



General approach

- Ulceration of the oral mucosa may be due to trauma, infection, immune-related disease, or neoplasia. Vesiculobullous blistering disorders frequently also present as ulceration due to rupture of initial lesions (Chapter 3, p. 42).
- Oral ulcers are invariably painful, although an important exception is squamous cell carcinoma, which is often painless, particularly when the tumor is small.
- Ulceration may represent neoplasia and therefore biopsy should be undertaken if there is any suspicion of malignancy or there is uncertainty of alternative diagnoses.
- Due to the good vascularity of the oral tissues the majority of ulcers in the mouth heal relatively quickly. Therefore, any ulcer persisting beyond 14 days should be considered neoplastic until proven otherwise.

Table 1 shows patterns of ulceration and likely diagnoses.

Table 1 Patterns of ulceration

Single or small number of discrete ulcers

- Traumatic ulceration
- Minor and major recurrent aphthous stomatitis
- Cyclic neutropenia
- Behçet's disease
- Squamous cell carcinoma
- Necrotizing sialometaplasia
- Tuberculosis
- Syphilis

Multiple discrete ulcers

- Herpetiform recurrent aphthous stomatitis
- Behçet's disease
- Acute necrotizing ulcerative gingivitis

Multiple diffuse ulceration

- Erosive lichen planus
- Lichenoid reaction
- Graft versus host disease
- Radiotherapy-induced mucositis
- Osteoradionecrosis

Traumatic ulceration

ETIOLOGY AND PATHOGENESIS

Traumatic causes of oral ulceration may be physical or chemical. Physical damage to the oral mucosa may be caused by sharp surfaces within the mouth, such as components of dentures, orthodontic appliances, dental restorations, or prominent tooth cusps. In addition, some patients suffer ulceration as a result of the irritation of cheek chewing. Oral ulceration caused during seizures is well-recognized in poorly-controlled epileptics. Chemical irritation of the oral mucosa may produce ulceration; a common cause is placement of aspirin tablets or caustic toothache remedies on the mucosa adjacent to painful teeth or under dentures. Situations also occasionally arise where a patient with psychologic problems may deliberately cause ulceration in their mouth (factitial ulcers).

CLINICAL FEATURES

Traumatic ulceration characteristically presents as a single localized deep ulcer (36, 37) with, as would be expected from physical injury, an irregular outline. In contrast, chemical irritation may present as a more widespread superficial area of erosion, often with a slough of fibrinous exudate (38).

DIAGNOSIS

The cause of a traumatic lesion is often obvious from the history or clinical examination. Factitial ulceration is usually more difficult to diagnose since the patient may be less forthcoming with the history; therefore a high index of suspicion is necessary to establish the diagnosis. Biopsy is often needed to establish the diagnosis and to rule out infection or neoplasia.

MANAGEMENT

If traumatic ulceration is suspected and it is possible to eliminate the cause, such as smoothing of a tooth or repairing a denture or restoration, and if the mouth can be kept clean, healing will result within 7–10 days. If the lesion is particularly painful then the use of sodium bicarbonate in water or antiseptic mouthwashes, such as chlorhexidine or benzydamine, may be helpful. A biopsy, to exclude the presence of

neoplasia such as carcinoma, lymphoma, or salivary gland tumor, should be taken from any ulcer that fails to heal within 2 weeks of the removal of the suspected cause. A patient who is thought to be deliberately self-inducing an ulcer may be challenged with this diagnosis, although admission by the patient is uncommon, and the underlying psychologic problems should be explored with appropriate specialist help.



36 Ulcer on the lateral margin of the tongue induced by trauma from the edge of a fractured restoration in the first lower molar.



37 Irregular ulcer that was self-induced by the patient.



38 Diffuse ulceration in the palate due to the placement of salicylic acid gel by the patient onto the fitting surface of her upper denture.



Recurrent aphthous stomatitis

ETIOLOGY AND PATHOGENESIS

In Western Europe and North America, recurrent aphthous stomatitis (RAS) is the most frequent mucosal disorder, affecting approximately 15–20% of the population at some time in their lives. Although many etiologic theories have been proposed for RAS, no single causative factor has as yet been identified. Hematinic deficiency involving reduced levels of iron, folic acid, or vitamin B₁₂ has been found in a minority of patients with RAS and correction has led to resolution of symptoms. Other predisposing factors implicated include: psychologic stress, hypersensitivity to foodstuffs, cessation of smoking, and penetrative injury. However, in the majority of sufferers, it is difficult to identify a definite cause for their RAS.

CLINICAL FEATURES

Clinically, RAS may be divided into three subtypes: minor, major, and herpetiform. All types of RAS share common presenting features of regular, round or oval, painful ulcers with an erythematous border that recur on a regular basis.

The large majority of patients with RAS suffer from the minor form (MiRAS) characterized by either a single or a small number of shallow ulcers that are approximately 5 mm in diameter or less (39, 40). MiRAS affects the nonkeratinized sites within the mouth, such as the labial mucosa, buccal mucosa, or floor of the mouth. Keratinized mucosa is rarely involved and therefore MiRAS are not usually seen in the hard palate or on the attached gingivae. The ulcers of MiRAS typically heal in 10–14 days without scarring, if kept clean.

