Course 9148: “Diagnosis and Treatment of Recurrent Oral Ulcers”

Friday, April 6
9 am - 12 pm
Diagnosis and Treatment of Recurrent Oral Ulcers

If I Knew I Was Going To See This Stuff, I Would Have Studied It Harder In School

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Outline
- Recurrent aphthous stomatitis
- Human herpes virus, type I
- Mucous membrane pemphigoid
- Pemphigus vulgaris
- Lichen planus
Synopsis

- Major clinical signs and symptoms
- Diagnostic criteria and tests
- Currently accepted therapeutic modalities

References

References

References
Aphthous Ulcers

**Etiology and Epidemiology**
- Immune dysfunction
- Microbial cross-reactivity
- Nutritional deficiency
- Hormonal imbalance
- “Stress”
- Most common oral ulcer
  - 50% of adults in USA affected

**Clinical Features**
- Never preceded by vesicles
- Only affect non-keratinized mucosa
  - NOT hard palate
  - NOT attached gingiva
- Multiple clinical forms
**Minor Aphthous Ulcers**
- Most common form
- Small (<1.0 cm)
- Shallow ulcer
- Pseudomembranous covering
- Erythematous halo
- Persist for 7 – 10 days
- Heal without scarring

**Major Aphthous Ulcers**
- More severe form
- Larger (>1.0 cm)
- Deeper (into muscle)
- Persist for 2-6 weeks
- Heal with scarring

**Herpetiform Aphthous Ulcers**
- NOT due to infectious agent
- Cluster of multiple small aphthae
- Extremely painful
- Soft palate
- Alveolar mucosa
Behçet’s Syndrome
- Oral ulcers
- Ocular ulcers
- Genital ulcers

Differential Diagnosis
- Other viral infections
- Traumatic ulcers
- Pemphigus vulgaris
- Cicatricial pemphigoid
- Other systemic disease

Diagnosis
- History
  - Clinical signs and symptoms
  - Biopsy ONLY to rule out other entities
## Treatment

- OTC medications
- Immunosuppressives
- Occlusive dressings
- Chemical cautery
- Ablation
- Topical antimicrobials
- Thalidomide

## Lynch’s Law

*When in doubt, treat conservatively*

## Lynch’s Corollary

*When something works, keep using it until it doesn’t*
Lynch’s Paradox

What works for me may not work for you and vice versa

Occlusion

Chemical Cautery
Herbals and Lysine

Sodium Lauryl Sulfate
- Extracted from palm oil and coconut oil
- Anionic surfactant (detergent)
  - Makes toothpastes "foamy"
- At higher concentrations, also an effective biocide, pesticide and shark repellent (!)
- Decreases effectiveness of topical F⁻
- Triggers oral aphthae in some patients

Topical Anesthetics
Coating Agents

Non-steroidal Anti-inflammatory Agents

Corticosteroids
Cortisone

- Described in 1935
- Converted to hydrocortisone in the liver (active form)

Topical Corticosteroid Potency

- Class I (superpotent) – clobetasol
- Class II (high potency) – fluocinonide
- Class V (moderate potency) – triamcinolone
- Class VII (low potency) – hydrocortisone

Kenalog in Orabase

- Only FDA-approved topical corticosteroid for oral mucosal use
- Least potent topical corticosteroid used in dentistry
Systemic Corticosteroids

- Increased glucocorticoid activity
  - Prednisone (converted to prednisolone in the liver (active form))
  - Prednisolone
  - Methylprednisolone

Daily Cortisol Production

- 20-30 mg (equivalent to 5 - 7.5 mg prednisone)
- 50-75 mg minor stress production
- 300 mg maximum stress production

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<th>CORTICOSTEROID</th>
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Prognosis
- Excellent
- Variable recurrences

Recurrent Herpes Simplex

Etiology and Epidemiology
- Human Herpes Virus 1 (HHV-1)
- #2 most common viral disease
- Majority of individuals in USA exposed
- 50% of individuals give history of contact
- 15% asymptomatic shedders
Clinical Features

- Prodrome
  - Burning
  - Itching
  - Tingling
- Recurrences due to stress
  - Trauma
  - Emotion
  - Endocrine

Clinical Features

- Herpetiform cluster of vesicles
  - Vermilion border
  - Attached gingiva
  - Hard palate
- Infectious for 5-7 days
- Heal in 14 days

Differential Diagnosis

- Impetigo
- Recurrent aphthous ulcers
- Traumatic ulcers
- Other viral stomatitis
Diagnosis

- History
- Clinical signs and symptoms
- Serology
- Viral culture
- Tzanck test

Treatment

- Non-prescription topical antiviral drugs
  - Abreva®
- Prescription topical antiviral drugs
  - Denavir®
  - Zovirax®
- Prescription systemic antiviral drugs
  - Zovirax®
  - Famvir®
  - Valtrex®

Lysine
Topical Antivirals

Systemic Antivirals

Treatment
- OTC remedies
- Iontophoresis
- Do not use corticosteroids
Prognosis

- Excellent prognosis
- Variable recurrence pattern

Mucous Membrane Pemphigoid

Also Known As . . .

