Common Non-systemic Causes of Oral Ulcers

Introduction

Patients may complain of a sore mouth or pain and yet have no obvious organic cause, but in most an organic lesion can be observed. In some patients this is an obvious ulcer or erosion, in others mucositis or an atrophic mucosa may be seen.

Ulcers and erosions can be the final common manifestation of a spectrum of conditions (Table 2.1) ranging from the simplest traumatic breach of the epithelium, to epithelial damage resulting from an immunological attack as in pemphigus, pemphigoid, lichen planus and aphthae; to damage because of an immune defect as in human immunodeficiency virus (HIV) disease and leukaemia; to infections as in herpesviruses, tuberculosis and syphilis; to nutritional defects such as in vitamin deficiencies and some intestinal disease; or to neoplasia. The term ‘ulcer’ is used usually where there is damage to both epithelium and lamina propria, and a crater, sometimes made more obvious clinically by swelling caused by oedema or proliferation in the surrounding tissue. The term ‘erosion’ (desquamation if involving the gingivae) is often used for breaches of the epithelium in which there is little damage to the underlying lamina propria. Such lesions, if penetrating the epithelium only partially, usually have a red or red and yellow appearance. If they penetrate the full thickness of the epithelium, however, they are typically covered by a fibrinous exudate and may then have a yellowish appearance. If they penetrate the full thickness of the epithelium, however, they are typically covered by a fibrinous exudate and may then have a yellowish appearance. This chapter discusses the causes and management of common non-systemic ulcerative disorders of the oral mucosal ulcers.

Most ulcers or erosions are due to local causes such as trauma or burns, some are caused by aphthae or malignant neoplasms.

**Table 2.1 Causes of mouth ulcers.**

- Local causes:
  - trauma
  - burns
- Drugs
- Recurrent aphthous stomatitis
- Malignant ulcers
- Systemic disease:
  - blood disorders
  - gastrointestinal disorders
  - mucocutaneous disease
  - connective tissue disease
  - vasculitides
  - infective diseases
- Others

ULCERS OF LOCAL AETIOLOGY

Trauma from bites or from dentures and orthodontic appliances is common. Self-induced lesions due to lip-biting after a local anaesthetic injection, cheek-biting (a neurotic habit) and in some syndromes (Fig. 2.1 and 2.2) may cause ulceration. Rarer causes include ulceration of the lingual frenum caused by repeated coughing or cunnilingus, and palatal bruising, petechiae and ulceration from fellatio. Other local causes include burns from heat or cold, chemicals, electrical injury or irradiation (Fig. 2.3).

Clinical Features

Usually a single ulcer is seen, with an obvious cause (e.g. a denture flange). The patient is otherwise well, although there may be a small degree of ipsilateral cervical lymph node enlargement. Chronic irritation may cause hyperplasia or hyperkeratosis of the adjacent mucosa, but induration should raise the suspicion of malignancy.
Management

Remove aetiological factors and prescribe a chlorhexidine 0.2% mouthwash. Maintenance of good oral hygiene and the use of benzydamine or hot saline mouthbaths may help (Table 2.2). Most ulcers of local cause heal spontaneously in about 1 week if the cause is removed and such supportive care given. Biopsy is needed if there is any suspicion of malignancy (see below) or if the ulcer does not heal within 3 weeks of removal of the apparent cause – it may be a neoplasm or another serious disorder.

DRUG-INDUCED LESIONS

A wide spectrum of drugs can occasionally cause mouth lesions, by various mechanisms. Ulcers are common in those treated with cytotoxic drugs. The more common examples of drug reactions include:

- Cytotoxic agents, particularly methotrexate, producing ulcers.
- Agents producing lichen-planus-like (lichenoid) lesions, such as non-steroidal anti-inflammatory agents, some antihypertensives, antidiabetics, gold salts, antimalarials and other drugs.
- Agents causing local chemical burns (especially aspirin held in the mouth).
- Agents causing erythema multiforme (especially sulphonamides and barbiturates).

