140TH ANNUAL MEETING
MAY 6 – MAY 7, 2010

JEWEL OF THE GREAT LAKES

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FRIDAY, MAY 7, 2010
9:00 A.M. TO 12:00 NOON

ORAL CANCER AND RELATED PREMALIGNANCY
Oral Cancer and Premalignancy

Contemporary Diagnosis, Treatment and Management

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Outline

- Leukoplakia

  - Screening and diagnostic methods

  - Squamous cell carcinoma

  - Management of treatment complications
Synopsis

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

References

Leukoplakia
Leukoplakia

- White patch or plaque that cannot be removed or characterized clinically or pathologically as any other disease
- Exclusively clinical definition

Etiology

- Tobacco
- Alcohol
- Ultraviolet radiation (lower lip)
- Trauma
- Microorganisms
  - T. pallidum, C. albicans, HPV
- Idiopathic

Epidemiology

- Most common oral lesion
  - 3% of adults
- Middle-aged and older adults
  - 8% of men over 70
- More common in males (3:1)
Epidemiology

- Dysplasia found in 5-25% of leukoplakias
- Malignant transformation in 4-50% of leukoplakias
  - Average 4%

Clinical Features

- 70% involve lips, tongue or gingiva
- Multiple clinical forms
  - Thin
  - Thick
  - Nodular
  - Proliferative verrucous

Actinic Cheilitis

- Due to UV radiation of the lower lip
- Usually fair-skinned, older adults
- Usually males (10X)
- Atrophy, scaling and ulceration
- Biopsy advisable (5-10% malignant)
- Treated surgically
- Excellent prognosis
Tobacco-associated Leukoplakia

- Due to tobacco “tars”
- Usually involve tongue and FOM
- Asymptomatic, well-circumscribed plaque
- Biopsy essential
- Treatment varies (monitoring – excision)
- Fair prognosis

Family Smoking Prevention and Tobacco Control Act of 2009

- June 22, 2009
- Allows FDA regulation of tobacco products
- Establishes Center for Tobacco Products
  - Funded by user fees
  - $235M in 2010; $712M by 2020
  - Regulates tobacco products to protect the health of the public

Center for Tobacco Products

- Require ALL ingredients, compounds and additives be reported
- Harmful products may be banned
- Nicotine may be regulated
- Flavorings are banned (except menthol)
- All new tobacco products must get FDA approval
Center for Tobacco Products

- Regulate modified risk tobacco products
- "light", "low", or "mild" terms not permitted unless risk reduction is verified
- Warning labels more graphic and in color
- Tobacco companies may not sponsor sporting events

Family Smoking Prevention and Tobacco Control Act of 2009

- Allows stricter state and local government regulation
- Reinstates 1996 Tobacco Rule
  - Restricted advertising
  - No outdoor advertising with 1000 feet of a school

Family Smoking Prevention and Tobacco Control Act of 2009

- Why is this important?
- 435,000 American die annually from tobacco-related illnesses
- Tobacco-associated health care expenditures are $96 billion annually
Erythroplakia

- Due to the loss of ability to make keratin
- 50% malignant transformation (highest)
- Asymptomatic red, velvety patch, often with leukoplakia (speckled leukoplakia)
- Biopsy essential
- Treatment varies (monitoring – excision)
- Fair prognosis

Differential Diagnosis

A list, in decreasing order of probability, of the diseases or conditions that are consistent with the patient’s clinical signs and symptoms

- Morsicatio buccarum
- Leukoedema
- Lichen planus
- Genodermatosis
Diagnostic Methods

Screening and Diagnosis
- History
- Clinical signs and symptoms
- Vital dye (toluidine blue)
- ViziLite® / ViziLite® Plus with TBlue630
- VELscope
- Identafl
- Exfoliative cytology
- Brush biopsy
- Punch /scalpel biopsy

Variations on a Theme
- Microlux™
- OraScoptic™
Oral Cancer Detection
- 80% survival with localized disease
- 20% survival with distant metastasis

**EARLY DETECTION = BETTER SURVIVAL**
- 50% with metastasis at diagnosis
- 65% with clinical symptoms at diagnosis

Visual Clinical Examination
- High sensitivity
  - detect abnormality with ease
- Low specificity
  - diagnose abnormality with difficulty

Problem
- 15% of patients have mucosal abnormality (Bouquot, 1986)
- 25% of malignant lesions appear benign (Sandler, 1962, 1966)
- 30% of soft tissue lesions are misdiagnosed (Dimitroulis, 1992)
Problem