Major recurrent aphthous stomatitis (MaRAS) occurs in approximately 10% of patients with RAS and, as the name implies, the clinical features are more severe than those seen in the minor form. Ulcers, typically 1–3 cm in diameter (41), occur either singly or two or three at a time and usually last for 4–6 weeks. Any oral site may be affected, including keratinized sites. Clinical examination may reveal scarring of the mucosa at sites of previous lesions, due to the severity and prolonged nature of MaRAS.

Herpetiform RAS (HU) presents with ulcers similar to those of MiRAS but in this form the number of ulcers is increased and often involves as many as 50 separate lesions (42). The term ‘herpetiform’ has been used since the clinical presentation of HU may resemble primary

herpetic gingivostomatitis, but at the present time members of the herpes group of viruses have not been found to be involved in this or in either of the other two forms of RAS.

DIAGNOSIS

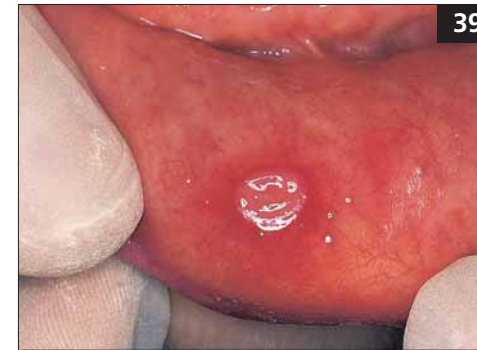
Diagnosis of RAS is made relatively easily due to the characteristic clinical appearance of the ulcers and the recurrent nature of the symptoms. A biopsy may be necessary in some patients with MaRAS since a solitary lesion may resemble neoplasia or deep fungal infection.

MANAGEMENT

A wide range of treatment has been recommended for the symptomatic management of RAS. However, in addition to providing treatment to reduce pain and aid healing of lesions, it may be helpful to identify predisposing factors. All patients with RAS should be advised to avoid foods containing benzoate preservatives (E210–219), potato chips, crisps, and chocolate since many sufferers implicate these foods in the onset of ulcers. Any relationship to gastrointestinal disease, menstruation, and stress should be investigated. Hematologic deficiency should be excluded, particularly if the patient has gastrointestinal symptoms, heavy menstrual blood loss, or a vegetarian diet. Blood investigation should include a full blood count and assessment of vitamin B₁₂, corrected whole blood folate and ferritin levels. Patients may also relate the onset of ulceration to periods of psychologic stress.

Many patients obtain symptomatic relief from use of a mouthwash (sodium bicarbonate in water, chlorhexidine, or benzydamine) or application of topical corticosteroids preparations (hydrocortisone, triamcinolone, beclomethasone or betamethasone). A mouthwash based on tetracycline (250 mg capsule broken into water and used 4 times daily for 1 week) has also been found to be helpful.

Systemic immunomodulating drugs and other agents, such as prednisolone (prednisone), levamisole, monoamine oxidase inhibitors, thalidomide or dapsone, can successfully control RAS, but their use should be considered carefully and they are best prescribed in specialist units for patients who do not respond to topical therapy.



39 Small round ulcer (MiRAS) affecting the labial mucosa.



40 Small round and oval ulcers (MiRAS) affecting the soft palate.

41 Large round ulcer (MaRAS) in the buccal mucosa.



42 Multiple small round and oval ulcers (HU) in the soft palate.





Behçet's disease

ETIOLOGY AND PATHOGENESIS

The etiology of Behçet's disease remains unclear but is known to involve aspects of the immune system. There is a strong association between Behçet's disease and the HLA B51 haplotype.

CLINICAL FEATURES

Behçet's disease is a multi-system condition with a range of manifestations including oral and genital ulceration, arthritis, cardiovascular disease, thrombophlebitis, cutaneous rashes, and neurologic disease. The condition usually begins in the third decade of life and is slightly more common in males than in females. Behçet's disease is more common in certain Mediterranean countries and in some Asian countries, especially Japan. The oral lesions consist of ul-

ceration that may be any of the three forms of recurrent aphthous stomatitis, although the lesions tend to be of the major type (43), which heal with scarring (44).

DIAGNOSIS

Recurrent oral ulceration is an essential feature of Behçet's disease, but a number of other criteria are required to be fulfilled to establish the diagnosis. HLA typing may be of value.

MANAGEMENT

Oral lesions should be managed symptomatically in the same way as recurrent aphthous stomatitis. The systemic manifestations are managed by the patient's physician.

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43 An ulcer of major aphthous stomatitis in the palate of a patient with Behçet's disease.

44



44 Scarring following the resolution of major aphthous stomatitis.

Cyclic neutropenia

ETIOLOGY AND PATHOGENESIS

Neutropenia is defined as an absolute reduction in circulating neutrophils. Prolonged or persistent neutropenia is associated with leukemia, some blood dyscrasias, many drugs, and radiation or chemotherapy. Cyclic neutropenia is a rare disorder of unknown etiology where there is a severe, cyclical depression of neutrophils from the blood and bone marrow.

