Lumps, Bumps and Lid Lesions

Know when to hold them & know when to fold them

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Disclosures

- Financial disclosures:
  - Speakers Bureaus/Consultant:
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Cancer

- Definitions:
  - A group of diseases characterized by uncontrolled growth and spread of abnormal cells
  - Any of various malignant neoplasms characterized by the proliferation of anaplastic cells that tend to invade surrounding tissue and metastasize to new body sites

Cancer

- Characteristics:
  - Can affect any tissue or organ at any age
    - ~77% of all cancers occur in patients > 55 yo
  - All cancers begin with a defect in a single cell (monoclonal)
  - This is followed by unrestrained growth
    - Benign tumors may damage localized tissue by occupying space but they do not spread

Cancer

- Characteristics:
  - Malignant tumors invade surrounding tissue and may metastasize
    - A one cm tumor contains one billion cells
    - One trillion cells usually means a lethal tumor
  - Cell division is controlled by genes that promote it and genes that suppress it
    - Cancer is the result of some combination of defects in this genetic functioning

History

- Duration
- Bleeding
- Discharge
- Change in size
- Change in color
- History of skin cancer
Cancer

- Risk factors:
  - Only ~5% of cancers are strongly hereditary
  - Environmental factors account for 75%-80%
    - Tobacco
    - Poor nutrition
    - Obesity
    - Infectious agents
    - Sunlight/Radiation
    - Carcinogens

- The 5 leading non-skin cancers in the U.S.
  - Prostate
  - Lung (90% in tobacco use)
  - Breast
  - Colo-rectal
  - Urinary/bladder
- Cancer accounts for 25% of the deaths in the U.S.
  - 25% of people will be personally affected in their lifetime

Cancer

- Basal Cell Carcinoma (BCC)
  - The most common malignancy in humans
  - 50% of all U.S. cancer, is skin cancer
    - 80% of that is BCC!
  - Greater risks exist for BCC & SCC in patients:
    - White
      - 19X greater whites:blacks
    - Light colored eyes & hair
    - Freckle easily and tan poorly
    - Increases with UV exposure
      - Tanning beds = 1.5X relative risk

- Basal Cell Carcinoma (BCC)
  - 80% of BCC cases are on the head & neck
    - 15% on the trunk
  - Greater risk of recurrence of BCC on eyelids (lower), nose & ears
  - There is no precursor to BCC

Cancer

- Basal Cell Carcinoma (BCC)
  - 20% of all eyelid neoplasms
    - 90% of all malignant eyelid neoplasms
      - Spread is by local invasion (almost exclusively)

Types:
- Superficial
- Nodular
- Morpheaform
Cancer
- Basal Cell Carcinoma (BCC)
  - 20% of all eyelid neoplasms
    - 90% of all malignant eyelid neoplasms
  - Spread is by local invasion (almost exclusively)

Basal Cell Nevus Syndrome (Gorlin-Goltz Syndrome)

16 weeks of Erivedge® (Vismodegib)

16 weeks of Tarceva® (Erlotinib)

Cancer
- Squamous Cell Carcinoma (SCC):
  - SCC is increasing in incidence
    - Greater rate of increase for SCC vs BCC
    - 200% for SCC vs 80% for BCC
  - Estimated BCC:SCC = 4:1
  - SCC is most common skin cancer in blacks (30%)
  - 60% of cutaneous SCC occurs on the head & neck (sun-exposed)
  - 90% of head & neck cancer = SCC

Cancer
- Squamous Cell Carcinoma (SCC):
  - 2nd most common eyelid malignancy
    - 10% of all eyelid malignancy
  - Demographics
    - Older population
    - Fair complexion, sun damage
  - intraepithelial spread or deep invasion with potential rare regional lymph node metastasis
Cancer

- Squamous Cell Carcinoma (SCC):
  - Risks:
    - Cumulative UV-B exposure is the primary risk factor
    - UV-A is less indicated but data is unclear
    - Smoking = 2X risk
    - Tanning beds = 2.5X risk
    - Born in high UV exposure area = 3X risk
    - Light skin & hair = 2-5X risk
    - Outdoor occupation = 5X risk

- SCC vs BCC:
  - SCC grows faster, ulcerates, bleeds & scabs more than BCC
  - SCC recurs more frequently than BCC
  - Since SCC extends deeper (not local), more severe
  - Lesions on the ear & lips are at greater risk for recurrence
    - Scalp, forehead, temple, eyelid, nose and hands are close behind

