Education in practice

Oral manifestations of inflammatory bowel disease: a guide to examination

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ABSTRACT

Orofacial symptoms are common in patients with inflammatory bowel disease (IBD). They may present as a primary manifestation of the disease in the oral cavity with oral Crohn's disease, or as a secondary manifestation of the disease such as iron deficiency, or due to side effects to medications used in treatment. Orofacial manifestations of IBD may result in significant morbidity which can impact patients' quality of life. Systematic examination and a timely diagnosis are fundamental in initiating appropriate management.

This article provides a guide for gastroenterologists to systematically perform an extraoral and intraoral examination of the orofacial region. The extraoral examination includes evaluation of lymph nodes, lips and perioral skin. Common extraoral features of IBD include lip swelling, lip fissuring, angular cheilitis, perioral erythema and cervicofacial lymphadenopathy. The intraoral examination involves a systematic inspection of all areas of the oral cavity. Intraoral IBD features include ulceration, cobblestoning of the buccal mucosa, gingival erythema and mucosal tags.

Examining the orofacial region is important in the complete assessment of patients with IBD, to diagnose orofacial conditions, to initiate tailored treatments and to identify those patients who would benefit from input from oral medicine specialists.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal (GI) tract consisting principally of ulcerative colitis (UC) and Crohn's disease (CD). Patients with IBD may present with orofacial signs as a primary manifestation of the disease or with secondary manifestations such as aphthous ulceration due to iron deficiency, or due to the side effects of medications.

Orofacial manifestations are often overlooked in a non-dental setting leading to suboptimal disease management. Up to 50% of gastroenterologists find it challenging to identify oral lesions compatible with oral CD compared with experienced dental professionals.[1] Orofacial symptoms associated with IBD may result in significant physical and psychological morbidity.[2] Early recognition of these signs and symptoms, and an appreciation of their relevance in the context of diagnosis and disease control, are vitally important for gastroenterologists.

CD can affect the mucosa anywhere along the alimentary canal. It is estimated that up to 60% of patients with CD have oral lesions at some point.[3] The true incidence of oral CD has been reported to be approximately 6%.[4] Orofacial signs are more common in males and those who have been diagnosed with CD at a younger age.[3] Those who develop features consistent with orofacial IBD alone, particularly childhood onset, are at increased risk of developing intestinal CD.[5] In addition, oral signs may be associated with perianal disease and follow a protracted course.[6] Orofacial disease, like perianal CD, can remain active despite control of luminal disease. Orofacial signs may involve the perioral structures and/or intraoral tissues including changes such as perioral erythema, angular cheilitis, lip swelling, oral ulceration and cobblestoning. These may be the only presenting features of IBD and can predate the onset of intestinal symptoms by 10 years.[7]

Oral findings are less common in UC than CD, but pyostomatitis vegetans (PV) is associated with UC and may indicate active colonic disease. Non-specific oral signs including aphthous ulceration, atrophic glossitis, angular cheilitis, taste disturbance, halitosis and periodontal

(gum) disease have also been identified in patients with UC.[8]

Oral symptoms which are more prevalent in, but not necessarily specific to IBD, include halitosis, oral discomfort, odynophagia and dysphagia.[6] Non-specific signs include dental erosions, dental decay and candidiasis.[9] It has been reported through case–control studies that adult patients with CD had a higher prevalence of decayed, missing and restored teeth compared with matched controls.[10] Similar findings have been shown in children with a diagnosis of CD when compared with those without CD.[11] There is growing evidence demonstrating a higher prevalence of gum disease in patients with IBD that can lead to tooth mobility and eventual tooth loss.[12] Oral features specific to IBD are explored later in this article.

This article provides a guide for gastroenterologists to examine the orofacial region, with examples of common features seen in patients with IBD and in the non-IBD cohort.

THE ORAL CAVITY AND EXAMINATION

A good understanding of the anatomy of the oral cavity lays the foundation for identifying and appreciating variations of normal anatomical structures and those associated with pathology. The oral cavity is divided into soft tissues and hard tissues. The soft tissues include the gums, non-keratinised mucosa such as the buccal mucosa (inside of cheeks) and floor of mouth (beneath tongue), along with keratinised mucosa such as the dorsal surface of the tongue and hard palate (roof of mouth). These sites are easily examined. Figure 1 shows the key anatomical sites within the oral cavity.

