Bumps in the Night II
Conjunctival Neoplasms

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Neoplasm – Definition
- A New growth
  - From Greek
  - Benign or malignant
- Tumor – synonym
  - A new and abnormal proliferation of cells serving no physiological function
- Conjunctival or corneal
  - From anterior ocular tissues and coverings

Risk Factors
- Advanced age
- Male gender
- Light complexion
- Repeated, intense sun exposure
- Outdoor occupations
- Cigarette smoking
- H/o squamous cell carcinoma (head/neck)
- AIDS

Rising Incidence
- Increased UV exposure
- Older population
- Increases in outdoor activities
- Changes in clothing styles
- Changes in ozone protection
- Rising incidence of disease
  - HIV ~ 10-fold ↑ risk of conjunctival neoplasm

Concerning Characteristics of Ocular Neoplasms
1. New or rapidly growing lesion
   - Overall size
   - Depth of tissue invasion
2. Changes in size or shape
   - Particularly irregular borders
3. Change in appearance
   - Particularly color
   - Particularly increasing pigmentation
4. Changes in surface characteristics
   - Crusting, ulceration, bleeding, oozing
5. Adjacent tissue changes
   - Swelling, redness, satellite lesions
6. Changes in or significant symptoms
   - Tenderness pain or itching
**General Management Principles**

1. **History**
   - Document lesion history well

2. **Observation**
   - Main management of choice for most benign, asymptomatic tumors
   1. Describe
   2. Draw
   3. Document well
     - Measure lesion at largest diameters

3. **Photo document**
   1. Critical for any level of suspicion
   2. Or even if thought relatively safe?
   - Slit lamp camera
   - Cheap hand-held digital camera

4. **Follow closely**
   - Frequent follow-ups for concerning lesions

5. **Biopsy or refer**
   - Growth or change (color, vasculature, etc.)
   - When in doubt

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**Ocular Tumor Organization**

**Anatomical Location**
- Eyelids and adnexa
- Conjunctiva and cornea
- Uvea: iris, choroid
- Orbit

**Tissue Involvement**
- Epithelial
- Melanocytic
- Glandular
- Vascular
- Lymphoid
- Lacrimal based
- Metastatic

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**Conjunctival Neoplasms**

**Benign**
- Choristomas
- Conjunctival Cysts
- Papilloma
- Phlyctenule
- Pterygium
- Capillary Hemangioma
- Pyogenic Granuloma

**Malignant**
- Conjunctival Intraepithelial Neoplasia
- Carcinoma in situ
- Squamous Cell Carcinoma
- Malignant Melanoma
- Kaposi's Sarcoma
- Lymphoma
- Metastatic Tumors

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**Red Eye in Sjögren's Syndrome**

- 68-year-old woman with 15 yrs Sjögren's
- CC: itching attributed/treated as KCS
- 6 Mo - painful eye with increasing redness

**Red Eye in Sjögren's Syndrome**

- MRI – thickened left lateral rectus beyond orbital rim
- Conjunctival B Cell lymphoma (MALT)
- Radiation with remission > 2 years

Ocular Tumor Organization

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Benign Neoplasms
- Choristomas
- Conjunctival Cysts
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Malignant Neoplasms
- Conjunctival Intraepithelial Neoplasm
- Carcinoma in situ
- Squamous Cell Carcinoma

Conjunctival Choristomas
- Choristoma contains tissue not normally present at the site
- Congenital (or shortly after birth)
- Not hereditary

Caruncle Oncocytoma is a glandular tumor

Dermoid
- Congenital, skin containing lesions
- Solid, isolated, white-yellow, focal mass
- Usually at inferotemporally limbus
- Often displays thin white hairs

Ossseous Choristoma
- Very solid nodule encapsulating bone
- Usually super temporal
- Calcium confirmed by ultrasound or CT

Complex Choristoma
- Contain tissue: dermal appendages, lacrimal gland tissue, cartilage, bone, etc.
- Appearance based on majority of tissue
- Can be quite large

Conjunctival Cysts (Epithelial Inclusion Cyst)
- Formed spontaneously
- Epithelial cells pushed into forming epithelium lined sacs
- Stimuli: trauma, inflammation, surgery
- Contain clear fluid and cellular debris
- Transilluminate
- Management:
  - Observe
  - Excise completely
Cyst Video

