The Dorsal Tongue
Cancer and Other Maladies

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The Basics
Form and Structure

• The tongue surface
  • Filiform papillae
  • Fungiform papillae
  • Vallate papillae
  • Foliate papillae
Papilla Types

Filiform  Fungiform  Circumvallate
Filiform Papillae

H: hair-like
S: skin-like
LM: lining mucosa-like
Filiform Papillae

Anterior compartment
• Hair-like pattern of keratin differentiation
  • Keratin expression: K 4, 6, 13, 16 & KHG proteins

Posterior compartment
• Skin-like keratin differentiation pattern 1, 10

Intervening area / between compartments
• Resembles lining / buccal mucosa
Filiform Papillae

Functions

• Help stabilize the food bolus during mastication and swallowing
• Offer cleansing action on mucosa and tooth surfaces
• In animals for grooming
Filiform Papillae

Further Characteristics

• Epithelial cells contain keratin-bundling proteins
  • Filaggrins
    • Co-localize with trichohyalin protein
    • Crucial in the keratinization process

• Nerve supply
  • Three types of nerve endings
    • Free unmyelinated—extend to subepithelial CT
    • Epithelial nerve endings—near BMZ or within basal / suprabasal cells
    • Complex nerve endings—lamellar corpuscles: sensory mechanoreceptors
      • Spatial perception: magnified by a factor of 1:6
Foliate Papillae

- At posterolateral location
- Deeply folded mucosa
- Cornified surface
- Lymphoid stroma deep to surface
- Numerous taste buds along lateral walls early in life
  - Atrophy later in life
Fungiform Papillae

- Contain terminal epithelial differentiation products
  - K1 / K10 keratins
  - Filaggrin
- Richly innervated/well vascularized
- Concentrated in anterior 2/3
- Most with taste buds in apical epithelium
Circumvallate Papillae

- 2.5 mm wide-1.0 mm deep
- Richly innervated and vascularized
- Each papilla is trenched
  - flushed by von Ebner glands
    - Up to 35 ducts rim the base of each papilla
- Lateral surfaces w/ hundreds of taste buds
The Taste Bud
A Bioengineering Marvel
Taste Bud Facts

- Number: about 2,000 in man
- Distributed over non-keratinized surfaces
  - 50% in circumvallate papillae
  - Balance in foliate and fungiform papillae, also over the soft palate and laryngeal surface of the epiglottis
- Contain 5 types of cells
  - I: “dark” cells; contain GAG granules into taste chamber (TC); support types II and III cells
  - II: at apical plasmalemma with microvilli extending into TC; stereochemical activation generates signal along nerve endings
Taste Bud Facts

- **III:** contain “densities” and synaptic vesicles
  - vesicles contact nerve endings
  - Similar to type II cells
- **IV:** small basal cells
  - Differentiate into other taste bud cells
- **V:** perigemmal cells
  - At taste bud periphery
  - Contain perigemmal nerve endings
The Lingual Follicle

- In aggregate form the lingual tonsil
- Are small lymphoepithelial organs
- Contain mucous glands opening into crypts (Cr)
- Lining is non-keratinizing
Diseases and Conditions
Diseases of the Tongue.

By

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Intemperance
Dental Indentations
Idiopathic Excoriations
Chronic Ulcer
Dental Trauma
TB
Lupus
Ruptured Gumma
Mucous Patch
Gummatous Ulcer
Leucoma
Ulcerated Leucoma
Leucoma w/ Warty Growth
Wandering Rash
Mucous Patches
Mucous Patches
Tertiary Syphilis
Degenerated Nevus
Carcinoma
Protuberant Carcinoma
Cancerous Growth in a Leucoma
Ulcerated Carcinoma
• Systemic illness location / dorsum of tongue correlation
Tongue in Diagnosis

Traditional Chinese Medicine

• Parameters
  • Color
  • Size
  • Shape
  • Mobility
  • Symmetry

• Reflects state of the body
Tongue Coating
Traditional Chinese Medicine

• A by-product of digestion
  • Reflects quality of digestion
  • Ideally thin, white to slightly yellow
  • Cannot be easily removed

• Loose or detached coating
  • Indicates weak energy, cold in the body
    • Affects spleen and stomach energy first, later the kidneys