- Unsure which lesions require testing
- Uncomfortable performing scalpel biopsy
- Patients resist incisional biopsy
- **NOT ALL LEUKOPLAKIAS BIOPSIED**

Leukoplakia / Erythroplakia

- Affect 3% of population
- 4-40% malignant transformation
- Only 25% biopsied
- **ALL LEUKO/ERYTHROPLAKIAS SHOULD BE EVALUATED**

General Dental Practice

- 5-10% with benign-appearing oral lesion
  - 95-98% are truly benign
- Can't biopsy 10% of population to detect <1% of clinically false benign lesions
- **CLINICAL INSPECTION ALONE CANNOT ADEQUATELY DETECT ORAL CANCER**
Sandler (JADA, 1966)

- 118,000 VA patients
- 2,758 with visible mouth lesions
- 592 had cytology and biopsy

- 70 of 287 SCC THOUGHT BENIGN
- 20 of 28 CIS THOUGHT BENIGN
- 11 of 1,801 (-) cytologies BECAME MALIGNANT

Diagnostic Goal

- Decrease false negative clinical findings

- Develop non-intimidating technique
  - practitioners
  - patients

Traditional Cytology

- 300,000 - 500,000 cells per smear
- Less than 0.005% abnormal cells
- Searching for a “needle in a haystack”
- People are not good searchers (proof reading)
Traditional Cytology

- Psychological habituation
  - eye sees abnormality
  - brain imposes expected pattern

- Sensitivity below threshold
  - don't detect abnormal cells

Oral Cytology

- Bigger “haystack”
  - more rapid cell turnover
  - more normal cells; bigger dilution

- Fewer “needles”
  - keratinization
  - decreased availability of abnormal cells

Folsom (Oral Surgery, 1972)

- 158,996 patients screened over 3 years
- 6,897 (4%) had oral lesions
- 148 cancers (2%) among oral lesions
- 41/148 (31%) FALSE NEGATIVE CYTOLOGY
Oral Brush Biopsy

Oral CDx™

- Effective
- Easy to use
- Bridges the gap between visual exam and incisional biopsy
- Helps to determine which lesions merit an incisional biopsy
- ADA Seal of Acceptance

Oral CDx™

- Optimal sample – full transepithelial sampling
- Optimal search – adaptive, non-algorithmic computing
- Optimal interpretation – oral cytology specialists
Clinical Technique

- May be done by RDH in many states
- No anesthesia necessary
- Identify area to be sampled
- Rotate end/side of brush 5-10 times

Clinical Technique

- Rotate brush on slide to transfer cells
- Apply fixative quickly
- Submit specimen and completed form

Laboratory Technique

- Computer scans slide (400 billion / second)
  - Optimized for Papanicolaou-stained oral mucosal cells
  - Looks for several dozen "needles" in "haystack" of 500,000 cells
  - Identifies 200 most atypical cells
Laboratory Technique

- Integrated analysis
  - computer DOES NOT replace pathologist

- Pathologist scans slide
  - selects 20 representative atypical cells
  - signs out case

Treatment

- Nothing
- Periodic follow-up
- Excision
- Laser ablation
- Electrosurgery
- Chemotherapy (retinoids)

Prognosis

- Good
- 4% average life-time risk of malignancy
- Malignancies arise 2-4 years later
- Dysplastic lesions more likely to become malignant (10-30%)
- Nodular (10%) and thick (5%) lesions more likely to become malignant
Oral Cancer

Etiology

- Intrinsic factors
  - Nutrition
  - Anemia
  - Immunosuppression
  - Oncogenes

- Extrinsic factors
  - Tobacco
  - Alcohol
  - Tobacco AND alcohol (40x risk)
  - Ultraviolet radiation
  - Microbes
Epidemiology
- 3% of all cancers (#6 - males; #12 - females)
- Increasing incidence begins in middle age
  - 8 per 100K overall; 30 per 100K after age 75
- 35% associated with pre-existing leukoplakia
- 31,000 new cases annually
- 8,500 deaths annually

Clinical Features
- 90% of cases
  - lower lip
  - ventral tongue
  - floor of mouth
- Most cases present for at least 1 year as an asymptomatic lesion

Clinical Features
- Leukoplakic (white)
- Endophytic (ulcerating)
- Exophytic (fungating)
- Erythroplakic (red)
Differential Diagnosis

