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Clinical Features

Oral Ulceration - Clinical Feature

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General Dental Practitioners (GDPs) frequently encounter patients presenting with oral ulceration. Oral ulceration has a variety of aetiologies and clinical presentations, which can aid in the diagnosis and management of the condition. This article discusses the different aetiologies, classical clinical findings, and management regimes for oral ulceration. Furthermore, this article will also support GDPs to identify cases of oral ulceration that may require referral to a secondary care setting.

Learning outcomes

- To recognise the common causes of oral ulceration and their classic clinical appearance;
- to discuss appropriate management strategies for oral ulceration in the primary dental setting; and,
- to develop an awareness of when patients with oral ulceration should be referred to secondary care.

INTRODUCTION

Oral ulceration is a painful, common clinical finding, affecting up to 25% of the population, with many seeking advice and treatment from their general dental practitioner (GDP). The aetiology of oral ulceration can range from trauma to the oral mucosa, to an underlying systemic disease, a side effect to medications, or recurrent aphthous stomatitis (RAS). Rarely, an ulcer may be the presenting finding of an intraoral malignancy. Therefore, it is essential to understand the aetiology of the ulceration as this underpins its management.

Ulceration may be managed within the primary dental care setting by removing any causative factors, such as trauma sources if present, and managing the patient's symptoms with topical treatments such as local anaesthetic sprays and topical corticosteroids. In some cases, liaising with the patient's general medical practitioner (GMP) may be necessary, in order to investigate any underlying deficiency states (iron, B12, folate) or systemic diseases. However, in cases involving ulceration resistant to topical treatments, severe ulceration or suspected malignancy, referral to a local oral medicine or oral and maxillofacial unit is required.

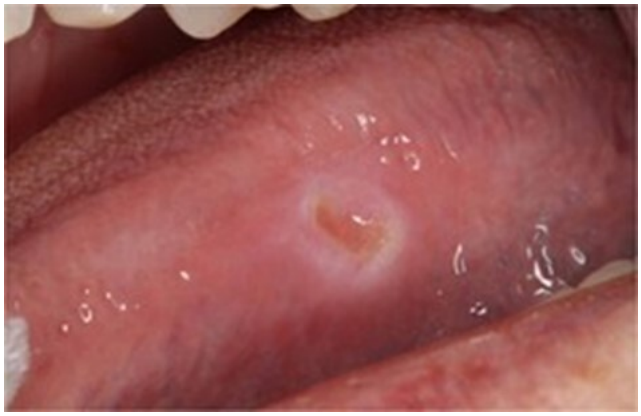

Figure 1. Traumatic ulcer.

AETIOLOGY OF ORAL ULCERATION

TRAUMATIC ULCERATION

Trauma to the oral mucosa from a fractured tooth, a sharp cusp or a denture clasp may result in the formation of an ulcer (**Table 1**). In these cases, ulcers are variable in size and appearance (**Figure 1**). They are often painful with raised white borders with a yellow base, and tend to affect the buccal mucosa, tongue, and lower lip.

RECURRENT APHTHOUS STOMATITIS

RAS ulceration usually affects the non-keratinised mucosa. Its aetiology is unclear, but it is thought to be driven by a dysfunctional cell-mediated immune response (Table 2).[1] Predisposing factors include: stress; trauma; deficiency states (iron, B12 or folate); smoking cessation; menstruation; or, the use of sodium lauryl sulfate- (SLS) containing toothpaste. There are three distinct forms of aphthous ulceration, which are characterised by:

- the size of the ulcer;
- the number of ulcers present at one time;
- the length of time to resolve; and,
- the presence of any scarring after healing.

Table 1. Traumatic ulceration aetiology, management and review.

Aetiology	• Direct trauma to the intraoral mucosa
Management	• Photograph of ulcer (to aid monitoring at review appointment) • Removal of any identified traumatic sources • Benzydamine oromucosal spray 0.15% may be prescribed for symptomatic relief
Review	• Review the patient two weeks following the removal of the suspected traumatic cause • Consider referral to oral medicine/oral and maxillofacial surgery (OMFS) if no improvement to ulcer after two-week review

Table 2. RAS ulceration aetiology, management and review.