Orofacial examination

The examination requires adequate lighting, gloves, a tongue depressor and dental mouth mirrors, if available. Ideally, the patient should be seated upright in a chair with the neck adequately exposed to the clavicles. Establish if the patient has any pain in the orofacial region prior to proceeding with the examination.

Extraoral examination

Inspection and palpation

a. Inspect the face, lips and neck noting any obvious asymmetry, skin changes, lumps and scars along with their anatomical location.
b. The perioral skin and lips should be inspected. The corners of the mouth should be carefully assessed for cracking and redness, termed angular cheilitis. The upper and lower outer surfaces of the lips should be assessed for swelling, fissures and cracking.
c. Systematically examine the anterior and posterior triangles of the neck identifying any abnormal pathology.
d. Examine the lymph nodes in the neck by starting below the chin where the submental nodes are located and then moving along below the lower jaw to palpate the submandibular lymph nodes. Then, examine the lymph nodes of the face in the pre-auricular, posterior auricular and occipital region.

   Carefully examine the anterior and posterior cervical lymph node chains, one side at a time, guided by the

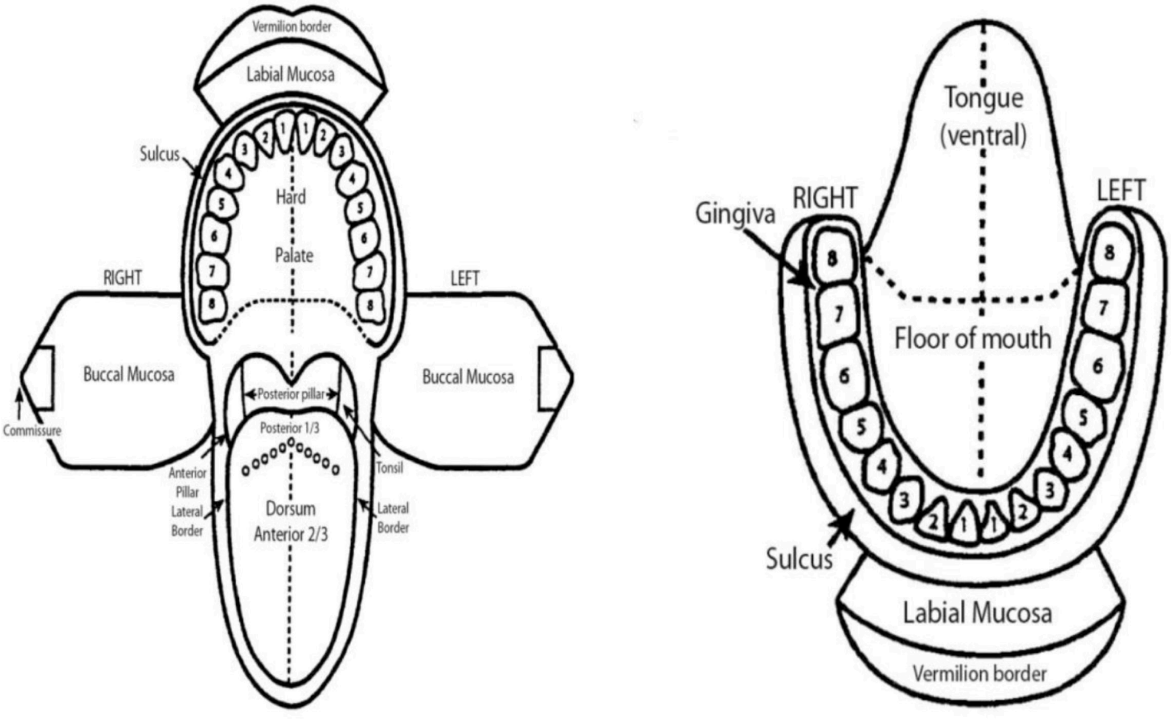

Figure 1 A labelled diagrammatic representation of the oral hard and soft tissues.