Other drug reactions are uncommon or rare.

Table 2.2 Dental clinical team roles in the management of patients with oral ulcers of local cause.

<table>
<thead>
<tr>
<th>Dental surgeon</th>
<th>Ancillary, hygienist, nurse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understand disease and management in order to extend education of, and reassure, patient</td>
<td>Understand disease and management in order to extend education of, and reassure, patient</td>
</tr>
<tr>
<td>Remove any obvious irritating cusp, restoration or appliance. Initiate topical treatment with analgesics (benzydamine) and antiseptics (chlorhexidine). Biopsy, consult or refer to specialist if concerned, or ulcer not healing in 3 weeks</td>
<td>Oral health education of patient</td>
</tr>
<tr>
<td>Oral healthcare; in particular to avoid causes of irritation</td>
<td>Prophylaxis if chlorhexidine causes staining</td>
</tr>
<tr>
<td>Oral health education of patient</td>
<td>Alert dental surgeon to any changes, or possible adverse effects of treatment</td>
</tr>
</tbody>
</table>
Clinical Features

- Radiotherapy-induced ulceration (mucositis): these are superficial ulcers in the path of (usually external) radiotherapy.
- Cytotoxic induced ulcers: these have a non-specific appearance, but are widespread and very painful.
- Lichenoid lesions: resemble lichen planus clinically and histologically (see Ch. 3).
- Chemical burns: are usually solitary lesions with sloughing of mucosa.
- Erythema multiforme: ulcers and lip swelling (see Ch. 3).

Management

Diagnosis of a drug reaction is made from the drug history and sometimes by testing the effect of withdrawal. Skin patch tests are, unfortunately, rarely of real practical value.

Treatment is to stop the causative drug and treat the ulceration symptomatically with topical benzydamine and, possibly, aqueous chlorhexidine.

APHTHAES (Recurrent Aphthous Stomatitis)

Recurrent aphthous stomatitis (RAS) are recurrent mouth ulcers which affect up to 20% of the population, are the most common lesions seen in practice, and typically start in childhood (Tables 2.3 and 2.4). The natural history is improvement with age.

Aetiology

The aetiology of aphthae is unknown and most patients with RAS are otherwise apparently well. There appears to be a genetically determined immunological reactivity to unidentified antigens, possibly microbial.

<table>
<thead>
<tr>
<th>Table 2.3</th>
<th>Aphthae (recurrent aphthous stomatitis (RAS)).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aetiology</strong></td>
<td>Unclear</td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td>Typically early onset with recurrent ulcers usually lasting 1 week or 1 month. Three distinct clinical patterns:</td>
</tr>
<tr>
<td></td>
<td>● <strong>Minor</strong> – small ulcers (&lt;4 mm) on mobile mucosae, healing within 14 days, no scarring</td>
</tr>
<tr>
<td></td>
<td>● <strong>Major</strong> – large ulcers (may be &gt;1 cm), any site including dorsum of tongue and hard palate, healing within 1–3 months, with scarring</td>
</tr>
<tr>
<td></td>
<td>● <strong>Herpetiform ulcers</strong> – multiple minute ulcers that coalesce to produce ragged ulcers</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Up to 20% of population</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>● Diagnosed from history and clinical features</td>
</tr>
<tr>
<td></td>
<td>● No diagnostic test of value</td>
</tr>
<tr>
<td></td>
<td>● A blood picture is useful to exclude possible deficiencies and coeliac disease</td>
</tr>
<tr>
<td></td>
<td>● Treat any underlying predisposing factors. Treat aphthae with chlorhexidine aqueous mouthwash or topical corticosteroids</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2.4</th>
<th>Dental clinical team roles in the management of patients with aphthae.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dental surgeon</strong></td>
<td>Understand disease and management in order to extend education of, and reassure, patient</td>
</tr>
<tr>
<td></td>
<td>Initiate investigations, and treatment with, for example, topical corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Refer to specialist if there is cause for concern</td>
</tr>
<tr>
<td></td>
<td>Oral healthcare; in particular to avoid causes of irritation or trauma</td>
</tr>
<tr>
<td></td>
<td>Be alert to any changes or possible adverse effects of treatment, such as candidosis after steroids</td>
</tr>
<tr>
<td></td>
<td>Oral health education of patient</td>
</tr>
<tr>
<td><strong>Ancillary, hygienist, nurse</strong></td>
<td>Understand disease and management in order to extend education of, and reassure, patient</td>
</tr>
<tr>
<td></td>
<td>Oral health education of patient</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis if oral hygiene impaired or chlorhexidine causes staining</td>
</tr>
<tr>
<td></td>
<td>Alert dental surgeon to any changes, or possible adverse effects of treatment</td>
</tr>
</tbody>
</table>
Thus a family history may be present and there are some weak human leukocyte antigen (HLA) associations, but none that are sufficiently strong to help establish the diagnosis. Immunological changes are detectable, but there is no reliable evidence of autoimmune disease. Various microorganisms have been tested, but none have been unequivocally incriminated in RAS. It is possible that RAS may be due to changes in cell-mediated immune responses and cross-reactivity with *Streptococcus sanguis* or a heat shock protein.