Aetiology	• The aetiology of RAS is unclear but is likely due to a dysfunctional cell-mediated immune response
Management	• Trial an SLS-free toothpaste • Ask patient to keep an ulcer diary to record features of ulcers between appointments • Liaise with the patient's GMP for blood investigations (full blood count, haematinics) • Benzydamine 0.15% mouthwash or benzydamine spray for symptomatic relief • Consider topical corticosteroid preparations if local analgesic measures are insufficient
Review	• Review with results from blood investigations and assess management of symptoms • Refer to oral medicine/OMFS if symptoms are poorly controlled or RAS is severe

TYPES OF RAS

Minor aphthae: painful small ulcers (usually <1cm), have a fibrinous base surrounded by a red inflammatory halo and occur on the non-keratinised mucosa. Ulcers appear in crops of one to six that heal within 10 days in the absence of scarring (**Figure 2**).

Major aphthae: differ from minor aphthae in their size (>1cm), pain and healing time, which will usually be several weeks. When major aphthae heal there can be scarring present.

Herpetiform ulceration: the least common form of RAS. These are multiple pinpoint ulcers ranging in size from 1-3mm that are markedly painful and coalesce into larger ulcers after a few days. They can take approximately 14 days to heal but do not scar helping to differentiate them from major aphthae. They tend to affect the ventral tongue and upper lip (**Figure 3**).

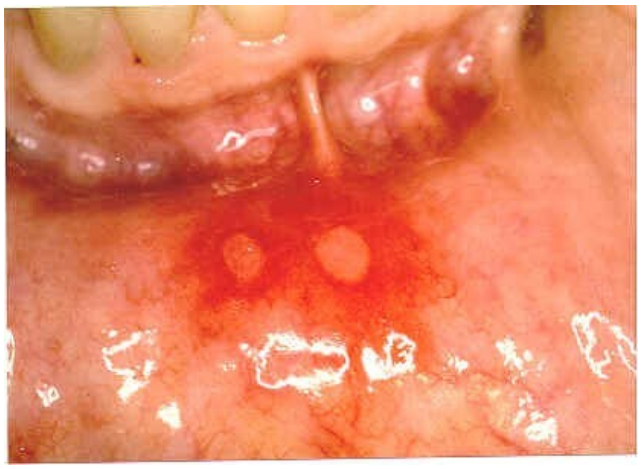

Figure 2. Minor aphthous ulcer.

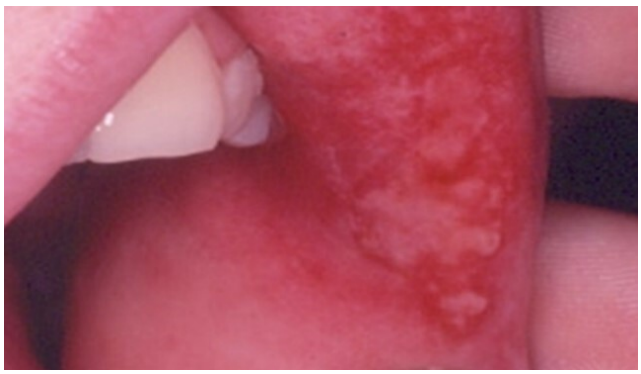

Figure 3. Herpetiform ulceration.

SYSTEMIC CAUSES

Systemic disease can result in ulceration, which has the same clinical features as ulceration in RAS. However, the aetiology differs from RAS as the ulceration is secondary to the systemic disease rather than due to immune dysregulation in RAS.

Gastrointestinal diseases such as coeliac disease or Crohn's disease may cause oral ulceration. It can be helpful to ask any patient presenting with ulceration whether they have had any gastrointestinal symptoms (**Tables 3** and **4**). An onward referral to the patient's GMP would be prudent for further investigation. This may initially include blood investigations to detect any deficiency states resulting from blood loss or malabsorption, and a faecal calprotectin test, which may be elevated in patients with active gastrointestinal inflammation. The patient's ulceration can be managed symptomatically in the same way as with RAS. However,

Table 3. Systemic-cause ulceration aetiology, management and review.

Aetiology	• The aetiology for ulcers occurring secondary to systemic disease is varied depending on the underlying condition
Management	• Enquire whether a patient with ulceration is experiencing any other symptoms, e.g., skin rashes, genital ulceration, change in bowel habit • Manage oral ulcers with topical corticosteroids and local analgesic preparations • Refer to GMP for further investigation and management of systemic disease • Refer to oral medicine/OMFS for biopsy if unusual or very extensive ulceration with systemic features
Review	• Once the patient's systemic disease is under control and ulceration managed, the GDP should review the patient at least every six months for any relapses with regard to their oral symptoms

Table 4. Oral ulceration and oral signs secondary to systemic disease.