Ideal

intensely white
yellow
grey
black
Color of the Tongue

Healthy: Light pink

- Very white: cold exposure
- Yellow: stomach, gall bladder, liver
- Blue: urinary bladder, kidneys
- Green: liver, gall bladder
- Purple: liver, pericardium (alcoholism)
- Grey/black: heart / kidneys
- Red/deep red: exhausted organic fluids, excessive heat exposure
Pathology

Dorsum of the Tongue
Oral Lichen Planus
Lichen Planus
Pathogenesis

Antigenic stimulation → cytokines released from keratinocytes, Langerhans cells, resident pmn’s → ICAM-1 upregulation → binding of lymphocyte integrins → lymphocyte adherence to basal keratinocytes with subsequent trans epithelial trafficking
Apoptosis Mechanisms

- TNF-α
- Granzyme B
- Caspase Cascade
- Apoptosis

- TCR
- Ag
- MHC1
- FAS-L
- FAS
- TNF-αR
OLP
Malignant Transformation

0.4 to 5.6 % of cases

The 800 pound gorilla: is chronic inflammation acting as a transformation factor ???

Lichen Planus
Neoplastic Considerations

Chronic stimulation from epithelial and stromal cells cytokine-based signaling allowing:

• Deranged epithelial cell growth control
• Altered cell cycle control
  • Caspase 3 apoptotic pathway activation
  • Simultaneous increased epithelial proliferation
• Genotoxic stress replication errors
  • p53 elevation initially followed by selective inactivation
Lichen Planus
Neoplastic Considerations

• NF-κβ and IL-1a, IL-6, IL-8, TNF-α
  • Increased levels demonstrated in saliva
  • NF-κβ: inhibits apoptosis, promotes cellular proliferation; higher in OLP vs CLP
  • Cytokines plus TNF may result in promotion of senescence-related growth arrest

• DDR pathway activation (CD 167a)
  • TK activity receptor signaling pathway
Lichen Planus
Neoplastic Considerations

Similarities between OLP-associated SCCa and IBD, colorectal carcinoma, Barrett’s esophagitis:

• Possible relation to NF-κβ activation of neuronal axon guidance molecule netrin-1 and its receptors

OLP
The Role of Inflammation

• Inflammasome participation in OLP ???
  • A multiprotein complex
    • Orchestrates innate and adaptive immune responses
    • A link established between colorectal inflammation-induced cancer and the inflammasome
      • The role of caspase-1 and NLRC4

• Complex

Amyloidosis
Amyloidosis

Facts

• Most cases related to plasma cell dyscrasias
  • Amyloid protein composed of Ig light chains (AA)
• May be nodular or diffuse
• Formerly associated with long term dialysis (AB)
  • Beta-2 macroglobulin (AB amyloid)
  • Less common now with improved dialysis filtration
• Simple biopsy will confirm
Granular Cell Tumor

Granular Cell Myoblastoma
Granular Cell Myoblastoma

Facts

• Schwann cell origin
• Widely distributed
  • >50% in oral cavity; over 1/3rd on dorsum of tongue
  • May be multiple
• Can arise at any age; most between 30-60 years
• Pathologic features:
  • Large polygonal cells in sheets and septate aggregates; granular eosinophilic cytoplasm (lysosomal/autophagic)
  • Positive for S-100, NSE, laminin, myelin proteins
• *Often induce remarkable surface PEH
  • May also be + in MRG, histoplasmosis, KA, deep fungal inf.
Oral Leukoplakia
Median Rhomboid Glossitis
Median Rhomboid Glossitis

Facts

• Common; asymptomatic; benign-remains so
• Ovoid to rhomboid shape; flat to nodular
  • May be associated with corresponding palatal erythema at area of resting contact
• Chronic presence of Candida organisms thought to produce atrophic papillary changes, inflammation
• Often responds to extended topical antifungal treatment
Median Rhomboid Glossitis

Facts

• Usually erythematous but may be hyperkeratotic
• Filiform papillae absent or fewer in number
• Likely due to Candida presence
• Trial of antifungal therapy may be helpful
• Lesions are harmless
Submucous Fibrosis
Submucous Fibrosis