Although most patients with RAS are apparently well, about 10–20% of patients prove to have associations with a deficiency of a haematinic such as iron, folate or vitamin B₁₂.

A very small number of patients may have RAS related to:
- coeliac disease (2–3%)
- menstruation
- stress
- food allergy
- Behçet’s syndrome
- immunodeficiencies, including HIV disease and cyclic neutropenia.

Aphthae sometimes appear when smokers give up the tobacco habit; they are less common in smokers than in non-smokers.

**Clinical Features**

Episodes begin usually in childhood and the natural history is of spontaneous remission after some years. Aphthae may present different clinical appearances and behaviours, but all typically (Fig. 2.4):
- are ovoid or round
- recur
- have a yellowish floor
- have a pronounced red inflammatory halo.

*Minor aphthae* (Mikulicz’s aphthae (MiRAS)) are small, 2–4 mm in diameter (Fig. 2.5), last 7–10 days, tend not to be seen on the gingiva, the palate or the dorsum of tongue, and heal with no obvious scarring. Most patients develop not more than six ulcers in any single episode.

*Major aphthae* (Sutton’s ulcers (MaRAS)) are recurrent, often ovoid ulcers with an inflammatory halo, but are less common, much larger and more persistent than minor aphthae, and can affect the dorsum of tongue and the soft palate, as well as other sites (Fig. 2.6). Sometimes termed periadenitis mucosa necrotica recurrens (PMNR), major aphthae can be well over 1 cm in diameter and can take several months to heal. In any one episode there are usually fewer than six ulcers present. Major aphthae may leave obvious scars on healing.

*Herpetiform ulcers* (HU) are so termed because patients have a myriad of small ulcers that clinically resemble those of herpetic stomatitis (Fig. 2.7). HU are, however, a distinct entity, lacking the associated fever, gingivitis and lymph node involvement of primary herpetic stomatitis. Pinpoint herpetiform aphthae enlarge and fuse to produce irregular ulcers.
Management

Aphthae are diagnosed from the history and clinical features. There is no diagnostic test of value. Blood tests may be useful for excluding possible deficiencies or other conditions (see Table 2.3).

Features that might suggest a systemic background, and indicate referral include:

- Any suggestion of systemic disease from extra-oral features such as:
  - genital lesions
  - skin lesions
  - ocular lesions
  - gastrointestinal complaints (e.g. pain, altered bowel habits, blood in faeces)
  - loss of weight or, in children, failure to thrive
  - weakness
  - chronic cough
  - fever
  - lymphadenopathy
  - hepatomegaly
  - splenomegaly.

- An atypical history or behaviour such as:
  - onset of ulcers in later adult life
  - exacerbation of ulcers
  - severe aphthae
  - aphthae unresponsive to topical hydrocortisone or triamcinolone.

