

Making sense of mouth ulceration: part three

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Viral infections

The clinical appearance of an oral ulcer on its own is rarely diagnostic. Any ulceration with fever or with other orofacial or extraoral lesions may be suspect. In the light of multiple causes, some systematic way of dealing with ulceration is needed, such as my system of splitting causes into:

- Systemic
- Malignancy
- Local
- Aphthae
- Drugs.

This article discusses the second of the systemic causes – infections, which include those mentioned in Table 1.

The main infective viral disorders that may present with mouth ulceration include: herpes simplex stomatitis; varicella zoster virus (VZV) infections; Epstein-Barr virus (EBV) infections; cytomegalovirus; Coxsackie and ECHO viruses; chikungunya fever, and HIV/AIDS.

Herpes simplex stomatitis

The primary infection with herpes simplex virus (HSV) may present, usually in a child or teenager, with a stomatitis manifesting with:

- A sore mouth, with gingival swelling plus scattered vesicles leading to multiple ulcers affecting any area of the mouth (Figure 1)
- Fever
- Cervical lymphadenopathy
- Malaise.

The diagnosis is clinical, though rising antibody titre is confirmatory. The differential diagnosis is from other mouth

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Table 1: Infections

Viral:
<ul style="list-style-type: none"> • Herpes simplex virus (HSV) • Varicella zoster virus (VZV) • Epstein–Barr virus (EBV) • Cytomegalovirus (CMV) • Human immunodeficiency virus (HIV) • Coxsackie viruses • ECHO viruses • Chikungunya fever
Bacterial:
<ul style="list-style-type: none"> • Mycobacteria • Treponema pallidum
Mycotic:
<ul style="list-style-type: none"> • Candidiasis • Histoplasmosis • Paracoccidioidomycosis
Parasitic:
<ul style="list-style-type: none"> • Leishmania • Others

ulcers especially other viral infections, and viral DNA studies can help.

Management is mostly symptomatic – controlling pain and fever with paracetamol, and there is typically spontaneous remission within seven to 10 days. If the patient is symptomatic, or immunocompromised, systemic aciclovir may be indicated.

Herpes labialis is a recurrence that affects the lips with prodromal paraesthesia, erythema and vesicles. It heals in seven to 14 days.

Penciclovir 1% or aciclovir 5% cream applied in prodrome may help and, in immunocompromised people, systemic aciclovir, valaciclovir or famciclovir are indicated.



Figure 1: Herpetic stomatitis

Recurrent intraoral herpes may arise, often in the hard palate, from trauma or HIV.

For some, HSV may also be responsible for facial palsy and erythema multiforme.

Varicella zoster virus (VZV) infections

Chickenpox is the primary infection with VZV infections. Shingles (zoster) is recurrence of VZV latent in dorsal root nerve ganglia. Predisposing factors include:

- Older age
- Immunocompromised
- Leukaemia
- Cancer.

Zoster presents with:

- Pain
- Rash – unilateral vesiculating then scabbing in dermatome
- Mouth ulcers (mandibular) – ipsilateral on the buccal and lingual mucosa
- Maxillary-ipsilateral on palate vestibule
- Post-herpetic neuralgia – pain persists long after rash has healed.

Zoster is a clinical diagnosis, the disorder being managed with:

- Analgesics
- Aciclovir orally
- Valacyclovir or famciclovir may help pain and healing and prevent post-herpetic neuralgia
- Systemic corticosteroids
- In ophthalmic zoster, an ophthalmological opinion is important (likelihood of corneal ulceration).

The shingles vaccine is now offered to people over the age of 70, as a prophylaxis.

Epstein-Barr virus (EBV) infections

EBV infections may be responsible for mouth ulcers in



Figure 2: Candidiasis

infectious mononucleosis, and also in lymphomas and HIV/AIDS.

The Paul-Bunell test and antibody studies can be diagnostically helpful. There are no cures or drug treatments; symptomatic treatment usually suffices.