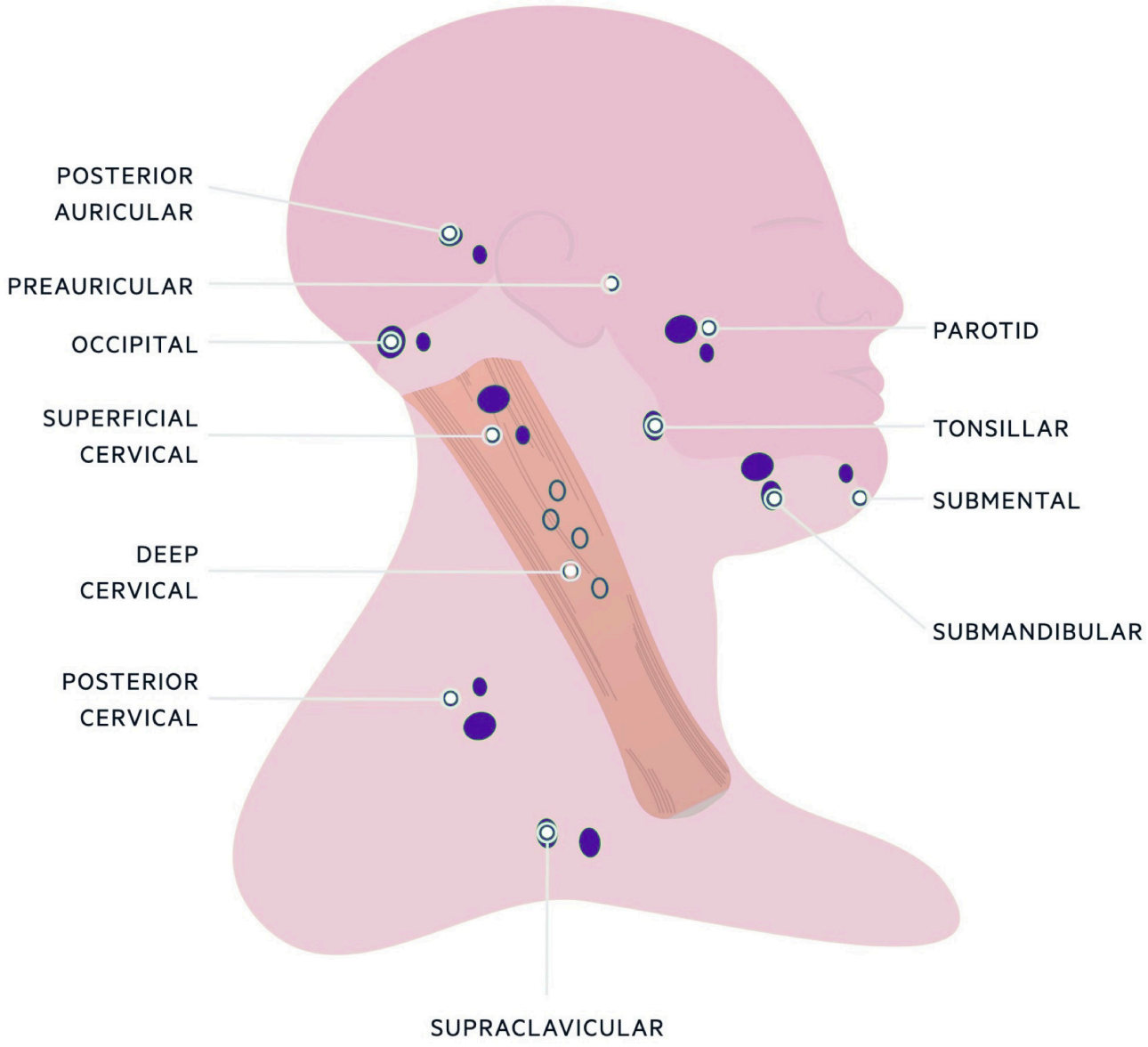

Figure 2 The regional position of lymph node chains within the head and neck.

location of the sternocleidomastoid muscle. Finally, palpate the supraclavicular region for lymphadenopathy. Lymphadenopathy must be noted and classified as either benign lymph nodes (<1 cm, smooth, rounded, mobile and non-tender), reactive lymph nodes (tender, smooth, rounded, mobile and may be associated with other infective symptoms) or associated with metastatic cancer (hard, firm, irregular and may be tethered). Figure 2 illustrates the facial, anterior and posterior chains of cervical lymph nodes. Cervical lymphadenopathy is reported to affect 20.4%[13] of patients with orofacial granulomatosis (OFG).