- Presence of other oral lesions, especially:
  - candidosis (including angular stomatitis)
  - glossitis
  - purpura or gingival bleeding
  - gingival swelling
  - necrotizing gingivitis
  - herpetiform lesions
  - hairy leukoplakia
  - Kaposi’s sarcoma.

Table 2.5 Patient information sheet: aphthous ulcers.

Any underlying predisposing factors should be treated where possible, and the aphthae controlled with:

- chlorhexidine 0.2% aqueous mouthwash, or
- topical corticosteroids such as hydrocortisone hemisuccinate 2.5 mg pellets, or
- 0.1% triamcinolone acetonide in Orabase used four times daily or
- in adults, tetracycline rinses.

A benzydamine rinse or spray may help ease the discomfort. Rarely, more potent topical corticosteroids (e.g. betamethasone or beclometasone (beclo)metasone) or other agents such as thalidomide may be needed, but these should be given by a physician since there may be adverse effects (Table 2.5).

BEHÇET’S SYNDROME (Behçet’s Disease)

Aphthae of any of the RAS types described above may rarely be a manifestation of Behçet’s syndrome (Table 2.6 and Fig. 2.8), where they are associated with systemic disease, manifesting usually with genital ulcers and uveitis. This rare condition affects mainly young adult males and is most common in people from the Middle East, Japan, China and Korea, along the ancient silk route from Europe to the Far East.

Aetiology

Behçet’s syndrome appears to have an immunogenetic basis, with a specific association with HLA genetic type HLA-B5101. Immune-logical changes are like those in aphthae. The precipitating factor is unknown but may be Streptococcus sanguis. There appears to be a subset of T cells which react to an immunostimulatory human heat shock protein with cross-reactivity to streptococci, and...
produce tumour necrosis factor (TNF) and interleukin 8 (IL-8). The interleukin leads to the chemo-attraction of neutrophils, which are also hyperactive and release superoxide, leading to vasculitis.

### Clinical Features

Behçet’s syndrome is a multisystem disease affecting the mouth in most cases and many other sites including, commonly:

- **Genitals**: ulcers resembling oral aphthae (Fig. 2.9).
- **Eyes**: uveitis is one of the more important ocular lesions and visual acuity is often impaired.
- **Skin**: erythema nodosum (painful red lumps on the shins), various rashes may develop as well as pustules at the site of venepuncture (pathergy).
- **Joints**: large joint arthropathy is not uncommon.
- **Neurological system**: headache, psychiatric, motor or sensory manifestations.
- **Vascular system**: thrombosis of large veins may be life-threatening.

### Diagnosis

Behçet’s syndrome is a clinical diagnosis, the cardinal features being oral and genital ulceration, uveitis and erythema nodosum. Other causes of this constellation of lesions, such as ulcerative colitis, Crohn’s disease, mixed connective tissue disease, lupus erythematosus and Reiter’s syndrome, must be excluded.

Diagnostic criteria for Behçet’s syndrome are not completely agreed but include:

- recurrent oral ulceration
- plus two or more of the following:
  - recurrent genital ulceration
  - eye lesions
  - skin lesions
  - pathergy.

### Treatment

Oral ulcers are treated as for aphthae. Systemic manifestations require immunosuppression using, typically, corticosteroids, colchicines or thalidomide.

### MALIGNANT ULCERS

Most malignant oral ulcers, probably more than 90%, are squamous cell carcinomas (Fig. 2.10). Other primary malignant neoplasms can be Kaposi’s sarcoma, lymphoma, antral carcinomas or salivary gland tumours. Metastases, especially