- benign mucous membrane pemphigoid (but it’s not a neoplasm)
- cicatricial pemphigoid (but oral lesions rarely scar)
- ocular pemphigus (no relationship to pemphigus)
Etiology and Epidemiology

- Auto-immune phenomenon
  - Attack basement membrane proteins
  - BP-180; epiligrin (laminin-5); other
- Middle-age
- Females >> males

Clinical Features (Skin)

- Skin lesions uncommon
- Face, neck and upper trunk
- Scalp
  - Scarring
  - Atrophy
  - Alopecia

Clinical Features (Mucosa)

- Mucosal lesions common
  - Oral
  - Ocular (symblepharon)
  - Genital
Clinical Features (Ocular)

Clinical Features (Genital)

Clinical Features (Oral)
- Pain
- Gingival erythema
- Intact blisters rare
- Scarring uncommon
- Variable Nikolsky’s sign
Differential Diagnosis
- Periodontal disease
- Pemphigus vulgaris
- Lichen planus
- Erythema multiforme
- Primary herpetic gingivostomatitis

Diagnosis
- Routine biopsy
  - Sub-basilar cleft
  - No acantholysis
  - No Tzanck cells
- Direct immunofluorescence
  - IgG and C3 at the BMZ
- Indirect immunofluorescence not useful

Treatment
- Corticosteroids
- Antimetabolites / immunosuppressants
  - Dapsone
  - Cyclophosphamide (Cytoxan®)
  - Azathioprine (Imuran®)
  - Calcineurin inhibitors (Tacrolimus®)
  - Tetracycline and niacinamide (B3)
  - Thalidomide (Thalomid®)
- Ophthalmology consult
Etiology and Epidemiology

- Auto-immune phenomenon
- Attack desmosome-tonofilament complex
- Multiple clinical forms
  - Vulgaris is the most severe
- Middle age
- No gender differences
- More common in Ashkenazic Jews
Clinical Features (Skin)
- Fragile blisters
- Wide-spread distribution
- Rupture with minimal manipulation
- Shallow ulcers

Clinical Features (Oral)
- Oral lesions precede skin disease (65%)
- Blisters and ulcers
- Stomatodynia
- Fetor oris
- Positive Nikolsky’s sign

Differential Diagnosis
- Cicatricial pemphigoid
- Primary herpetic gingivostomatitis
- Bullous lichen planus
- Erythema multiforme
- Dermatitis herpetiformis
Diagnosis

- Routine biopsy
  - Supra-basilar cleft
  - Acantholysis
  - Tzanck cells
- Direct immunofluorescence
  - Interepithelial IgG and C3
- Indirect immunofluorescence
  - Titers parallel clinical disease

Differential Diagnosis

- Cicatricial pemphigoid
- Primary herpetic gingivostomatitis
- Bullous lichen planus
- Erythema multiforme
- Dermatitis herpetiformis

Diagnosis

- Routine biopsy
  - Supra-basilar cleft
  - Acantholysis
  - Tzanck cells
- Direct immunofluorescence
  - Interepithelial IgG and C3
- Indirect immunofluorescence
  - Titers parallel clinical disease
Treatment
- Corticosteroids
- Antimetabolites / immunosuppressants
  - Azathioprine (Imuran®)
  - Cyclophosphamide (Cytoxan®)
  - Mycophenolate mofetil (CellCept®)
  - Cyclosporine (Sandimmune®)
  - Methotrexate (Trexall®)
  - Niacinamide (B3) with tetracycline
- Plasmapheresis

Prognosis
- Fair
  - High morbidity
  - <5% mortality

Lichen Planus
### Etiology
- T-cell mediated autoimmune damage to basal keratinocytes that express altered self-antigens on their surface
- Multiple potential triggers
  - Hepatitis C; HBV immunization
  - Primary biliary cirrhosis
  - Other viruses – HHV-6, HHV-7
  - Contact allergens
  - Drugs

### Epidemiology
- Middle age
- Females >> males
- Exacerbated by “stress”

### Clinical Features (Skin)
- Purple, polygonal, pruritic papules
- Peripheral Wickham’s striae
- Flexor wrists, dorsal hands, ankles, feet, thighs, glans penis
- >65% with oral lesions
Clinical Features (Nails)
- 10% of patients
- May be the only feature in children
- Lateral thinning
- Longitudinal ridging and splitting
- Onycholysis
- Red lunula
- Pterygium formation

Clinical Features (Genital)

Clinical Features (Esophagus)
Clinical Features (Oral)

- Widespread involvement
  - 75% buccal mucosa and tongue
  - 20% labial mucosa and gingiva
  - <5% palate and floor of mouth
  - <35% with skin lesions
- Multiple clinical forms
  - Reticular/plaque forms - asymptomatic
  - Erosive/atrophic/bullous forms - symptomatic

Differential Diagnosis

- Leukoplakia
- Lupus erythematosus
- Aphthous ulcers
- Pemphigus vulgaris
- Cicatricial pemphigoid
- Erythema multiforme

Diagnosis

- Biopsy is mandatory
- Routine histopathology
- Direct immunofluorescence
  - BMZ fibrinogen to rule out LE
Treatment

- No treatment for asymptomatic cases
- Corticosteroids
- Antimetabolites
- Dapsone
- Cyclosporine
- Occlusive dressings

Prognosis

- Good prognosis
- Moderate morbidity (symptomatic forms)
- Exacerbations and remissions
- (?) premalignant potential
  - <2%
  - Lichenoid dysplasia
Recurrent Oral Ulcers Post-Test

Which if the following statements regarding recurrent aphthous ulcers is incorrect?