Cranial nerve examination

A cranial nerve (CN) examination is performed with an emphasis on CN V (trigeminal nerve) and CN VII (facial nerve). A condition such as Melkersson-Rosenthal syndrome, a rare neurological disorder, is characterised by a triad of tongue fissuring, a facial nerve palsy and OFG. The facial palsy is a lower motor neuron type and may be permanent. The syndrome may be unilateral or bilateral, and partial or complete. The trigeminal nerve is the main sensory nerve to the face and provides motor innervation to the muscles of mastication. Sensory or motor deficits should prompt appropriate referral to neurology.

Intraoral examination

All non-fixed dental prostheses should be removed to allow assessment of the mucosa. The examination should be performed systematically.

Soft tissues

a. Ask the patient to partially open the mouth and inspect the labial mucosa (inside of lips), labial sulcus (recess created by reflection of the labial mucosa on to the gums),

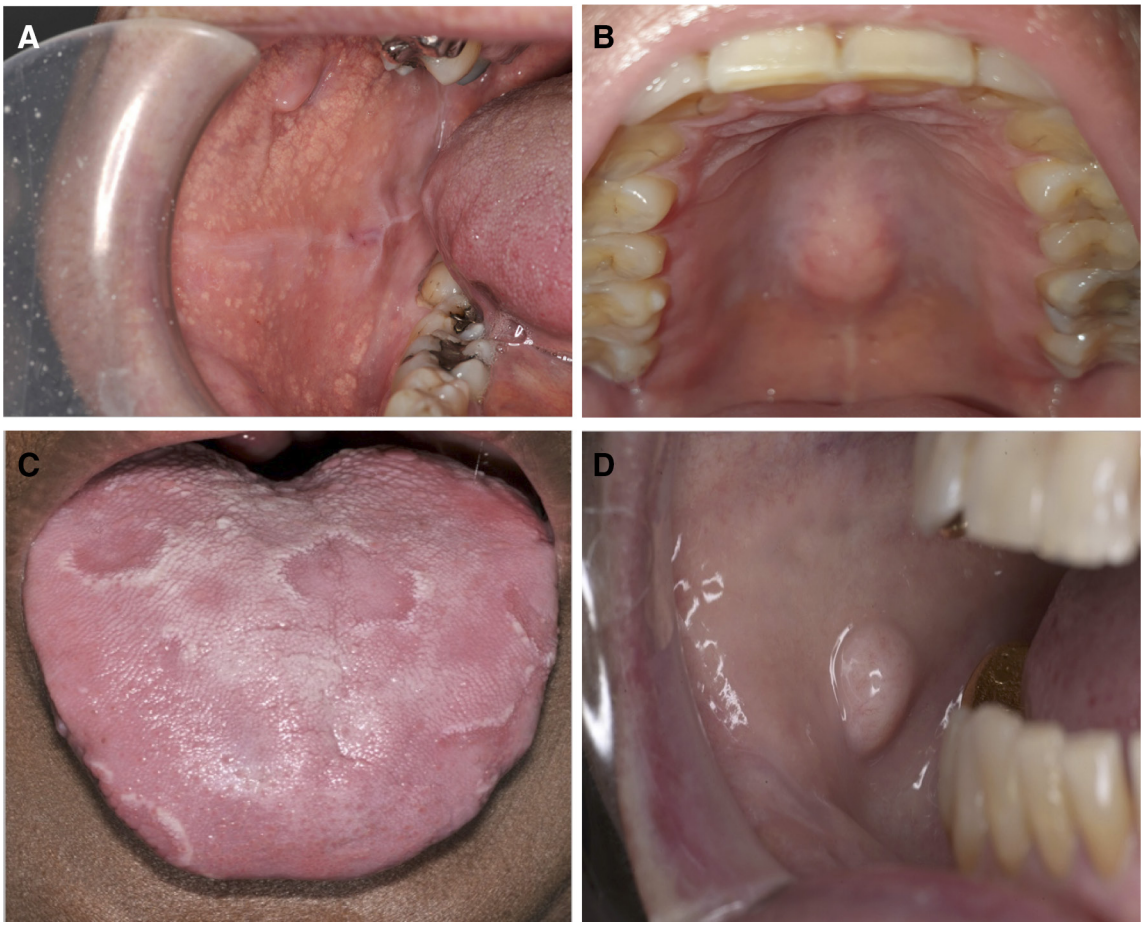

Figure 3 (A) Fordyce spots involving the right buccal mucosa, (B) palatine torus involving the midline of the hard palate, (C) geographical tongue involving the dorsum tongue and (D) fibroepithelial polyp of the right buccal mucosa.