---

**Table 2.6** Behçet’s syndrome.

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Immunological</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td>multisystem disorder</td>
</tr>
<tr>
<td>● Oral aphthae</td>
<td>almost invariably</td>
</tr>
<tr>
<td>● Eye disease:</td>
<td>reduced visual acuity, uveitis,</td>
</tr>
<tr>
<td></td>
<td>retinal vasculitis</td>
</tr>
<tr>
<td>● Skin disease:</td>
<td>erythema nodosum and others</td>
</tr>
<tr>
<td>● Arthralgia:</td>
<td>of large joints</td>
</tr>
<tr>
<td>● Neurological disease:</td>
<td>various syndromes</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>No test of reliable value, except HLA typing</td>
</tr>
<tr>
<td>● Oral ulcers:</td>
<td>treat as for aphthae</td>
</tr>
<tr>
<td>● Systemic</td>
<td>manifestations: immunosuppression</td>
</tr>
</tbody>
</table>
from breast, lung and prostate malignancy may also arise. The incidence of oral carcinoma, lymphoma and Kaposi’s sarcoma is rising, the latter two virus-related tumours because of HIV infection and the increasing use of iatrogenic immunosuppression.

**Oral Carcinoma and Potentially Malignant Lesions**

Oral squamous cell carcinoma is uncommon in most parts of the developed world, where it generally affects elderly males (Table 2.7). It is common in parts of northern France, however, and especially in the developing world such as South-East Asia.

**Table 2.7 Oral squamous cell carcinoma.**

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Predisposing factors include tobacco and alcohol use and sometimes UV irradiation (sun)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td></td>
</tr>
<tr>
<td>Intraoral</td>
<td>a lump or ulcer with induration commonly on the posterolateral tongue</td>
</tr>
<tr>
<td>Lip</td>
<td>thickening, induration, crusting or ulceration, usually at vermilion border of lower lip just to one side of midline</td>
</tr>
<tr>
<td>Incidence</td>
<td>Uncommon in most parts of the UK</td>
</tr>
<tr>
<td>Management</td>
<td>Biopsy is mandatory</td>
</tr>
<tr>
<td>Intraoral</td>
<td>surgery or radiotherapy; 5-year survival is 30%</td>
</tr>
</tbody>
</table>

**Aetiology**

There is no doubt that aetiological factors acting on a genetically susceptible host who may have impaired metabolism of carcinogens, may include:

- tobacco habits (including betel use)
- alcoholic beverages
- diet poor in fresh fruit and vegetables and thus in vitamins such as vitamin A
- and, in the case of lip carcinoma, exposure to sunlight.

Most oral squamous cell carcinomas in developed societies arise in the absence of any obvious clinical premalignant lesions. In other societies where the incidence of oral cancer is apparently higher, clinically recognizable premalignant or potentially malignant lesions are more common. Such potentially malignant lesions or conditions include:

- all erythroplasias (Fig. 2.11)
- some dysplastic leukoplakias (Fig. 2.12)
- some lichen planus (see Ch. 3) (Fig. 2.13)
- some oral submucous fibrosis (Fig. 2.14)
- some chronic immunosuppression (lip cancer mainly)
- rare conditions such as
– discoid lupus erythematosus
– Paterson–Kelly syndrome (sideropenic dysphagia)
– tertiary syphilis.

The definition of premalignancy is difficult. In practice, lesions can only be termed malignant after malignant change has developed, since there is, as yet, no means of predicting with certainty the risk of cancerous transformation. ‘Potentially malignant’ may be a better term.

Potentially malignant oral lesions frequently show epithelial atrophy and hence appear clinically particularly as red lesions, or erythroplasia (see Ch. 5). These are rare, isolated lesions or they may be associated with white lesions as erythroleukoplakia (speckled leukoplakia). The majority of erythroplasias have histopathological features of severe oral epithelial dysplasia.

Other potentially malignant oral lesions may be associated with epithelial thickening and appear clinically as white lesions, ‘leukoplakias’, although this term is usually now restricted to those white lesions where no defined cause can be identified (see Ch. 5). Leukoplakia is more common than erythroplasia. Lichen planus may also be potentially malignant (see Ch. 3).