Facts

• Not common in US; very common in India, SE Asia
• Associated with use of Areca nut, tobacco, betel leaf quid
• Oral cavity, oropharynx, vocal cords affected
• Lips tighten, decreased oral opening, submucosal scar bands develop
• Up to 10% of users develop oral SCCa
• Follow-up care required / biopsy prn
Geographic Tongue

A Psoriasiform Mucositis
Geographic Tongue

Facts

• Affects 2% of population; noted in up to 15% of teenagers and young adults

• Usually asymptomatic; may be painful
  • Appearance often drives office visits

• May affect other areas of mouth (migratory stomatitis)

• Patches evolve quickly / resolve / reform

• Histologically similar to psoriasis
  • Clinical relationship unclear

• Treatment usually not necessary
Hairy Tongue
Hairy Tongue

Facts

• A benign hypertrophy of filiform papillae
  • Defective desquamation in central column of filiform papillae
• Etiology:
  • Xerostomia
  • Poor oral hygiene
  • Medications: antibiotics, psychotropics, xerogenic drugs
  • Substances: methamphetamines, smoking, EtOH
• Treatment: id causative agent(s); scraping / removal

NB: This is not “hairy leukoplakia”
Cobblestone Surface

Chronic Xerostomia
Cobblestone vs Fissured Tongue
Fissured Tongue Facts

• 7% to 15% of the population
• May be inherited (AD)
• Usually asymptomatic
• May be seen in several syndromes:
  • Melkersson-Rosenthal Syndrome
  • Sjogren Syndrome
  • Acromegaly
  • Down syndrome
• 5% to 25% with concurrent geographic tongue
Vascular Lesions
Lymphangioma
Lymphangioma

Facts

- Superficial and deep types
- May be capillary, cavernous or mixed
- Most common cause of childhood macroglossia
- Usually accompanied by red areas and blood vessel presence
- Surgery usually successful
  - Circumscrip tum variety usually cured with argon or CO$_2$ laser
Hemangioma
Hemangioma Facts

• A common cause of macroglossia
• Often present at birth
• Tongue lesions can be well circumscribed—often infiltrate into muscle
• Often combined with lymphangioma
• Treatment approaches:
  • sclerotherapy; laser ablation; surgical excision; intralesional steroids
Squamous Cell Carcinoma
Dorsum of the Tongue

Squamous Cell Carcinoma
SCCa-Dorsum of Tongue

Facts

• Location: anterior to circumvallate papillae
• Pain or burning usual presenting symptoms
• Appearance ranges from
  • Flat and ulcerated
  • Exophytic / papillary
  • Mixed red / white
SCCa-Dorsum of Tongue

Facts

• Represents a minority of oral tongue cancers
• Associated with premalignant lesions
  • Leukoplakia
  • Erythroplakia
  • Sideropenic dysphagia
  • Oral submucous fibrosis
  • Oral lichen planus
  • Chronic syphilitic lesions
• Dorsal tongue carcinomas: 3% to 5% of all oral tongue cancers
SCCa-Dorsum of Tongue

Mimicking Pathology

• Granular cell myoblastoma
• Median rhomboid glossitis
• Erosive lichen planus
• Amyloidosis
## Dorsum Tongue SCCa

### Overall % of Tongue SCCa

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<th>Series</th>
<th>No. of Cases</th>
<th>% SCCa</th>
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<td>Frazell, 1962</td>
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<td>Flament, 1964</td>
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<td>Kari, 1994</td>
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<tr>
<td>Goldenberg, 1997</td>
<td>99</td>
<td>5</td>
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Dorsum of Tongue SCCa
Goldenberg Study

5 cases

Age range: 36-80 years / Average age 66 years

Gender ratio: 3:2 / M-F

Risk factors: 2 smokers; 2 no risk factors; 1 OLP
  NB: the 2 smokers died of their disease @ 3 years

Stage at diagnosis:
  1 with stage 1 disease
  3 with stage 2 disease
  1 with stage 3 disease-DOD at 2 years
Dorsum of Tongue SCCa

Prognosis

• Wide survival range from 0% at 5 years (Lam, et al) vs. 51% survival of lateral tongue lesions

• Goldenberg, et al 2/4 DOD @3 years; 2/4 A/W @ 5 years; 1/5 NED at 6 months