followed by the buccal mucosa (inside of cheeks) and the buccal sulcus (recess created by reflection of the buccal mucosa on to the gums). Use of dental mirrors or tongue spatula helps to retract soft tissues for complete inspection. Look for ulceration, mucosal tags, scarring, red/white patches and cobblestoning.

b. Next, inspect the dorsal surface of the tongue, followed by the lateral and ventral surfaces, documenting ulceration, mucosal lumps and evidence of depapillation (loss of taste buds) and red/white patches.
c. Inspect the gums in both the upper and lower arches noting areas of erythema, swelling, ulceration and evidence of plaque accumulation.
d. Inspect the mucosa of the hard and soft palate and oropharynx.

Hard tissues

a. Finally, inspect the dentition in the upper and lower arches for signs of dental erosion and decay.

Pertinent findings should be documented and where possible, clinical photographs taken. Figure 3 demonstrates the healthy oral cavity along with common intraoral features, often mistaken as pathology.

PRIMARY ORAL MANIFESTATIONS OF IBD

Oral CD

The clinical features of oral CD vary in severity and subtle signs may not be identified in the absence of GI symptoms. Several oral features may be asymptomatic.

Erythema and linear ulceration within the buccal sulci, especially in the posterior aspect of the oral cavity, is more commonly associated with oral CD.[7] Ulceration of the buccal mucosa and scarring has been demonstrated in a large cohort of patients with intestinal CD.[7] Swelling, mucosal tags (figure 4) and buccal mucosa cobblestoning are more often seen in patients with CD.[7] OFG, a non-caseating granulomatous condition, can also present with similar oral changes but tends to involve the anterior oral cavity, with a greater propensity for lip swelling. Bloods may reveal anaemia and raised C reactive protein.[7] Box 1 outlines features suggestive of oral CD.

Orofacial granulomatosis

OFG is a rare chronic inflammatory disease characterised by granulomatous inflammation of the orofacial region.[14] It presents with relapsing and remitting episodes of lip swelling but can also involve the buccal mucosa, gingiva (gums) and floor of mouth.[5] It tends