Conjunctival Papilloma (Squamous Papilloma)
- Benign
- Human papilloma virus (HPV)
- Fibrovascular, pink
- Pedunculated or sessile

Papilloma

Childhood/Young Adults
- Bulbar and Fornix
- Multiple, bilateral
- Often stable w/o growth
- Small
- Benign

Older Adults
- Limbus
- Single, unilateral
- Wide growth
- May be very large
- Significant corneal and conjunctival inv.
- Weeping blood
- Can mimic SCC

Papilloma Treatment
1. Monitor
2. Topical steroid
3. Cimetidine (Tagamet)
   - H-2 receptor blocker

Papilloma in a Child, Case 1
- 11-year-old boy
- CC sudden conjunctival bleeding
- What is it?
- 8-year h/o diffuse conjunctival papillomas
- Failed excisional biopsy, cryotherapy and mitomycin C
- Diffuse recurrence over entire conjunctiva

Papilloma in a Child, Case 2
- Treated with Cimetidine
  - Tagamet
  - H-2 receptor blocker
- 2 mo: dramatic regression
- 4 mo: resolution
**Phlyctenule**
Phlyctenular Keratoconjunctivitis
- Small, nodular, circumscribed limbal lesion
- Lymphoid tissue
- Ulcerates and heals 10 - 14 days
- Delayed hypersensitivity to antigens
  - Mainly bacterial by-products
  - Associated with tuberculosis
  - Indicates altered immune function

**Epithelial Based Carcinoma:**
A Continuum
1. Conjunctival Intraepithelial Neoplasm (CIN)
   - Superficial thickened or atypical epithelium (pre-malignant)
2. Carcinoma in situ
   - Full-thickness epithelium showing malignant like cells
   - Intact basement membrane
3. SCC
   - Breaks through basement membrane
   - Invades conjunctival stroma

**Conjunctival Intraepithelial Neoplasia (CIN)**
- Most common conjunctival malignancy
- 3rd most common ocular tumor in geriatrics
- Precancerous lesion
  - Epithelial cells variably atypical, dysplastic
- At limbus
  - Can involve cornea
- Stain with Rose Bengal
  - DDx pinguecula, pterygium or pannus

**Common Presentations for CIN, Carcinoma in Situ, SCC**
1. A raised vascular, gelatinous mass
   - Grey or slightly red
2. White, plaque-like lesion
3. Papilloma-like lesion
4. Opaque, membranous-like tissue spread onto peripheral cornea
Squamous Cell Carcinoma

- Incidence of 1:800
- Older, all races, both genders
- Dilated peri-lesional blood vessels
- Signs of malignancy
  - Bleeding
  - Invasion of underlying tissues
  - Dystal adhesion form limbus

Classification: Squamous Cell Carcinoma of the Conjunctiva

1. Leukoplakic
   - White perilimbal plaque
2. Papillomatous
   - Pinkish, limbal, corkscrew vessels
3. Gelatinous
   - Semi-translucent

Management: Squamous Cell Carcinoma

- In office management
  1. Serial photography
  2. Anterior segment ultrasound
     - R/o tissue invasion
  3. Excision or biopsy criteria
     1. If any of the characteristics described
     2. Any focal conjunctival thickening with prominent abnormal vasculature
Some Malignancies are Easier to Diagnose Than Others

A Black Eye
- A 77-year-old woman
- C/O OS had “turned black” past 6-9 mo
- OS extensive pig, inc. lid margin and cornea
- Primary acquired melanosis (PAM) of the conjunctiva with atypia (Confined to epithelium)
- Followed q 2-6 mo.