- Frictional hyperkeratosis
- Lichen planus
- Traumatic ulcer
- Erythematous candidiasis

Screening and Diagnosis

- History
- Clinical signs and symptoms
- HPV screening
- Scalpel biopsy
- Punch biopsy

Treatment

- Surgery
- Radiation therapy
- Combination therapy
- Periodic reassessment
Prognosis
- Depends on location and progression
- More anterior location
- No regional lymph node involvement
- No distant metastasis

Grading
- Assessment of biologic behavior based on microscopic features of pleomorphism, cellular maturation, keratin production, etc.
- Grade I – well-differentiated
- Grade II – moderately well-differentiated
- Grade III – moderately differentiated
- Grade IV – poorly differentiated

Staging
- Assessment of survival based on a combination of factors
  - tumor size (T)
  - regional lymph node involvement (N)
  - distant metastasis (M)
- TNM system
TNM Staging

- TX – not assessed
- T0 – no evidence of tumor
- Tis – carcinoma in situ
- T1 – <2 cm
- T2 – 2-4 cm
- T3 – >4 cm
- T4 – invading adjacent structures

TNM Staging

- NX – not assessed
- N0 – no nodal involvement
- N1 – single, ipsilateral node, <3 cm
- N2 – nodal metastasis, 3-6 cm
- N2a – single, ipsilateral node, 3-6 cm
- N2b – multiple ipsilateral nodes, <6 cm
- N2c – bilateral or contralateral nodes, <6 cm
- N3 – nodal metastasis, >6 cm

TNM Staging

- MX – not assessed
- M0 – no distant metastasis
- M1 – distant metastasis
TNM Staging

<table>
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<th>TNM</th>
<th>STAGE</th>
<th>5 YEAR SURVIVAL</th>
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<tr>
<td>T1N0M0</td>
<td>Stage I</td>
<td>85%</td>
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<td>T2N0M0</td>
<td>Stage II</td>
<td>66%</td>
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<td>T3N0M0</td>
<td>Stage III</td>
<td>41%</td>
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<td>Any T4</td>
<td>Stage IV</td>
<td>9%</td>
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<td>Any N2-3</td>
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<td>Any M1</td>
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Management of Treatment Complications

Radiation Therapy

- Maximum treatment to tumor limited by unavoidable damage to normal tissue
- Damage directly proportional to volume of tissue irradiated and total radiation dose
- Damage inversely proportional to number of fractions given and total dosage time
Radiation Changes

- Radiation dermatitis
- Acute mucositis
- Osteoradionecrosis
- Xerostomia
- Loss of taste

Radiation Dermatitis

- Erythema
- Tanning
- Transient hair loss

Acute Mucositis

- Radiation dose outpaces regenerative ability of normal mucosa
  - 180 cGy(rad) per day, 5 days per week
- Appear 14 days following initiation of therapy
- May require interruption of therapy
Acute Mucositis
- Topical anesthetics
- Systemic analgesics (usually narcotic)
- Antimicrobial (usually antifungal) therapy
- Systemic anti-inflammatory therapy

Osteoradionecrosis
- Higher risk in dentate patient
- Higher risk with post-therapy extraction
- Mandible >> maxilla
- Late complication (> 1 year post tx)
- Irreversible bone changes
- Focal sequestration progress to necrosis
- Intense pain
- Potential jaw fracture

Osteoradionecrosis
- Pre-therapy extraction of questionable teeth
- Antibiotics
- Hyperbaric oxygen
- Vascularized flaps
- Resection
Xerostomia
- Serous acini more sensitive
- Residual saliva, when present, is mucous
- Usually regenerates to some degree
  - May take up to 12 months

Variable therapy
- Water
- Artificial saliva
- Sialogogues
- Pilocarpine, cevimeline, bethanechol

Candidiasis
- Related to xerostomia
- Pseudomembranous or erythematous
- Better results with systemic therapy
  - Topical rinses ineffective
  - Difficulty in dissolving troches / tablets
  - Lidocaine viscous
  - Systemic analgesics
  - Salivary stimulants or replacement
Loss of Taste

- Hypogeusia (partial loss of taste)
- Ageusia (complete loss of taste)
- Dysgeusia (altered taste)
- Usually regenerate within 4 months
- Zinc supplements (100 mg/day) helpful

Dental Treatment Planning

- Anticipated bone dose
- Pre-therapy dental status
- Extraction techniques (primary closure)
- Extraction healing time before radiation (minimum 7-10 days)
- Patient compliance and motivation