Management of Oral Soft Tissue Conditions and the Use of Medications

29 August 2017

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Objectives

• Differential diagnosis of soft tissue conditions
• Describe more common soft tissue conditions
• Diagnosis of soft tissue conditions
• Management strategies of mucosal lesions
  • Treatment
  • Prevention
Differential Diagnosis-NIRDS

• Neoplastic
• Infectious
• Reactive
• Developmental
• Systemic
NEOPLASTIC
Leukoplakia- White

- Clinical diagnosis only
- Histologically: hyperplasia, mild, moderate, or severe dysplasia, carcinoma in-situ, invasive carcinoma
- Thin leukoplakia: seldom malignant change
- Thick leukoplakia: 1-7% malignant change
- Granular or verruciform: 4-15% malignant change
- Erythroleukoplakia: 28% malignant change
Neoplastic: Red Lesions

• SCCA
Diagnosis: Incisional vs. Excisional Biopsies
Dysplasia Management – Medical

- Systematic Review: 9 studies met criteria for low bias in prior review
- Three studies were reviewed based adequate study quality.
  - topical bleomycin
  - systemic retinoids
  - systemic lycopene
- No therapeutic recommendations for bleomycin and cis-retinoic acid
- Lycopene (4 and 8 mg) may have some efficacy in patients with risk factors similar to those found in a subcontinental Indian population, for the short-term resolution of oral epithelial dysplasia
Dysplasia Management – Surgical

• Lack RCTs that would allow to assess the effectiveness of surgical treatment, including lasers
• In non-RCTs the effectiveness of various surgical modalities in preventing malignant transformation of oral dysplasia have resulted in contradictory outcomes
INFECTIOUS
Candidiasis

- Pseudomembranous
- Erythematous
- Hyperplastic
- Angular cheilitis
Soft tissue diagnostic tests

• Fungal
  • Superficial:
    • Smear $\rightarrow$ potassium hydroxide or stained with PAS $\rightarrow$ hyphae
    • Culture
  • Deep fungal: $\rightarrow$ Biopsy
Treatment - Fungal

• Topical
  • 10 mg clotrimazole troches 5x/d for 7-10 days
  • Nystatin rinse- 100,000U/mL swish and spit 5mL 4x/d for 2 weeks
  • Chlorhexidine rinse 10 mL bid
  • Probiotics (reduced oral candida in elderly population- RCT J Dent Res x2)
  • Nystatin/triamcinolone cream- dab on corners of mouth 4x/d
  • Clotrimazole-betamethasone dipropionate (Lotrisone) cream
  • Miconazole (Monistat 7) nitrate vaginal cream 2%
  • Nystatin ointment (thin layer on denture) tid
Treatment - Fungal

- Systemic
  - Fluconazole
    - 200 mg day 1 followed by 100 mg/d 1-2 weeks
  - Ketoconazole
    - 200 mg/day for 14 days

- Both are potent inhibitors of cytochrome P-450: Check Pharmacology Reference-Drugs.com: 149 major drug interactions-Warfarin, Xanax, Lipitor, Plavix, hydrocodone...
Infectious: Red Lesions

• Fungal
  • Erythematous candidiasis
  • Immunocompromised
  • Histoplasmosis, Coccidioidomycosis, Blastomycosis, Cryptococcus (Solitary painful ulceration of tongue, palate, buccal mucosa)
  • Aspergillosis (sinus, after tooth extraction or endodontic treatment)
  • Mucormycosis (Maxillary sinus infection, swelling of alveolar process and/or palate)
    • Extensive tissue destruction due to preference for small blood vessels: infarction and necrosis disrupts blood flow
Infectious: Red Lesions

• Viral HSV
  • HSV-1 vs. HSV-2
  • Children: Acute herpetic gingivostomatitis—both moveable and attached mucosa
  • Adults: Pharyngotonsillitis—vesicles tonsils and posterior pharynx. Oral mucosa anterior to Waldeyer’s ring <10% of cases.
  • Most common recurrent site: lip (herpes labialis)
Soft tissue diagnostic tests

• Viral
  • Culture → 2-4 days for + ID
  • Cytology → Virally damaged epithelial cells
  • Serology → Rising titre of antibody
  • DNA in situ hybridization for specific virus identification

• Bacterial
  • Aerobic and anaerobic culture
Infectious: Red Lesions

• Viral VZV
  • Primary infection: chickenpox (oral lesion: palate and buccal mucosa most frequently involved: vesicles.
  • Recurrence: Herpes Zoster
    • 10-20% of older population.
    • One dermatome affected
    • Prodromal pain, fever, malaise 1-4 days before cutaneous/oral lesions.
Treatment - Viral