Cytomegalovirus

Cytomegalovirus can cause ulcers, especially in immunocompromised people. There are no cures or drug treatments though ganciclovir may help; symptomatic treatment usually suffices.

Human herpesvirus-8 (HHV-8) or Kaposi's sarcoma-associated herpesvirus (KSHV)

KSHV can cause Kaposi's sarcoma, especially in immunocompromised people. There are no cures or drug treatments; symptomatic treatment usually suffices.

Coxsackie and ECHO viruses

These enteroviruses can cause ulcers, especially in epidemics in children. Occasionally there can be cardiac, neurological or other sequelae. There are no cures or drug treatments; symptomatic treatment usually suffices.

Chikungunya fever

This is an RNA virus infection transmitted from a mosquito bite, mainly contracted from areas around the Indian ocean, with an incubation period of usually two to four days and symptoms such as:

- Oral ulceration
- Rash
- Headache, malaise
- Arthralgia
- Fever to 39 degrees.

There are no cures or drug treatments; symptomatic treatment usually suffices.

Table 2: September 1992 consensus classification of oral lesions associated with adult HIV infection

Group one: lesions strongly associated with HIV infection
<ul style="list-style-type: none"> • Candidosis <ul style="list-style-type: none"> - Erythematous - Pseudomembranous • Hairy leukoplakia • Kaposi's sarcoma • Non-Hodgkin's lymphoma • Periodontal disease <ul style="list-style-type: none"> - Linear gingival erythema - Necrotising (ulcerative) gingivitis - Necrotising (ulcerative) periodontitis
Group two: lesions less strongly associated with HIV infection
<ul style="list-style-type: none"> • Bacterial infections <ul style="list-style-type: none"> - Mycobacterium avium intracellulare - Mycobacterium tuberculosis • Melanotic hyperpigmentation • Necrotising (ulcerative) stomatitis • Salivary gland disease • Dry mouth caused by decreased salivary flow rate • Unilateral or bilateral swelling of major salivary glands • Thrombocytopenia purpura • Ulceration not otherwise specified • Viral infections <ul style="list-style-type: none"> - Herpes simplex - Human papillomavirus (wart-like) lesions - Condyloma acuminatum - Focal epithelial hyperplasia - Verruca vulgaris - Varicella zoster virus - Herpes zoster - Varicella
Group three: lesions seen in HIV infection
<ul style="list-style-type: none"> • Bacterial infections <ul style="list-style-type: none"> - Actinomyces israelii - Escherichia coli - Klebsiella pneumonia - Cat-scratch disease and epithelioid (bacillary) angiomatosis • Drug reactions (ulcerative, erythema multiforme, lichenoid, toxic epidermolysis) • Fungal infection other than candidosis <ul style="list-style-type: none"> - Cryptococcus neoformans - Geotrichum candidum - Histoplasma capsulatum - Mucoraceae (mucormycosis zygomycosis) - Aspergillus flavus • Neurologic disturbances <ul style="list-style-type: none"> - Facial palsy - Trigeminal neuralgia • Aphthous-like ulcers • Viral infections <ul style="list-style-type: none"> - Cytomegalovirus - Molluscum contagiosum

HIV/AIDS

Worldwide, the RNA human immunodeficiency virus (HIV), which progresses over months or years to the acquired immune deficiency syndrome (AIDS), is mainly heterosexually transmitted. Nevertheless, in general, infection is more common in:

- Young persons
- Travellers
- Men who have sex with men
- Urban areas
- Africa and people of heritage
- Asia
- The Americas
- Eastern Europe.

The UK has one of highest rates of new HIV diagnoses in Europe, outstripped only by Portugal, Ukraine, Estonia and Russia.

Most HIV infections are in heterosexuals, contracted on vacation. Many men who have sex with men have HIV. Transnational gay men sexual networks exist, as shown by syphilis and lymphogranuloma venereum (LGV) outbreaks among HIV-positive men, and high rates of migration and travel between Amsterdam, Barcelona, Berlin, London and Paris.