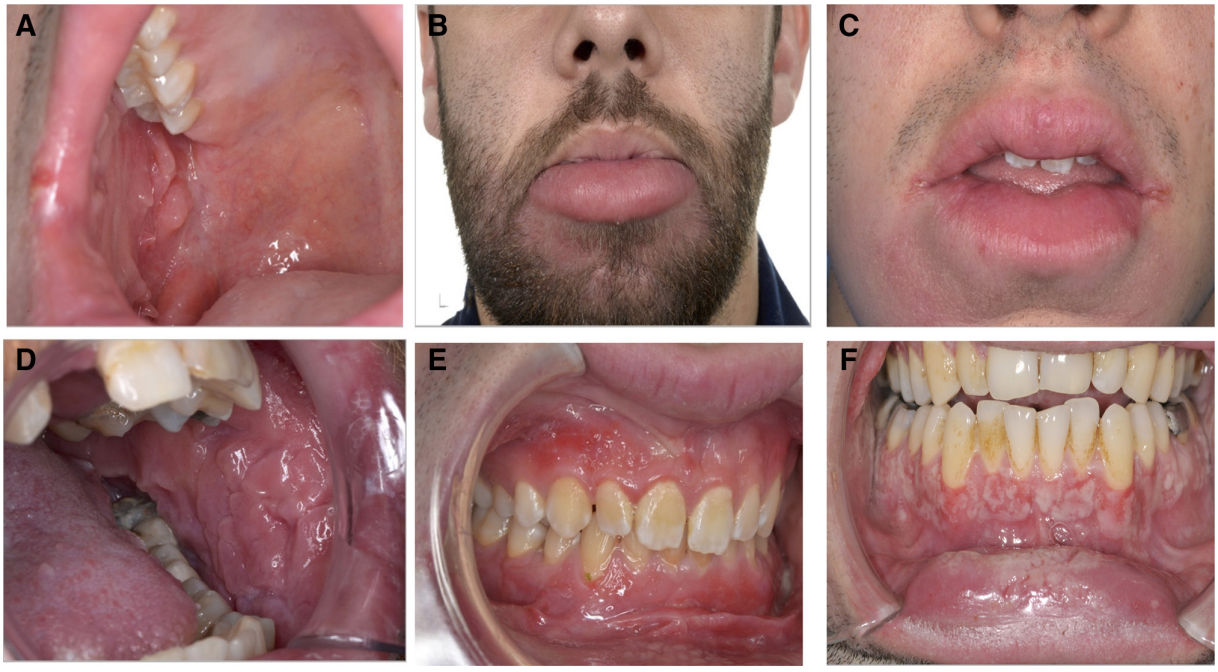

Figure 4 (A) Mucosal tags in the right upper posterior buccal mucosa, (B) diffuse swelling of lower lip, (C) angular cheilitis of the right and left corners of the mouth, (D) cobblestoning of the left buccal mucosa, (E) gingival erythema in the upper and lower arches, and (F) snail-track ulcers involving the gingiva in the lower arch.

to have an 'anterior' pattern of disease presentation with more lip involvement, compared with the 'posterior' pattern more characteristic of oral CD.

OFG classically presents as diffuse symmetrical or asymmetrical swelling of one or both lips, with a slight predilection for lower lip (figure 4), lasting weeks to months. The lower lip may have a vertical fissure in the midline secondary to oedema which predisposes this site to infection with skin commensals. Patients may present with angular cheilitis (figure 4) and cervicofacial lymphadenopathy.[15] There may be oedema of the cheeks with or without overlying erythema.[16]

The intraoral features of OFG include mucosal oedema, ulceration, cobblestoning (figure 4), gum erythema (figure 4) and hypertrophic changes in the floor of mouth called staghorning.[17] Though these features overlap with oral CD, the features identified in Box 1 are more specific to CD.

The histopathological features include lymphoedema and the presence of multiple non-caseating giant cell granulomas. Granulomas are not required for diagnosis and are present in only two-thirds of biopsies.[18]

Box 1 Features associated with Crohn's disease

⇒ Sulcal disease involvement, with erythema
⇒ Linear ulceration (sulcal, buccal mucosa and gingiva)
⇒ Mucosal scarring
⇒ Buccal mucosal swelling and mucosal tags
⇒ Anaemia
⇒ Raised C reactive protein

Biopsy of the labial mucosa is indicated in cases of diagnostic uncertainty or if the history and examination are suggestive of an alternative diagnosis.

Patients who develop signs and symptoms of OFG alone, without any GI-related symptoms, are at an increased risk of developing CD in the future. There is an approximate 25% chance of developing intestinal CD over 10 years when the diagnosis of OFG is made before age 16 years.[5]

Treatment strategies include a cinnamon and benzoate-free diet, with a success rate of 72%.[19] The exclusion diet is adhered to for 12 weeks prior to careful re-introduction of foods guided by a dietitian. Other treatment options include exclusive enteral nutrition, intralesional triamcinolone injections, azathioprine and biologics.[14] Patients with suspected OFG should be referred to an oral medicine specialist for confirmation of the diagnosis and for treatment planning, often undertaken jointly alongside a gastroenterologist.

Ulcerative colitis

Pyostomatitis vegetans

PV is a rare condition strongly associated with IBD[20] and may be the initial presentation of UC. It is more commonly seen in young adults with a male-to-female ratio of 3:1.[21] It presents as generalised oedema, yellow-white pustules and 'snail-track' ulcers[22] (figure 4) involving the buccal mucosa, labial mucosa, gingiva and palate.[23] The extent of oral mucosal involvement does not necessarily correlate with symptoms and it is often asymptomatic.[24] Histopathology demonstrates intraepithelial or subepithelial abscesses