Body system	Systemic disease	Key oral features of the condition
Gastrointestinal	Crohn's disease	• Aphthous-like ulceration and linear ulceration in sulci • 'Cobblestoned' appearance of buccal mucosa • Swelling of the labial and buccal mucosa • Angular cheilitis • Stag horning of the floor of the mouth
	Ulcerative colitis	• Aphthous-like ulceration • Pyostomatitis vegetans • Glossitis
Haematological	Leukaemia	• Generalised oral ulceration • Spontaneous gingival bleeding • Gingival hyperplasia • Petechiae haemorrhages • Opportunistic infections
	Anaemia	• Recurrent oral ulceration • Mucosal pallor • Glossitis
Mucocutaneous	Lichen planus (erosive type)	• Irregular, large painful erosions or ulcers occurring on the tongue, vermillion border or the buccal or labial mucosa, which are slow to heal • Scarring on the site of a healed erosion may occur • Desquamative gingivitis
	Beçhet's disease	• Recurrent aphthous-like ulceration is often the first sign prior to the onset of genital ulceration or ocular manifestations such as anterior uveitis • Arthralgia • Skin manifestations
Miscellaneous conditions	Reactive arthritis (Reiter's syndrome)	• Superficial small ulcers affecting the tongue, palate, and buccal mucosa • Lesions on the tongue, which closely resemble geographic tongue
	Lupus erythematous	• Superficial ill-defined ulcers affecting the palate, buccal mucosa and tongue, which lack an erythematous halo • 'Sun-ray'-like lesions • Xerostomia • Burning sensation affecting the oral mucosa • Butterfly malar rash
Infective	Primary herpetic gingivostomatitis	• Multiple yellow vesicles with a red halo affecting buccal mucosa, tongue, palate, pharynx, lips • Submandibular or cervical lymphadenopathy
	Herpangina	• Diffuse erythema affecting the soft palate and tonsillar region • Multiple vesicles and ulcers

appropriate management of their gastrointestinal disease may lead to the resolution of the ulceration.

Multisystem inflammatory disorders such as Beçhet's disease and MAGIC syndrome (a rare syndrome characterised by features of both Beçhet's disease and the recurrent inflammation of cartilage as seen in relapsing polychondritis) can also cause oral ulceration. These patients may also suffer from genital ulceration and ocular mani-

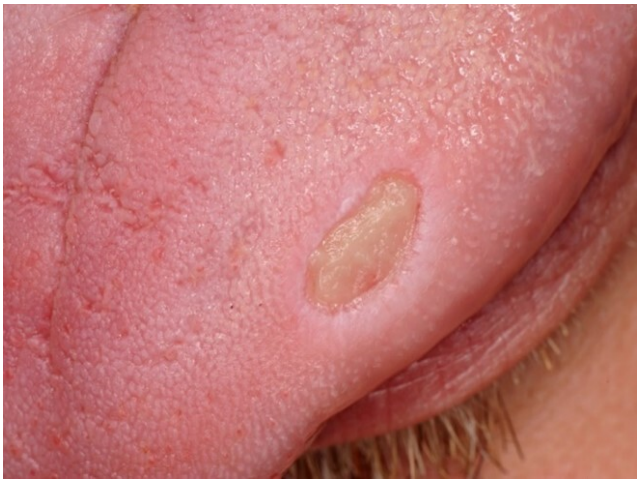

Figure 4. Nicorandil induced ulceration.

festations.[2] Therefore, when taking an ulcer history, it is important to enquire if patients experience ulceration on other body sites.

Various autoimmune conditions can cause extensive oral ulceration. Pemphigus vulgaris affects the oral mucosa (as well as other mucous membranes) causing vesicles, which quickly burst to leave superficial erosions with ragged edges before the onset of skin vesicles or bullae, which also break down to give painful ragged erosions. Patients presenting with these symptoms should be urgently referred to an oral medicine consultant or dermatologist for assessment and management, which involves immunosuppressive treatment.

More commonly seen in patients presenting to their GDP is lichen planus. In its erosive form, there are shallow areas of ulceration with a yellow fibrin plaque covering the surface of the erosion. Sometimes these patients will have striae at the periphery of the ulcerated area and may also have skin involvement with <5mm itchy purplish papules with a shiny surface, and striae often on the forearms and wrists.