Microscopy is still the best available prognostic guide. The histological findings of dysplasia indicate that a lesion has a malignant potential, but cannot be used for confident prediction of malignant change and, in any event, even the best pathologists by no means always agree on the degree of dysplasia. Furthermore, even though severely dysplastic lesions can proceed to malignancy or recur after excision, a few can undergo regression upon removal of aetiological factors or even spontaneously. For example, oral mucosal dysplasia has been seen in unsuspected vitamin B12 deficiency, regressing on replacement therapy. New technologies, such as DNA ploidy, may help resolve these dilemmas.

**Clinical Features**

A carcinoma (Figs 2.15 and 2.16) can present as an:

- ulcer
- red lesion
- white lesion
- mixed red and white lesion

---

**Figure 2.13** Lichen planus (see also Figs 3.11 to 3.16).

**Figure 2.14** Oral submucous fibrosis.

**Figure 2.15** Squamous cell carcinoma with surrounding leukoplakia.

**Figure 2.16** Squamous cell carcinoma.
● lump
● fissure.

Usually carcinoma forms a solitary chronic indurated ulcer, with a raised rolled edge and granular floor (Fig. 2.17). Cervical lymph node enlargement may be detectable (Fig. 2.18).

Intraorally carcinoma typically affects the posterolateral tongue as a lump or ulcer, with submandibular node involvement.

On the lip, carcinoma presents with thickening, induration, crusting or ulceration, usually at the vermillion border of the lower lip just to one side of midline. There is late involvement of the submental lymph nodes.

**Management**

Almost invariably indicated are:
● biopsy
● specialist referral.

It is essential to differentiate an intraoral carcinoma from other causes of persistent mouth ulceration, especially major aphthae or, rarely, chronic infections such as tuberculosis, or a deep mycosis such as histoplasmosis. A lip carcinoma must be differentiated from herpes labialis, keratoacanthoma and basal cell carcinoma. The prognosis is better with early detection, but is very site-dependent. The prognosis of:

● intraoral carcinoma is low, with a 5-year survival rate of about 30%, because of the high proportion of late-stage cases
● lip carcinoma, typically detected at an earlier stage, is much better, with a 5-year survival rate often of more than 70%.

Predisposing factors such as tobacco and alcohol use should be stopped; patients are liable to subsequent further primary tumours, especially in the mouth and respiratory tract.

It is essential to determine whether cervical lymph nodes are involved or there are other primary tumours, or metastases elsewhere. Oral carcinoma is now treated by surgery and/or irradiation. Occasionally, chemotherapy is used, but it is of little value in most instances.

The dental clinical team are crucial to the management of the patient who has received

| Table 2.8 Dental clinical team roles in the management of patients with oral malignancy. |
|---------------------------------------|-----------------------------|
| **Dental surgeon**                   | **Ancillary, hygienist, nurse** |
| Refer urgently to specialist. Understand disease and management in order to extend education of, and reassure, patient | Understand disease and management in order to extend education of, and reassure, patient |
| Alert specialist to any developments or possible adverse effects of treatment | Oral health education of patient, in particular dietary and preventive dental care advice |
| Oral healthcare; in particular to avoid causes of infection or pain, to treat xerostomia, to prevent caries | Alert dental surgeon to any changes, or possible adverse effects of treatment |
| Oral health education of patient | |
radiotherapy to an oral or perioral neoplasm (Table 2.8). Radiation-induced lesions are invariable if teletherapy (external beam) involves the oral mucosa and salivary glands. The consequences may include:

- **Mucositis**: diffuse erythema and ulceration (Fig. 2.19).
- **Xerostomia** (see Fig. 10.3): leading to
  - dysphagia
  - disturbed taste
  - radiation caries
  - candidosis
  - bacterial sialadenitis.

Xerostomia is managed as discussed in Chapters 1 and 10.

- **Liability to osteoradionecrosis** – surgery and tooth extraction should be avoided wherever possible
- **trismus**
- **telangiectasia**
- and, in children,
  - **jaw hypoplasia**
  - **hypoplasia and retarded eruption of developing teeth.**

**FURTHER READING**