CLINICAL FEATURES

During episodes of neutropenia there is fever, malaise, cervical lymphadenopathy, infections, and oral ulcers. Oral ulceration is common on nonkeratinized surfaces and may appear as single (45, 46) or multiple discrete lesions. Patients are also prone to severe periodontal disease.

DIAGNOSIS

Diagnosis is established on examination of the peripheral blood differential showing a reduction in circulating neutrophils during episodes of oral ulceration.

MANAGEMENT

There is no specific management for the condition. Medical investigations may be needed to rule out other causes of neutropenia. During episodes of neutropenia, antibiotics may be given to prevent oral infection. Scrupulous oral hygiene is needed to minimize periodontal disease.

45, 46 Minor aphthous stomatitis in cyclic neutropenia.

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46



Squamous cell carcinoma

ETIOLOGY AND PATHOGENESIS

The vast majority of intra-oral malignancies are cases of squamous cell carcinoma (SCC). A number of etiologic factors have been proposed for SCC but at the present time the two most important are believed to be tobacco and alcohol. The smoking of tobacco in the form of cigarettes, cigars, or a pipe accounts for the majority of tobacco usage and there is a direct relationship between the amount of tobacco used and the risk of developing oral SCC. Although there has been some suggestion that smokeless tobacco is also associated with oral SCC, this link remains weak and controversial. By contrast, the chewing of 'pan soupuri' (tobacco, areca nut, and slake lime) is a major cause of oral cancer in the Indian sub-continent.

Excessive drinking of alcohol is associated with an increased likelihood of occurrence of oral SCC. Interestingly, it has been observed that there is an adverse synergistic effect between tobacco and alcohol, with a greatly increased risk of SCC if a patient has both habits rather than just one. Other factors, such as deficiency of iron, vitamin A or vitamin C, fungal infection, viral infection, and stress have been proposed as being involved in the development of oral SCC, but their relative contributions and significance are unknown. While trauma itself would not appear to cause cancer, it has been implicated as a cofactor in the presence of another factor.

CLINICAL FEATURES

The clinical presentation of SCC can vary greatly and range from a small erythematous patch through to a large swelling or area of ulceration. SCC of the lip usually presents as a painless ulcer with rolled margins (47) and is associated with sun damage to the tissues. The majority of cases of SCC within the mouth develop in a previously clinical normal mucosa, although some may be preceded by a leukoplakia or an erythroplakia (Chapters 4, p. 74, and 5, p. 93). Approximately 70% of oral SCC develop in the floor of the mouth (48), tongue (49, 50), or retromolar region (51). Although the gingivae are rarely affected, painless areas of ulceration at this site should be regarded as suspicious (52). Unfortunately, SCC is often painless at an early stage and therefore most (60–70%) of patients present with advanced (late stage) lesions involving metastatic spread to regional lymph nodes.

DIAGNOSIS

Although there are presenting features, such as induration and rolled margins, that may suggest the presence of oral SCC, the disease *cannot* be diagnosed clinically. Biopsy and histologic examination of lesion material is mandatory. The use of exfoliative cytology, topical nuclear dye (tolinium chloride), and brush biopsy have all been suggested as a method for investigating suspicious mucosal lesions, but the usefulness of these techniques is uncertain and limited at the present time.

MANAGEMENT

Overall, the 5-year survival rate from oral cancer is approximately 40%, although this varies according to site. Lip cancer has the best 5-year survival rate of 90%, possibly due to the increased likelihood of detection of the tumor while small and the ease of treatment. By contrast, SCC of the floor of the mouth carries a poor prognosis, with a 5-year survival rate of around 20%. The most important predictor of outcome is the stage of the disease at presentation. The presence of metastatic tumor within the lymph node of the neck reduces the overall survival rate of oral SCC from any intra-oral site by 50%.

The treatment of oral cancer consists primarily of surgery, radiotherapy, or a combination of both approaches. Some patients may also receive chemotherapy prior (neo-adjuvant), during (concurrent), or after (adjuvant) treatment with radiotherapy. The development of microvascular surgery and use of free flaps in reconstruction has dramatically improved the quality of life for patients with SCC. Unfortunately, despite these surgical advances the post-operative survival rate of patients has changed little in the past 80 years, due to death from new primary lesions or metastases.

All patients with a history of SCC should be kept on long-term review to detect any recurrence of tumor or the development of further primary lesions. Obviously, patients should be given support to eliminate any tobacco and alcohol habit. Since outcome is influenced by early detection, all health care workers should regularly undertake examination of the oral mucosa of their patients. Dental surgeons are ideally placed to carry out this examination and represent one category of the key workers who could possibly improve the early detection of oral cancer. Any suspicious area of mucosa such

as a persistent area of ulceration, leukoplakia, or erythroplakia should be biopsied. This could be carried out in the general dental practice setting

but in cases of widespread mucosal involvement it may be more sensible to refer the patient to a specialist clinic.



47–52 Squamous cell carcinoma presenting as an ulcer with rolled indurated margins on the lip and at a variety of intra-oral sites.