A Black Eye
- Some progression, some regression

Racial Melanosis (Conjunctival Melanosis)
- Darkly pigmented persons
- Flat bulbar conjunctival pigmentation
- Usually
  - Bilateral
  - More dense at limbus
  - May extent on to cornea
- Rarely progresses to melanoma

Racial Melanosis (Melanocytosis)
- Axenfeld loop
Racial Melanosis
- Can spill over onto lid

Congenital Melanocytosis
1. Ocular
   - Eye only; least prevalent
2. Dermal
   - Skin only; 1/3 of cases
3. Oculodermal
   (Nevus of Ota)

Nevus of Ota
Oculodermal Congenital Melanocytosis
- Skin & eye; most prevalent
- Blue/grey pigment along 1st & 2nd trigeminal branches
- Dark pigmented people, Asians
- Rare in whites

Nevus of Ota
- Rarely this profound
- Note skin lesion along 1st & 2nd trigeminal branches

Congenital Ocular Melanocytosis
- Congenital pigmentation of scleral and/or peri-ocular tissues
- Easily confused with primary acquired melanosis (PAM)
- Conjunctival pigment
- 1:400 uveal melanoma risk
- Not conjunctival melanoma
- Usually whites
- Monitor every 6-12 months

Congenital Melanocytosis
Associations
- Hyper perpigmented trabecular meshwork
- Heterochromia iridis
- Iris mammillations
- Dark fundus
Conjunctival Nevus
- Most common conjunctival melanocytic tumor
- Visible by 2nd decade
  - Don’t appear after 35
- Benign
  - < 1% conversion to malignant melanoma
- Management
  - Photographic monitoring
  - Excision if documentable enlargement

Conjunctival Nevus
- Unilateral
- Minimal to slight elevation
- Varying pigment
  - Brown, reddish, amelanotic
- Clear cysts common

Conjunctival Nevus
- Usually found
  1. Limbal and perilimbal
  2. Plica and caruncle 2nd most common location
  3. Interpalpebral

Variously Pigmented Nevi

Primary Acquired Melanosis (PAM)
- Middle age (vs nevus)
- Common, 30% incidence in whites
- Flat (vs nevus)
- Diffuse and patchy
- Moves easily with conjunctiva
  - Vs. racial/ocular melanosis
Primary Acquired Melanosis (PAM)

1. PAM without atypia
   - Rarely progresses to melanoma
   - ↑ pigmentation in epithelium w/ normal melanocytes

2. PAM with atypia
   - 50%-90% conversion risk to malignant melanoma
   - Atypical melanocytes

Risks of Melanoma Associated with PAM

<table>
<thead>
<tr>
<th>General Classification</th>
<th>Conjunctival Melanoma Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAM without atypia</td>
<td>0%</td>
</tr>
<tr>
<td>PAM with atypia</td>
<td>46%</td>
</tr>
<tr>
<td>If atypical melanocytes show abundant cytoplasm</td>
<td>75%</td>
</tr>
<tr>
<td>If atypical epithelial melanocytes located in other than basal layer</td>
<td>90%</td>
</tr>
</tbody>
</table>

Folberg R, McLean IW, Zimmerman LE: Primary acquired melanosis of the conjunctiva. Hum Pathol 16:136, 1985. Adapted from Duane's

Indications for Biopsy

**Suspicious Signs**
- Focal, thickened, darker brown areas
- Darkly pigmented
- Rapidly progressive
- Large
- Multifocal

**Suspicious Locations**
- Palpebral conjunctiva
- Fornix
- Caruncle
- Distal to limbus (bulbar conjunctiva)

Malignant Melanoma of the Conjunctiva

- Typically Whites in the 5th decade
- Very Rare
  - 2% of ocular malignancies
  - 4 new cases per 10 million per year in whites
  - 8 X < for blacks
  - 3 fold ↑ incidence 1973 - 1999 (white males)
- Origins
  - 10% from nevi
  - 20% de novo
  - 70% from PAM with atypia
### Conjunctival Melanoma
- Strong metastatic tendencies
- Primarily lymph nodes
- Pre-auricular and submandibular node palpation
- Grow superficially for extended times
- Rarely invade uvea or globe
- Prognosis
  - 25% overall mortality
  - Up to 45% if the tumor arose from PAM
  - Many fold mortality rate if
    - >0.8 mm thickness
    - lymphatic invasion

### Malignant Melanoma Characteristics
- Localized
- Limbal & interpalpebral
- Pigmented
  - But can be amelanotic
  - Prominent abnormal blood vessels
  - Nodular 1 to >10 mm