HIV can cause infections and tumours in most tissues and, in the mouth, presents with (Table 2):

- Aphthous-like ulcers
- Candidiasis (Figure 2)
- Hairy leukoplakia
- HIV-related gingival and periodontal disease
- HIV salivary gland disease
- Kaposi's sarcoma
- Lymphomas (Figure 3)
- Viral infections
- Warts.

HIV is a diagnosis confirmed serologically and managed with anti-retroviral therapy (ART), which typically has considerable benefit and can alter oral sequelae, as these can be decreased or increased after ART.

Decreased after ART:

- Kaposi's sarcoma
- Hairy leukoplakia
- HIV-related gingival and periodontal disease
- Aphthous-like ulcers.

Increased after ART, as part of the immune reconstitution inflammatory syndrome (IRIS):

- HIV salivary gland disease
- Viral infections
- Warts.

Fungal infections

Fungal (mycotic) infections are mainly seen in immunodeficient people, in whom disseminated disease is



Figure 3: Lymphomas

common. Seriously ill patients (especially those who have immune defects) may be infected with other fungi, such as candida, mucor and aspergillus.

Increasing population mobility means a wide range of fungal infections (deep mycoses), formerly seen mainly in the tropics, may now also be seen globally. Healthy individuals in endemic areas (often in the developing world) are often infected with these fungi, typically involving the lungs, but often asymptomatic.

Even acute pulmonary and primary mucocutaneous symptomatic mycotic lesions, in otherwise healthy persons, may resolve spontaneously. Chronic pulmonary infections tend to progress and disseminated infections can be fatal.

Orofacial lesions caused by these mycoses are typically associated with lesions elsewhere, often in the respiratory tract. The diagnosis may be suggested by a tumour-like nodule or mass, chronic ulceration, chronic sinus infection, or bizarre mouth lesions, especially in immunocompromised patients, those who have been in endemic areas, or where there is granuloma formation found on biopsy.

Investigations include smear, biopsy, culture, sometimes serology, physical examination and chest radiography. Tissue forms of the fungus may be visible but special stains are often required.

Patients should be managed by a specialist, usually with systemic anti-mycotic drugs.

References

Gandolfo S, Scully C, Carrozzo M (2006) Oral medicine. Elsevier Churchill Livingstone (Edinburgh and London). ISBN 13: 29780443100376

Scully C, Almeida ODP, Bagan J, Diz PD, Mosqueda A (2010) Oral medicine and pathology at a glance. Wiley-Blackwell (Oxford) ISBN 978-1-4051-9985-8

Scully C, Flint S, Bagan JV, Porter SR, Moos K (2010) Oral and maxillofacial diseases. Informa Healthcare (London and New York). ISBN-13: 9780415414944

Scully C, Bagan JV, Carrozzo M, Flaitz C, Gandolfo S (2012) Pocketbook of oral disease. Elsevier, London. ISBN 978-0-702-04649-0

Scully C (2013) Oral and maxillofacial medicine. 3rd edition. Churchill Livingstone (Edinburgh). ISBN 9780702049484

Scully C (2012) Aide memoires in oral diagnosis: mnemonics and acronyms (the Scully system). Journal of Investigative and Clinical Dentistry 3(4): 262-3

Scully C (2013) RULE for cancer diagnosis. British Dental Journal 215: 265-6

Disclosure

This series offers a brief synopsis of the diagnosis and management of mouth ulceration – a complex topic that includes common disorders, and less common but life-threatening conditions. It does not purport to be comprehensive, and the series may include some illustrations from books written or co-authored by the author and colleagues from UK and overseas, published by Elsevier-Churchill Livingstone, Wiley-Blackwell, or Informa/Taylor & Francis – all of whose cooperation is acknowledged and appreciated.

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