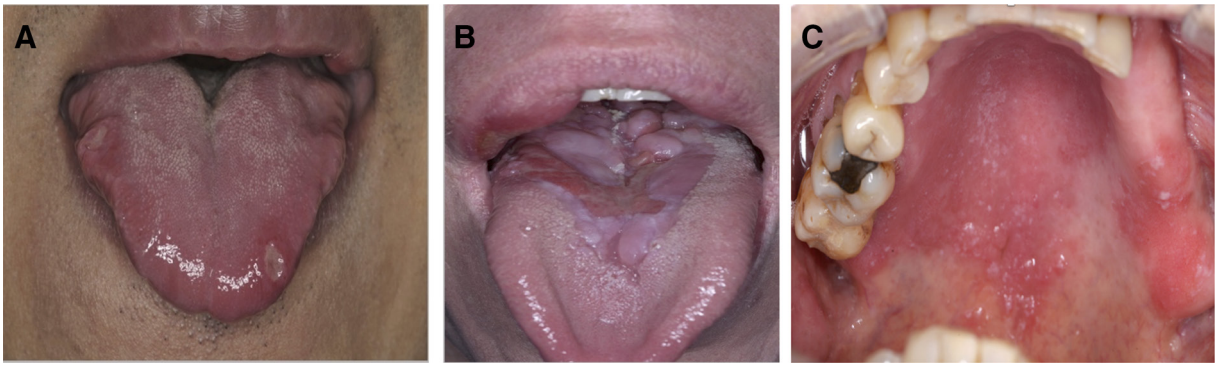

Figure 5 (A) Aphthous ulcers involving the right and left tongue, (B) stomatitis gangrenosum of the posterior dorsum tongue and (C) pseudomembranous candidiasis affecting the hard palate.

containing numerous eosinophils and neutrophils.[21] Confirmation of PV should raise suspicion for UC and colonoscopy should be undertaken.[25] A raised eosinophil count may be seen on blood monitoring. Treatment of PV is focused at controlling the underlying UC. When PV presents in isolation, topical corticosteroids are helpful.[20]

SECONDARY MANIFESTATIONS OF IBD

Aphthous ulceration

Oral ulceration can be secondary to a number of local or systemic factors. Clinical features help distinguish between a benign or neoplastic process. Aphthous ulcers classically appear as round or ovoid, well circumscribed, with grey-yellow centre and erythematous halo and can affect both non-keratinised and keratinised mucosa (figure 5).

Aphthous ulceration occurs in the context of haematinic deficiencies, and secondary to systemic conditions such as CD and coeliac disease. Approximately 3% of patients with coeliac disease experience aphthous-like oral ulcers. An increased incidence of coeliac disease in patients with CD has been reported. It should be considered as a possible diagnosis in the appropriate clinical setting.[26] Investigation of aphthous ulceration depends on the history and clinical features but should include a full blood count, haematinics and a screen for coeliac disease, if the history is suggestive. Management includes correcting predisposing factors, pain management with the use of topical anaesthetics, optimisation of oral hygiene and the use of topical corticosteroid mouth rinses.

Stomatitis

Specific forms of stomatitis have been reported with increased frequency in patients with IBD including stomatitis gangrenosum and staphylococcal mucositis.

Stomatitis gangrenosum

Stomatitis gangrenosum is the oral manifestation of pyoderma gangrenosum known to affect the skin, with necrotic ulcers with violaceous borders. It is rare and seen in only 1% of patients with IBD. The literature is limited to case reports but it is more commonly seen in males, with an average age of 48 years.[27] Clinically, it presents with foul-smelling deep ulcers of varying size with rolled margins and a grey fibrinous base. The oral sites most commonly affected are the buccal mucosa, tongue (figure 5) and soft palate.[27]

The lesions may extend to include large surface areas between 1 and 5 cm, and in cases of extensive involvement, bone destruction and loss of periodontal apparatus may occur.[28] Histology shows ulceration with a fibrinopurulent membrane and a chronic inflammatory infiltrate, though findings are non-specific.[29] The mainstay of treatment is aimed at adequately controlling the underlying disease with corticosteroids and/or immunosuppressive therapy.

Staphylococcal mucositis

This is a pan-oral erythematous stomatitis associated with *Staphylococcus aureus*. Prompt treatment with antibiotics can provide rapid improvement in symptoms. Infections caused by *S. aureus* include angular cheilitis and impetigo, but staphylococcal mucositis has also been reported in patients with IBD.[30]

DRUG-RELATED ORAL SIDE EFFECTS

An overview of management of oral CD/OFG has been published elsewhere.[14] Immunosuppressants, most commonly corticosteroids, can increase the risk of oral opportunistic infections, including oral candidiasis. This can present as classic acute pseudomembranous candidiasis (figure 5), denture stomatitis, angular cheilitis or median rhomboid glossitis, which is a depapillated rhomboid-shaped area on the middle of the dorsum tongue. The diagnosis involves identifying clinical signs, with microbiology demonstrating the presence of *Candida* organisms on microscopy. Treatment includes topical (eg, nystatin oral suspension, miconazole cream/oral gel) or systemic antifungal therapy (eg, azole antifungals).