DRUG-INDUCED ORAL ULCERATION

Oral ulcers may be induced by systemic medications and can present as single or multiple areas of ulceration.[3] Drug-induced ulcers are typically flat with a whitish base and a raised clear margin (**Figure 4**). These ulcers tend to be resistant to topical treatments. Below is a list of the classes of medications, which are often linked to drug-related ulceration:

- antihypertensives (e.g., bisoprolol);
- bisphosphonates (e.g., alendronic acid);
- immunosuppressants (e.g., methotrexate);
- potassium channel activators (e.g., nicorandil); and,
- antimalarials (e.g., chloroquine).

Should drug-induced ulceration be suspected, you should liaise with the patient's GMP or the consultant who prescribed the medication to enquire if the dosage could be reduced or temporarily stopped to allow healing of the ulcer (**Table 5**).

Patients undergoing chemotherapy (and those receiving radiation to the head and neck region) may develop oral mucositis. This is a very painful condition causing inflammation and widespread ulceration of the oral mucosa, which usually develops four to seven days after starting a chemotherapy regimen. The ulcers tend to be deep with an irregular outline occurring on the non-keratinised mucosa and have a fibrinopurulent exudate. These patients will usually be closely reviewed by their oncologist, who will often manage the oral mucositis. Typical management involves chlorhexidine digluconate 0.2% mouthwash to prevent secondary infection, as well as local analgesics and mucosal coating agents such as Gelclair. The patient will also often receive systemic analgesia and their dose of chemotherapy may be adjusted to enable the resolution of the mucositis, which usually occurs in two to four weeks.

MALIGNANCY

The most common intra-oral malignant neoplasm is oral squamous cell carcinoma (OSCC), which clinically can present as a non-healing ulcer (**Figure 5**). While an OSCC can develop at any site within the mouth, the most common sites are the floor of the mouth, the postero-lateral tongue border, and the gingivae.

A clinician should be suspicious of OSCC in any patient who is presenting with a solitary unexplained ulcer, which is persistent (>14 days), particularly if they have any risk factors for the development of an OSCC including tobacco or betel nut use, heavy alcohol consumption, or past or family history of oral cancer (**Table 6**). Other worrying symptoms include unexplained paraesthesia of the lower lip or tongue, and an unexplained persistent lump in the neck.

The classical clinical features of an ulcerated OSCC involve an ulcer with raised rolled margins and which is indurated on palpation. These ulcers rarely cause pain, but patients may report discomfort in the later stages, as well as a tendency of the ulcer to bleed to mild trauma or spontaneously.

After taking a thorough history from the patient and examination, if a practitioner suspects the ulcerated area represents oral cancer the patient should be referred urgently to their local oral medicine/oral surgery or maxillofacial department for assessment, confirmation of diagnosis and onward management.

CASE REPORT

A 56-year-old female was referred to the Oral Medicine Department at Belfast Royal School of Dentistry for a non-healing ulcer on the left lateral border of her tongue. She reported that this ulcer was painful on contact with foods and had been present for six weeks. The patient had no recollection of any preceding trauma or cause.

Her past medical history included eosinophilic granulomatosis with polyangiitis that was being managed with rituximab. She was otherwise fit and well. She was a non-smoker and did not consume alcohol regularly.

Table 5. Drug-induced oral ulceration aetiology, management and review.

Aetiology	• Drug-induced ulceration is commonly linked to starting or increasing dosages of antihypertensive, immunosuppressant, bisphosphonate, potassium channel activator, or antimalarial medications
Management	• Benzydamine 0.15% spray applied directly to the ulcer to aid symptomatic relief or mouthwash if ulceration is widespread or inaccessible • Contact the patient's GMP to enquire if the dose of the medication can be temporarily reduced or stopped to allow for healing of the ulcer
Review	• Review at three weeks • Refer to oral medicine/OMFS if the ulcer still persists after three weeks with no sign of improvement

Extraoral examination did not display any cervical lymphadenopathy or facial asymmetry. However, the patient did have notable pallor of the face. Intraoral examination revealed a large 3x3cm raised ulcerated lesion on the lateral border of the tongue, with rolled margins and a speckled surface. The ulcer was indurated and painful to palpate (**Figure 6**) and lay adjacent to a lingually positioned LL5 with a fractured restoration. The differential diagnoses considered were:

- traumatic ulcer;
- squamous cell carcinoma; and,
- granulomatosis disease.

