal mucosa and uvula.
Dermatitis herpetiformis	Superficial ulcers, Enamel hypoplasia in children
Peutz-Jegher's syndrome	Vesicles, bullae, Desquamative gingivitis
Congenital hepatic disease and biliary atresia	Enamel hypoplasia (in children)
Hepatitis C virus infection	Perilabial pigmented macules, Cystic fibrosis Enamel hypoplasia,
Primary biliary cirrhosis	Tetracycline staining of teeth
Crohn's disease	Superficial oral ulcers
Ulcerative colitis	Pigmentation of the gingivae
Colonic malignancy	Xerostomia, Salivary gland disease, Lichen planus
	Telangiectasia, Xerostomia
	Labial (and facial) enlargement, Fissuring of the tongue, Linear ulcers of the buccal and labial vestibules, Superficial oral ulcers
	Gingival enlargement, Facial nerve palsy
	Pyostomatitis vegetans, Pyoderma gangrenosum
	Superficial oral ulcers, Acanthosis nigricans



Fig. 1: Ulceration on the sublingual caruncula region



Fig. 2: Irregular superficial ulcers on ventral surface of tongue in Crohn's disease



Fig. 3: Pyostomatitis vegetans in a patient with ulcerative colitis

form of burning mucosal sensation, halitosis and mucosal erythema of palatal mucosa and uvula.^[13]

CONCLUSION

The present article has presented an overview of the common clinical presentations of oral ulceration as with gastrointestinal disorders. Gastrointestinal disease particularly undiagnosed

Celiac disease, Crohn's disease and ulcerative colitis, can give rise to ulcers of the mouth. Hence, it is important to ask patients who present with oral ulcers about their symptoms and to examine the mouth carefully when assessing patients with possible disease of the gastrointestinal tract. In other circumstances, the severity or prognosis of the disease can be monitored by the presence or extent of oral manifestations, and the success of the management of GI diseases may be reflected in the response of oral tissues..

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