Diagnosis & Management of Oral Mucocutaneous Disease

- One of the most important considerations with some of these conditions is that they are often confused with the inflammatory gingival diseases such as ANUG, gingivitis or even periodontitis!

APHTHOUS ULCERS

- Affects non-keratinized mucosa
- Not observed on attached gingiva. Hard palate, vermilion border of lip.
- Single or multiple painful areas
- Covered by yellow membrane and erythematous halo
- More painful than they look!!

Aphthous Ulcers Cont’d…

- Minor aphthous ulcers heal within 7-10 days
- Major aphthous ulcers may take up to 6 weeks to heal
- Differential: herpes simplex, trauma, pemphigus, pemphigoid

Small Aphthous Ulcer

- This is an aphthous ulcer
- These can be painful enough to mimic a toothache!
Herpes Simplex (I)

- Self-limiting
- Passed through physical contact
- Eruption expected at site of inoculation within 3-14 days

Herpes Simplex (I) – 3 Variants

- **Primary Gingivostomatitis** - usually small children; multiple painful ulcerations preceded by vesicles
- **Secondary Herpes or Herpes Labialis** - common in adults and may be activated by stress, sunlight, latent virus
- **Herpetic Whitlows** - eruptions on digit; seen in dentists

Herpes Simplex (1) Cont’d…

- Differential Diagnosis should include:
  - ANUG
  - trauma
  - chemical burns
  - contact allergy
  - streptococcal pharyngitis
  - erythema multiforme
  - aphthous ulcer

Herpetic Lesion

- **Herpetic lesions**
  - In contrast to aphthous ulcers, these are seen on keratinized tissue and also have a very erythematous border see arrow.

Herpetic Lesions

Primary in Child

Recurrent in Adult (labialis)
Varicella Zoster Virus

- Varicella Zoster primary infections: common in children (chicken pox), painful, pruritus vesicles on trunk, face and oral mucosa

Varicella Zoster Virus Cont’d…

- Herpes Zoster: adult (shingles). Seen commonly in immunosuppressed and elderly
  - Due to reactivation of latent virus causing unilateral painful vesicles and ulcers along V-2 and V-3 distribution
  - Prolonged and painful course and may also lead to post-herpetic neuralgia and ophthalmologic disorders

Varicella Zoster

- Varicella Zoster
  - Note that this erythematous tissue does not cross the midline (Arrow delineates boundary). This is the clue that would tell you that this is a recurrent viral lesion.

Herpes Zoster on Face

Lichen Planus (5 Forms)

- Reticular: interlacing keratotic striae commonly on buccal mucosa
- Plaque: leukoplakia-like in appearance, primarily on buccal mucosa and dorsum of tongue...biopsy may be indicated
- Atrophic: painful red areas surrounded by white striae

Lichen Planus Cont’d…

- Erosive: granular, brightly erythematous erosions covered by pseudomembrane: painful
- Bullous Variant: uncommon form, short lived bullae or vesicles which rupture and leave painful eroded surfaces...difficult to treat
Lichen Planus

These demonstrate various presentations of oral lichen planus. Note that in cases where the lichen planus lesions are localized on attached gingiva, they have been readily mistaken for chronic gingivitis. Note that these lesions don’t have to be removed!

Lichen Planus

Note that this form of lichen planus on the cheeks is of little consequence BUT it does appear to be heading towards ulceration, which can be painful and would then require treatment as outlined in later slides. But…

Lichen Planus

(continued from previous slide) Even after treatment, the white striae will not disappear. This patient was actually made to feel quite guilty for not looking after her ‘gingivitis’! (See also next slide). Arrow pointing to marginal lesion.

Lichen Planus

Lichen Planus. This is seen as white striae shown by arrow on the gingiva only. This lesion did not have to be removed. As with the previous slide, the patient with this lesion was feeling rather guilty because she could not look after her gingival condition by proper OH!