• Observe/supportive care
  • Immunocompetent patient
  • Maintain hydration and nutrition

• Topical
  • MBX- care with lidocaine (esp. children and elderly)
  • Aquaoral with SPF
  • Penciclovir (Denavir) cream 1%
  • Docosanol (Abreva)
Treatment - Viral

• Systemic
  • Acyclovir caps 200 mg: 2 caps 3x/day for 7 days
  • Valacyclovir 500 mg: 1 g 2x/day for 7-10 days (initial episode)
  • Valacyclovir 500 mg: 4 caps when prodromal symptoms start
  • Valacyclovir 500 mg: 1 cap 2x/day for 3 days
Prevention - Viral

• Systemic
  • Acyclovir caps 200 mg: 2 caps 2x/day
  • Valacyclovir 500 mg: 1 cap daily
REACTIVE
Reactive-White
Reactive lesions

- Focal (frictional) hyperkeratosis
  - Response to low-grade irritation (sharp edge)
  - Buccal mucosa along occlusal line
  - No dysplastic changes
Reactive lesions

• Tobacco pouch keratosis
  • Muccobuccal fold, granular to wrinkled appearance
  • Gingival, periodontal destruction possible
  • 15% chewing tobacco, 60% snuff users
  • Malignant potential

• Nicotine stomatitis
  • Palatal mucosa: elevated papules with red centers are inflammed minor ducts
  • Not pre-malignant. May revert when discontinues smoking
Reactive-Red
Reactive: Red Lesion

• Aphthae
  • Unknown etiology, incidence 20-60%
  • 3 Clinical forms (minor, major, herpetiform)
  • Non-keratinized mucosa
  • Diagnosis by elimination
  • Rule out allergies, hematologic abnormalities, infectious agents, nutritional imbalances, trauma, stress.
Management/prevention of RAS

- Clobetasol (0.05% gel) on lesion immediately when first symptoms occur
- Chlorhexidine start 1-2x/day for 2 weeks and decrease to every other day or every 3rd day
- Vitamin B12 supplement
- Alteration of diet?
Topical steroid by strength

- **Ultrapotent**
  - Clobetasol 0.05%
  - Halobetasol 0.05%

- **Potent**
  - Dexamethasone 0.5 mg/5 mL
  - Fluocinonide 0.05%

- **Intermediate**: Triamcinolone acetonide (Kenalog) 0.1%

- **Low**: Hydrocortisone 1%

- Gel, Ointment, Cream, Compounded
Topical Steroids

- "for external use only"
- High cost
- Atrophy of mucosa
- Fungal side effects...
Topical Steroids and Fungal Infection: Study Objectives

• **Primary**
  Determine the incidence of oral candidiasis in patients treated with topical steroids for oral lichen planus (OLP)

• **Secondary**
  Determine if different antifungal therapies are more effective than others in preventing the development of clinical fungal infections

Methods

Multicenter, retrospective chart review of a well-characterized group of Lichen Planus patients

• Carolinas Medical Center (CMC)
• University of Florida College of Dentistry (UF)
• University of Texas Health Science Center at San Antonio (UTHSCSA)
• Georgia Regents University College of Dental Medicine (GRU)
Methods

Inclusion Criteria

• Patients diagnosed with clinical oral lichen planus.

• Patients at CMC, UF, UTHSCSA, and GRU

• Patients treated for lichen planus with topical steroids for at least 2 weeks AND a follow-up visit within 5 weeks of the initiation of daily topical steroids.
Methods

Treatment regimen for oral lichen planus

• Topical Steroid Used: Y/N
• Generic name and % of topical steroid
• Systemic Steroid Used: Y/N
• Antifungal Preventive Therapy Used: Y/N
• Generic name and % (if applicable) of antifungal therapy
Methods

Follow-up Data

• Clinical appearance:
  • Improved/Worsening/No change
• Clinical symptoms (burning/pain):
  • Improved/Worsening/No change
• Oral Fungal Infection? Y/N
  • If yes, describe appearance
• Treatment of oral fungal infection
Results

Topical steroids were used in 303 (96.2%) patients.

Systemic steroids were used in 12 (3.8%).