1. Aphthous ulcers initially present as a vesicle.
2. Aphthous ulcers frequently affect the hard palate.
3. Aphthous ulcers frequently affect the attached gingiva.
4. Aphthous ulcers frequently heal with scar formation.
5. All of the above statements are incorrect.

Under normal circumstances, how is the diagnosis of recurrent aphthous ulcers made?

1. Routine biopsy
2. Direct immunofluorescence
3. Cytology
4. History, clinical signs and symptoms
5. Serologic test(s)

What is the most commonly used pharmacologic therapy for minor aphthous ulcers?

1. Topical calcineurin inhibitors
2. Topical corticosteroids
3. Injectable corticosteroids
4. Systemic corticosteroids
5. Thalidomide

Which if the following statements regarding herpetiform aphthous ulcers is incorrect?

1. Herpetiform aphthous ulcers have a viral etiology.
2. Herpetiform aphthous ulcers occur in clusters.
3. Herpetiform aphthous ulcers frequently affect the soft palate.
4. Herpetiform aphthous ulcers frequently affect the alveolar mucosa.
5. All of the above statements are incorrect.
Which of the following is not characteristic of Behçet syndrome?

1. Oral ulcers
2. Ocular ulcers
3. Genital ulcers
4. Cutaneous ulcers

Which of the following statements regarding recurrent Human Herpesvirus Type I (Herpes simplex) is incorrect?

1. Lesions are often preceded by a prodrome.
2. Intraoral lesions are limited to non-keratinized mucosa.
3. Recurrent oral Human Herpesvirus Type I lesions are indistinguishable from recurrent oral Human Herpesvirus Type II (Herpes progenitalis) lesions.
4. Occasional, otherwise uncomplicated lesions are best treated symptomatically rather than pharmacologically.

How is the diagnosis of recurrent Human Herpesvirus Type I (Herpes simplex) routinely made?

1. History, clinical signs and symptoms
2. Serology
3. Viral culture
4. Tzanck test

Which of the following statements regarding mucous membrane pemphigoid is incorrect?

1. Mucous membrane pemphigoid is an autoimmune disease.
2. Mucous membrane pemphigoid is most commonly found in middle-aged women.
3. Mucous membrane pemphigoid is characterized microscopically by a sub-basalar cleft.
4. Mucous membrane pemphigoid may also affect ocular and genital mucosa.
5. All of the above statements are correct.
Which of the following statements regarding mucous membrane pemphigoid is incorrect?

1. The immune system attacks the connections between individual epithelial cells.
2. Mucous membrane pemphigoid is more common in Ashkenazic Jews.
3. Skin lesions are common.
4. Genital lesions are called symblepharons.
5. All of the above statements are incorrect.

Which of the following is not a microscopic feature of mucous membrane pemphigoid?

1. Full-thickness separation of the epithelium from the underlying connective tissue
2. Acantholysis
3. Absence of Tzanck cells

Which of the following statements regarding pemphigus vulgaris is incorrect?

1. Pemphigus vulgaris is an autoimmune disease.
2. Oral lesions frequently precede skin lesions.
3. Patients frequently exhibit a positive Nikolsky sign.
4. Direct immunofluorescence is useful in the diagnosis of pemphigus vulgaris.
5. All of the above statements are correct.

Which of the following statements regarding pemphigus vulgaris is correct?

1. Tzanck cells are prominent in the microscopic slide.
2. Acantholysis is prominent in the microscopic slide.
3. The separation of tissue is interepithelial.
4. Indirect immunofluorescence is useful in monitoring clinical disease.
5. All of the above statements are correct.
Which of the following statements regarding lichen planus is incorrect?
1. Lichen planus is most commonly found in middle-aged women.
2. Cutaneous lesions are frequently found in patients with oral lesions.
3. A biopsy is required to definitively diagnose lichen planus.
4. Reticular lichen planus is often asymptomatic.
5. Symptomatic lesions of lichen planus are routinely treated with corticosteroids.

What is the classic lesion associated with reticular lichen planus?
1. Symblepharon
2. Wickham’s striae
3. Pseudomembranous ulcer
4. Alopecia

In addition to skin and oral involvement, what other anatomic sites can be involved in patients with lichen planus?
1. Nails
2. Genital mucosa
3. Esophageal mucosa
4. All of the above can be involved in patients with lichen planus.

Which of the following diseases may be confused with lichen planus both clinically and microscopically?
1. Mucous membrane pemphigoid
2. Pemphigus vulgaris
3. Lupus erythematosus
4. Erythema multiforme