Benign Mucous Membrane Pemphigoid

- Inflammatory disease characterized by vesicles and bullae of mucous membrane of oral cavity, eyes
- Bullae rupture and may present as desquamative gingivitis
- Diagnosis: clinically, biopsy, immunofluorescence (antibodies localized on basement membrane)
Pemphigoid

These patients have benign mucous membrane pemphigoid. These patients were also treated, in most cases, for "routine", periodontal or gingival problems before diagnosis of their mucocutaneous disease was made.

Of course, no amount of oral hygiene improvement would resolve their problems! These patients find it difficult to brush because mechanical home care can injure the very fragile tissues, and so plaque accumulation is often seen and this may mislead the clinician into focusing on oral hygiene alone. VERY difficult to treat as must treat perio and mucocutaneous condition.

In cases like this, oral hygiene and plaque removal are essential but treatment of the underlying inflammatory condition is crucial.

Pemphigus Vulgaris

- Affects skin and oral mucosa as vesicles or bullae which rupture and leave painful lesions
- Positive Nikolsky’s sign
- **Differential:** pemphigoid, erythema multiforme, aphthous stomatitis
- **Biopsy:** lost adhesion of basal and prickle cells, immunofluorescence showing antibodies between epithelial cells

- Slide courtesy Dr. David Mock

Note the raw bleeding mucosa. Such patients may have numerous soft relines for their dentures with little help because the underlying disease has not been treated!
Candidiasis

- Candida Albicans: a commensal organism in the oral cavity
- Opportunistic: becomes pathogenic as a result of local inflammation or systemic disease (i.e., long-term antibiotics, HIV) in the host

Candidiasis (candidosis for our friends south of the 49th parallel!). Note the white plaque in the vestibule (arrow). This is a colony of candidal organisms that can be wiped off readily (unlike what one could do with the white striae of lichen planus for example).

Severe oral candidiasis with large area of palate colonized by candidal organisms. This patient was suffering from terminal AIDS.

Candidiasis (AIDS Patient)

Biopsy Types

- Routine Histopathology: specimen is fixed in formalin after removal. Normal and diseased tissues should be sampled
- Immunopathology: specimen frozen in liquid nitrogen. In some cases, fixed tissues can be used but antigenic sites could be destroyed by fixation

Pemphigus Histology

- The histopathological slide on top is courtesy Dr. David Mock.
- This demonstrates intra-epithelial breakdown that is consistent with a diagnosis of pemphigus
Pemphigoid (micro)

The epithelium has separated from the underlying connective tissue. This is consistent with a diagnosis of benign mucous membrane pemphigoid.

Blood Tests

- **Serum Cutaneous Antibodies**: pericellular distribution = pemphigus, basement membrane distribution = pemphigoid
- Usually reported in “dilutions” (e.g. 1:20)
- **Serum Anti-nuclear Antibodies**: also reported in dilutions with 0-1:40 considered as normal while ≥ 1:80 may suggest SLE. May supplement with anti-DNA and/or rheumatoid factor

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Blood Tests

Immunofluorescence stain. Note the bright green staining. This demonstrate localization of autoantibodies directed against epithelial cell surface antigens as seen in pemphigus.

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Blood Tests

- **T4/T8 Ratio**: This test is used to assess the ratio between CD4 (helper) and CD8 (suppressor) cells
- A ratio of less than 0.8-0.9 could be suggestive of immunodeficiency
Cytological Smear
- Used to detect candidal organisms
- Not reliable for assessing malignant cells in mouth
- Less sensitive than culture, but more specific
- Use a steel spatula or periodontal probe instead of wood

Treatment: Aphthous Ulcers
- Tetracycline (250 mg): Open one capsule in 15 ml of water and rinse QID. This method may be more effective than the prepared tetracycline, which is no longer available anyway.

Biofilm Control in Mucocutaneous Diseases

Treatment of Mucocutaneous Diseases
- Mild to Moderate: Betnovate ointment (0.1% betamethasone). Apply to affected areas QID (may be applied on gauze) or Topsyn Gel (0.05% fluocinomide).
- Moderate to Severe: Dermovate (0.05% clobetasol). Apply 2-4 times per day.