Topical Steroids
- Clobetasol gel
- Dexamethasone rinse
- Fluocinonide gel
- Lotrisone®
Results

• Objective improvement
  • Clobetasol
    • 91.1% with clobetasol
    • 81.5% without clobetasol (p=0.02)
  • Use of any preventive antifungal
    • 90.6% with antifungal
    • 80.5% without antifungal (p=0.02)

• Subjective improvement
  • Clotrimazole
    • 94.3% with clotrimazole
    • 85.4% without clotrimazole (p=0.04)
Results

• Oral fungal infections at follow-up
  • Total: 43 (13.7%) patients

• No significant difference between sites (p=0.36).
  • CMC - 24/155 (15.5%)
  • UF - 11/67 (16.4%)
  • UTHSCSA - 6/59 (10.2%)
  • GRU - 2/34 (5.9%)
Results

• **Fungal infections at follow-up, by steroid treatment**
  - Clobetasol - 32/183 (17.5%), (p=0.02)
  - Dexamethasone - 11/98 (11.2%), (p=0.39)
  - Fluocinonide - 1/22 (4.6%), (p=0.33)
  - Lotrisone® - 4/20 (20%), (p=0.50)

• Preventive antimycotic agents were used in 203 patients and no antimycotic in 111, with fungal infections occurring in 29 (14.3%) and 14 (12.6%), respectively.
Results

• Salivary flow testing was completed in 51 patients of which 10 developed OFI.
  
• Low stimulated salivary flow group (≤ 0.7 ml/min)
  • 9 (90%) OFI patients

• High stimulated salivary flow (>0.7 ml/min)
  • 1 (10%) OFI patient

• No difference in unstimulated flow
Conclusions

• The incidence of oral fungal infections in OLP patients following steroid therapy was higher than anticipated (13.7%).
• Clobetasol had a significantly higher incidence of fungal infection compared to all other steroid therapies.
• Low saliva is a major risk factor for a fungal infection
Reactive: Red Lesion

- Allergic reaction to systemic drugs
  - Erythema multiforme
  - Lichenoid
  - Lupus erythematosus-like eruptions
  - Pemphigus-like lesions
Reactive: Red Lesion

• Erythema Multiforme
  • Immunologically mediated
  • 50% of cases preceding infection or exposure to drug
  • Oral: erythematous patches that develop shallow erosions and ulcerations.
  • Target skin lesions in 50% of cases
  • More severe: erythema multiforme major (Stevens-Johnson syndrome) and Toxic Epidermal Necrolysis (Drug involved)
Management – Erythema Multiforme

• Prednisone start of lesions

• Preventive:
  • Acyclovir 400 mg 2x/day
  • Valacyclovir 500-1000 mg /day
DEVELOPMENTAL-White
Hereditary conditions

• Leukoedema
  • Natural variant. Asymptomatic, symmetric gray-white, filmy or milky surface
  • Stretching removes clinical appearance
  • More frequent in African Americans
Fordyce granules

• Sebaceous glands that occur on the oral mucosa. Normal variant
• Found in up to 80% of the population
• Multiple yellowish-white papular lesions.
• Most common buccal mucosa.
Developmental: Red Lesion

• Benign Migratory Glossitis (Geographic Tongue)
  • Red Lesion with white border
  • Usually asymptomatic
  • Moves
• Diagnosis
  • Elimination
  • Rule out fungal etiology of symptoms
Management of Benign Migratory Glossitis

• Topical Steroids
• Antifungals
• Rule out hematinic deficiencies
SYSTEMIC
Lichen Planus

• The reported prevalence rates of oral lichen planus (OLP) vary from 0.5% to 2.2% of the population
• Often develops between 30-60 years, and it is more frequently seen in women
• Intra-oral: Reticular, plaque-like, erosive, bullous forms, desquamative
• Extra-oral: PPPP: purple, polygonal, pruritic papules- Flexural surfaces, scalp, nails, genitals
• Etiology unknown
• Lichenoid reactions (drugs, amalgam, gold)
Treatment for symptomatic OLP- systematic review

- Topical corticosteroids (+/- topical anti-mycotics) are the first-line treatment for localized lesions
- Insufficient evidence regarding different dosages, formulations or modes of delivery of topical steroids (eg. paste, spray, mouthwash) to make an evidence based recommendation about which is best
- Systemic corticosteroids (+/- topical anti-mycotics) are the first-line treatment only for severe, wide-spread OLP and for lichen planus involving other muco-cutaneous sites (eg.: vaginal/vulval LP) recalcitrant /resistant to topical therapies
- Topical retinoids should be considered only as second line therapy for OLP; systemic retinoids are not recommended
- Topical calcineurin-inhibitors should be considered only as second-line therapy.
Management – Lichen Planus

• Topical steroids
  • Up to 2 weeks followed by 1 week break: repeat if needed
  • Concern of atrophy of mucosa and adrenal suppression with long-term use

• Optimize oral care

• Chlorhexidine with poor plaque control

• Tacrolimus (protopic) 0.1% ointment
  • No a steroid
  • BUT- black box warning
LP malignant transformation