### Conjunctival Melanoma
- Localized
- Pigmented
- Prominent abnormal blood vessels
- Nodular 1 to >10 mm

### Amelanotic Conjunctival Melanoma
- Benign
- Congenital or develop near birth
- May enlarge over several months
- Often spontaneously resolves

### Capillary Hemangioma
- Observation
- Surgical resection
- Local or systemic prednisone

### Which is the melanoma?
Both!
Pyogenic Granuloma

- Misnomer
  - Not pyogenic – puss forming (bacterial)
  - Inflammation not granulomatous
- Chronic inflammatory process from
  - Chalazia, foreign body, blepharitis
  - Surgery: chalazia, pterygium, strabismus, etc.
- Treatment
  - Steroid drops often successful
  - May require surgical excision

Pyogenic Granuloma

- Fast growing
- Pedunculated (stalk)
- Red
- Fleshy

Pyogenic Granuloma Video

- From FB
- Topical steroids for a few weeks

Pyogenic Granuloma Video

Conjunctival Neoplasms

- Epithelium
- Melanocytic
- Glandular
- Vascular
- Lymphoid
- Lacrimal based
- Metastatic

Benign
- Capillary
- Hemangioma
- Pyogenic Granuloma

Malignant
- Kaposi’s sarcoma
**Kaposi's Sarcoma**
- Most common HIV related ocular tumor
- Seen in healthy people w/ a rare sarcoma
- 70% of ocular lesions occur on the eyelids
- Conjunctival lesions most common in inferior fornix
- Differentials include
  - Hemangioma, pyogenic granuloma, other

**Kaposi's Sarcoma of the Conjunctiva**
- Quick growing neoplasms
- Capillary related
- Bright to dark red
- Spontaneous bleeding possible

**Lymphoid Tumors**
- Very rare
- Variable consequence
  - Benign - more common in children
  - Malignant - more common Mid to later age
  - Rarely sight or globe threatening
  - Most local, but can indicate systemic lymphoma
- Most slow growing
  - AIDS associated fast growing

**Lymphoid Tumors**
- Minimal symptoms
- Subepithelial mass
- Smooth
- Pink
- At bulbar conjunctiva or fornix
- Minimal vascular involvement

**Lymphoid Tumors**
- Local ocular lesions are manifestations of systemic disease
- “Salmon patch” termed from salmon color
- Usually located in the fornix and stroma
- Management
  1. Must biopsy as cannot clinically differentiate benign versus malignant
  2. Must do systemic workup on all patients
### Risk of Systemic Lymphoma Development based on Ocular Involvement

<table>
<thead>
<tr>
<th></th>
<th>% Systemic Lymphoma Development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 Year</td>
</tr>
<tr>
<td>Lymphoid Tumor</td>
<td>7%</td>
</tr>
<tr>
<td>Lymphoma specifically</td>
<td>12%</td>
</tr>
</tbody>
</table>


### Management of Lymphoid Tumors

- Complete history and review of systems
- Biopsy
- Blood workup
- CT or MRI of torso to rule out systemic lymphoma
- Treatment dependent on malignancy
  - Observation, steroids, radiation, chemotherapy

### Orbital Fat Prolapse

### Metastatic Carcinoma of the Conjunctiva

- Rare and predominantly breast cancer
- Also skin melanoma and other 1o tumors
- Usually flashlight, pink and vascularized in the conjunctiva stroma
- Metastatic melanoma is usually pigmented
- Very rare

Conjunctival metastatic breast cancers
Concerning Characteristics of Ocular Neoplasms

1. New or rapidly growing lesion
   - Size and depth
2. Changes in size or shape
   - Irregular borders
3. Change in appearance, particularly color
   - Increasing pigmentation
4. Changes in the surface
   - Crusting, ulceration, bleeding, oozing
5. Adjacent tissue changes
   - Swelling, redness, satellite lesions
6. Changes in or significant symptoms

Management Principles

1. History
   - Document lesion history well
2. Observation – describe, draw, document
   - Main management for most benign, asymptomatic tumors
3. Photo document – critical if any suspicion
   - Even lesions thought to be safe?
4. Follow closely – Close interval if concerned
3. Biopsy or refer – When in doubt
   - Growth or change
   - Just plain concerned

Thank You

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