NOTE: There may be a systemic effect with Dermovate. Therefore, consult MD

Treatment of Mucocutaneous Disease Cont’d…
- Benadryl Elixir 250 ml
- Distilled Water 250 ml
- Mycostatin Suspension 25 ml
- Hydrocortisone 2-4% (depending on severity of lesions, cortisone can be varied)

Label: Rinse with 15 ml of solution for 30 seconds TID and expectorate.

Note… does not taste very good! Patient-compliance can be an issue!

Treatment of Mucocutaneous Diseases Refractory Lesions
- Direct injection of lesions
- Dexamethasone (4 mg/ml)
- Place about 0.5-1.0 ml
- One to three injections over a treatment period of one to two months
**Pemphigus vulgaris: treatment**
- Dermatology referral
- Systemic corticosteroids
- Immunosuppressants
  - Mycophenolate mofetil
  - Azathioprine
- Rituximab – monoclonal antibody to B-lymphocytes

**Treatment of Oral Mycoses**
- **Nystatin Ointment** (100,000 U/gm) QID. Can be placed in a denture base
- **Nystatin Suppositories** (100,000 U/g). Dissolve 1 in mouth QID. *Note: These have no sucrose flavouring*
- **Oral Suspension** may be used but suppositories may be more effective

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**Treatment of Viral Lesions (Herpes)**
- **Topical**: Zovirax Ointment (acyclovir 5%). Apply to affected areas 4-6 times per day (10 days)
- **Systemic**: Zovirax (200 mg) Q4H up to 10 days... Valacyclovir (500-1000 mg Q8-12H)
- **Prophylaxis**: Zovirax (200 mg) Q8H daily and in consultation with MD (or Valacyclovir (500-1000 mg/day))

**Combination Therapy**
- In some cases, mycotic infections may develop secondarily to topical or systemic steroid therapy or tissue inflammation and mycotic infection exist concurrently
- Nystatin and Betnovate may be combined in various ratios:
  - Betnovate 70%:Nystatin 30%
- Apply to affected areas QID

**New Direction/Adjunctive to Steroids?**
- **Systemic subantimicrobial dose**
  - Doxycycline: (20 mg BID)
- This drug inhibits MMP activity for treatment of mucocutaneous. They can be used in combination with, for example, steroid rinses when there’s a poor overall response to the rinse.

**Periopatch®**
- Innovative Pharmaceutical...
PerioPatch®

PerioPatch Adheres to Mucosa: The Components Draw Out Inflammatory Cytokines

Evidently Leads to Long-Term Regulation of Inflammation by Returning the Inflammatory Response to a Constitutive Level

Gingival Cleft at Presentation As an Example of Prolonged Effect Even Following One Treatment Exposure

Gingival Cleft: PerioPatch in Place

Gingival Cleft 1 Week
More Clinical Evidence for Novel Treatment of Inflammation with PerioPatch

Note that this represents treatment of periodontal disease without scaling and root planing; PerioPatch only (and now ADA Recognized)

Now That You’re an Expert!

The histopathological features of these conditions were quite unclear too, but at most suggested chronic non-specific ulceration with localized inflammatory cell infiltrates
Factitious Injury

This patient had self-induced lesions! There are often associated psychiatric issues. Secondary gain is also an important factor here (i.e. sympathy from family, clinicians). In this case the patient had a form of anorexia and of course could not eat when mouth was 'ulcerated'.

Factitious Injury

1) When faced with an unusual presentation of an oral ulcerative lesion you must of course rule out the other forms of mucocutaneous diseases (as well as neoplastic diseases).
2) After having done that, and presuming no response to treatment, begin to consider factitious lesions (for reference see Kotansky et al J. Perio. 66:241-245, 1995).

Factitious Injury (Rules of Thumb)

- Rule out known mucocutaneous diseases
- Gentle suggestion
- Psychiatric consultation

Similar Case…