• The alleged annual malignant transformation rate for OLP is between 0.2% and 0.5%
• 10-50X increased risk of SCCA
• 2-4 /100 patients over 10 year follow up
• Patients should be encouraged to avoid or discontinue habits such as excessive tobacco and alcohol use, that are likely to increase the risk of malignant transformation
• Long-term monitoring may be problematic as this is resource intensive. At a minimum, annual monitoring of OLP is recommended
Oral Lichenoid Reactions

• Oral lichenoid contact lesions (OLCL’s) are seen in direct topographic relationship to an offending agent
• This reaction is most often attributable to dental restorative materials, most commonly amalgam
• With the removal and replacement of the putative causative material, the majority of such OLCL’s resolve within several months
• Patch testing?
Lupus

- Oral lesions approximately 25% of SLE.
- May appear lichenoid, ulcerative or granulomatous. May have more erosive quality.
Pemphigus

• Autoantibodies to desmosomes
• 50% have oral mucosal lesions prior to mucocutaneous lesions. Eventually all have intra-oral lesions.
• Prior to corticosteroids, 60-80% mortality
Pemphigoid

- Autoantibodies to basement membrane
- Average age 60
- Oral lesions most patients. Begin as vesicles or bullae. Painful and persistent if untreated.
- Ocular lesions in 25% of pemphigoid patients with oral lesions
Management - Pemphigoid

- Avoid hard/sharp foods
- Optimal plaque control
- Chlorhexidine
- Topical steroids
- Doxycycline 100 mg daily long-term
- Refractory: dapsone, prednisone
Gingival Differential

- Desquamative Gingivitis
  - Erosive LP (71%)
  - Pemphigoid (14%)
  - Pemphigus (13%)
  - Linear IgA Disease
  - Epidermolysis Bullosa Acquisita
  - Plasma Cell Gingivitis

- Mass on Gingiva (4 Ps)
  - Pyogenic Granuloma
  - Peripheral Ossifying Fibroma
  - Peripheral Giant Cell Granuloma
  - Parulis
White Lesions

Does lesion rub away?

Yes

Infections Etiology
- Pseudomembranous candidiasis
- Secondary syphilis
- Diphtheria

Reactive Etiology
- Thermal or chemical burn
- Allergy
- Mechanical trauma

No

Keratosis
- Hereditary
- Frictional
- Smoker’s

Lichen Planus/ Lichenoid Reaction

Lupus Erythematosus

Infections etiology
- Hairy leukoplakia
- Fungal

Dysplastic Tissue changes
- Mild, moderate, severe dysplasia
- Carcinoma in situ
- Squamous cell carcinoma

Does lesion rub away?

No
Erythematous Lesions

Generalized?

Yes

Dermatoses
- erosive lichen planus
- pemphigoid
- pemphigus
- epidermolysis bullosa acquista
- psoriasis

Nutritional Deficiency
- ferritin
- folate
- vitamin B12

Fungal Etiology

No

Center of tongue: Median rhomboid glossitis Glossitis

Palate:
- Denture stomatitis
- Fungal

Bilateral corners of mouth:
- Angular cheilitis
- Fungal; candidosis
- Staph or strep
- Hematogenic deficiency
- Oral Crohn’s disease
- Immuno compromised state (e.g. Diabetes, HIV)

Gingival:
- Plaque-associated gingivitis
- Dermatosis
- Allergy (plasma cell gingivitis)

Dysplastic Tissue changes (solitary lesion)
- Mild, moderate, severe dysplasia
- Carcinoma in situ
- Squamous cell carcinoma

Generalized?
Management of Oral Lesions

- Acute lesions (i.e. < 2 weeks)
- Chronic lesions (> 2 weeks)
- Long term follow-up of chronic oral lesions
- Transformation of oral lesions to oral cancer
Management of Acute Lesions

• New onset lesions
• CHLORIDE
• Head and neck examination
• Evaluate for etiologic factors
  • Social habit
  • Change in medication or oral care product
  • Parafunctional habits
  • Trauma- sharp areas
• NIRDS
Management of Acute Lesions

• Eliminate potential etiologic factors
• Treat with antifungals if on differential
  • Chlorhexidine 2x/day for 2 weeks
  • Clotrimazole troches 10 mg 5x/d for 7-10 days
  • Nystatin/triamcinolone cream dab corners of mouth 4x/d
  • Probiotic yogurt
  • Fluconazole 200 mg day 1 followed by 100 mg/d one week
  • Nystatin ointment (thin layer on denture) tid
• Return for reassessment in 2 weeks
• Consider incisional biopsy for definitive diagnosis
Questions?

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