An incisional biopsy was taken alongside routine blood investigations to aid in diagnosis. The biopsy revealed that the ulcer was consistent with a traumatic aetiology. The blood investigations found that the patient had a microcytic anaemia due to low iron. Therefore, a working diagnosis was made of a traumatic ulcer secondary to the fractured LL5 with delayed healing associated with low iron.

The patient's LL5 was temporised and Difflam Spray was prescribed for symptomatic relief. She was also referred to her GMP to correct her iron levels. At review after six weeks, the ulcer was significantly reduced in size and had resolved at a further two-month follow-up.

REFERRAL

The UK's National Institute for Health and Care Excellence (NICE) produced guidelines in 2015 for head and neck cancers, which recommend referral on a suspected cancer pathway for people with unexplained ulceration in the oral cavity lasting for greater than three weeks, or a persistent and unexplained lump in the neck. Furthermore, referral to an oral medicine or oral maxillofacial unit may be made for ulceration with the following features[4]:

- an ulcer that is indurated with a raised rolled margin;
- ulceration that cannot be adequately managed with topical treatments;
- investigations that cannot be undertaken in the primary dental care setting; and,
- recurrent ulceration of unknown aetiology.

SUMMARY

Oral ulceration can occur due to a variety of reasons. Investigations should be undertaken to identify any predisposing cause but most often ulceration will be due to trauma or RAS. Management is aimed at symptomatic relief through local analgesic preparations or, if unsuccessful, topical corticosteroid treatments. Patients who are resistant to treatment or who have red-flag symptoms should be urgently referred to oral medicine or oral and maxillofacial surgery units for further investigation.

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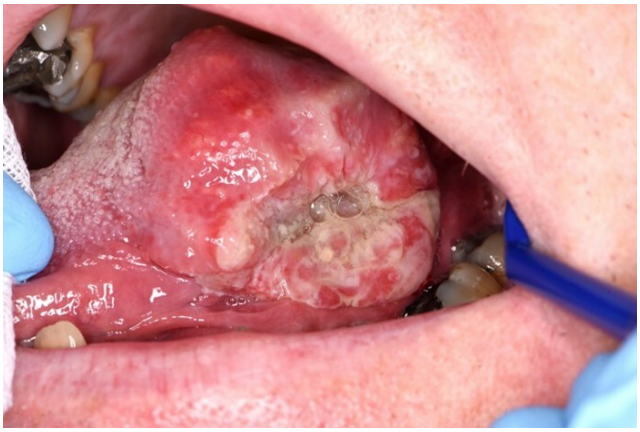

Figure 5. Ulcerated OSCC lateral border of tongue.

Table 6. Malignancy-caused ulceration aetiology, management and review.

Aetiology	• The aetiology of an OSCC is multifactorial – risk factors in the development of an OSCC include: 1) tobacco use; 2) betel nut or paan consumption; 3) excessive alcohol consumption; or, 4) past personal or family history of oral cancer
Management	• Thorough history and examination • Correct any potential traumatic causes of the ulcer if detected
Review	• Refer a suspected cancer pathway to a local oral and maxillofacial department for assessment plus or minus a biopsy if suspicious of malignancy

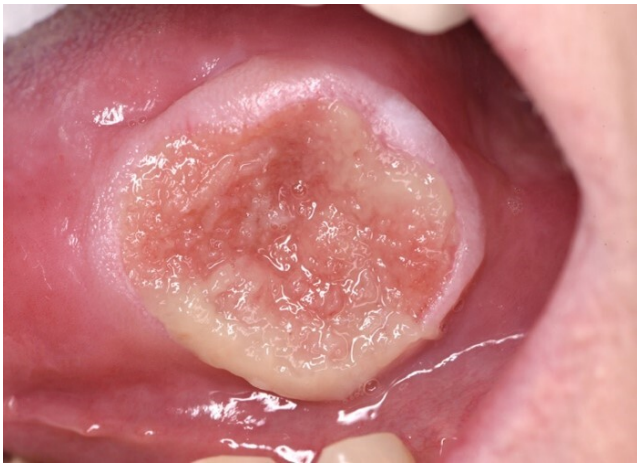

Figure 6. Raised ulcer lateral border of tongue.

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