Moreover, the use of intralesional corticosteroids, disease-modifying drugs such as methotrexate or

biological therapy has been shown to directly affect the oral mucosa.

Methotrexate

The most common oral side effects are ulceration, at any dosing regime, and mucositis, often reported at higher doses. These occur due to the anti-metabolite properties of the drug which impair cell turnover and its anti-folate activity.[31] Folic acid supplementation in patients taking methotrexate has been shown to reduce GI adverse effects and stomatitis.[32] Management of oral ulceration secondary to methotrexate should warrant evaluation of drug dose.[31] Management includes topical analgesia with benzydamine hydrochloride 0.15% (Difflam) and topical corticosteroid (eg, betamethasone 500 µg soluble tablet or prednisolone 5 mg tablet, used as mouthwash for 3 min before expectorating, up to four times daily).

Biologics

The literature identifying oral adverse effects secondary to biological agents is growing.[33] The most common orofacial adverse effect with the use of anti-tumour necrosis factor (TNF) agents is angioedema, mainly of the lips and face.[34] There have been reports of oral lichenoid lesions attributed to the use of both adalimumab and infliximab.[35] In this scenario, patients can be managed by switching to an alternative biological agent, providing topical corticosteroids in the form of a mouthwash (betamethasone, prednisolone) and monitoring. Infliximab-induced osteonecrosis of the jaw has been documented.[36] Osteonecrosis is treated conservatively in the majority of cases, but patients may undergo wide excision and debridement of the affected area in more severe cases. Reactivation of infections, such as oral herpes simplex and varicella zoster virus, has been reported in patients on anti-TNF agents.[37] These infections are generally self-limiting. Additional rare oral effects identified also include oral bleeding, transient ageusia (loss of sense of taste), gum inflammation and medication-induced pigmentation.[33]

Intralesional corticosteroids

Triamcinolone acetonide (40 mg/mL) is often used in the management of OFG involving the lips. The use of intralesional corticosteroids in the orofacial region carries the risks of atrophy, hypopigmentation and hyperpigmentation. Repeated intralesional corticosteroid injections also carry the risk of fibrosis and scarring, which is predictor of future failure to treatment.

CONCLUSION

In this article, we describe a simple but structured approach to the examination of the oral cavity for the gastroenterologist. We have also described the common oral findings in IBD, dividing them into those which are primary manifestations of IBD and secondary consequences of the disease, including common drug-related side effects.

As a tertiary UK centre with an active oral medicine practice, it is our experience that gastroenterology trainees rarely have experience in this area. While trainees have come through a standard UK gastroenterology training programme, which involves time spent at teaching hospitals, little training focuses on the oral manifestations of IBD or teaching a systematic approach to examining the oral cavity. Clinicians, therefore, complete training unconfident in diagnosing oral lesions, as supported by published evidence suggesting that gastroenterologists in general find this a challenging area.[1]

Learning to examine the oral cavity is relatively straightforward. Spending time in an oral medicine clinic would be beneficial for all trainees. Having a systematic approach to examination facilitates accurate description of the nature and severity of oral lesions. This is especially important in the most modern IBD practices in the National Health Service where it is often uncommon for patients to be seen by the same clinician twice. An ability to identify these conditions is of great relevance, as they are relatively common and well described as leading to significant symptoms with impaired quality of life. Furthermore, as we have illustrated, some oral manifestations of IBD may be associated with active luminal disease. In the context of an increased emphasis on achieving mucosal healing, if unrecognised, they represent a missed opportunity to reassess disease and consider appropriate treatment changes. While certain oral conditions such as isolated OFG are rare, it is important they are recognised, as they usually require referral to an oral medicine team for further management. Other oral conditions, such as aphthous ulceration, are far more common and can be due to a variety of associated conditions such as iron deficiency or coeliac disease. These, in turn, are easy to diagnose provided the appropriate tests are performed.

Given the increasing use of complex medical therapies within IBD, it is likely that oral drug-related side-effects will also become more common. It is therefore increasingly important that gastroenterologists are aware of these issues.

It is hoped this article will facilitate gastroenterologists to develop a systematic approach to examining the orofacial region. This will allow for a more successful approach the next time a patient attends the IBD clinic with oral symptoms. It is also hoped that this article will highlight a potential area for improvement in training for those wishing to pursue a career in managing IBD.

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