SCC- Conjunctival

- Unrelated to sun exposure
- Commonly misdiagnosed as conjunctivitis
- Higher incidence of metastatic disease if lesion extends into fornix
Solar lentigo
- Benign sun-induced area of darkening pigmentation
  - Commonly referred to as “Liver Spot”
  - Easily mistaken for melanoma

Seborrheic keratosis
- Common benign skin lesion in older adults
  - Proliferation of epidermal cells occurring on sun exposed areas of skin
    - Variable pigmentation
      - Pink – brown – dark brown – black
      - Can transition to solar lentigo
    - Usually begin as flat, brown, circumscribed areas that can increase in size and thickness
    - Causes suspicion for melanoma

Malignant Melanoma (MM): Risk factors:
- FHx offer 10% increase risk
- Dysplastic nevus syndrome can increase risk 100-500X
  - ~25% of nevi develop to MM
- Blondes = 2X risk
- Red heads = 4X risk
- Sun sensitive or inability to tan = 2X risk
- Frecklings = 2X risk
- Whites = 10X risk vs blacks/Asians/Hispanics
- Living near equator increases risk

Malignant Melanoma (MM):
- Increased incidence (~6% per year)
  - Greatest incidence increase amongst neoplasms
  - ½ the incidence of MM is between 35-65 ages
  - 80% of cases occurring between 20-74 ages
  - Survivability has improved
    - 60% in 1960s
    - >89% in 1990s
- Median age of diagnosis is 57

Malignant Melanoma (MM):
- Risks:
  - Sunlight exposure is primary risk factor
    - Past sunburn at ANY age = 2X risk
    - Childhood sunburns increase risk
    - Tanning beds = 1.25X risk
    - Living near equator increases risk
Malignant Melanoma (MM):
- **ABCDE** rule:
  - **A** symmetry,
  - **B** order irregularity,
  - **C**olor abnormality & **D**iameter (>6mm)
  - **E** has now been added:
    - Evolving = change in size, shape, surface (bleeding) or symptoms (itching or tenderness)

Dermal Melanoma

Now to the tour.....

Epithelium
- Stratified layer

Melanocytes

Langerhahn’s cells
- The sentry cells
  - Signal the immune system
  - NOT in the cornea!
  - They stimulate the system to cause scarring

Goblet cells

Fibroblasts

Nerve cells

Lymphatics
- Not IN the eye but in the conj & lids
- This allows for lymphatic related spread of disorders

Epithelium

Melanocytes

Langerhahn’s cells

Goblet cells

Fibroblasts

Nerve cells

Lymphatics

Tissues of the conjunctiva

Tissues of the conjunctiva

Tissues of the conjunctiva

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Tissues of the conjunctiva

- Blood vessels
- Mast Cells
  - At BV wall
  - Degranulate in allergy
    - Itch
    - Erythema
    - Edema

Early Phase Allergy

- Nerves
- Sensitized Mast Cell
- Antigen
- Other Mediators: Tryptase, Heparin, Prostaglandins
- H<sub>1</sub> nerve stimulation @ 3-5 min = Itching!
- Histamine
- Endothelial Gaping = fluid leakage = Swelling!
- Vasodilation @ 5-10 min = Redness

Tissues of the conjunctiva

- Limbal stem cells
  - Thickened area of conjunctiva
  - Source of replenishment of corneal epith
  - A highly mitotic & immunologic area
  - Explains why the limbal area can be the source of so many disorders

- Palpebral conjunctiva
  - Goblet cells
    - Mucus producing cells
    - Distribution of goblet cells in the conj is not uniform
    - Greater density away from the limbus temporally
    - Greater nasally then temporally

Clinical Identification tips

- Conjunctival lesions
  - Limbal Dermoids
  - Congenital choristoma
    - Definition
      - *Choristoma* is a congenital lesion composed of types of normal tissue that would not normally be found at that location of the body
      - *Hamartoma* is a congenital lesion of an abnormal density of normal tissue that would be found at that location
  - Freckle/nevus = hamartoma of pigment
  - Hemangioma = hamartoma of blood vessels

- Limbal Dermoids
  - Congenital choristoma
    - White - solid lesion
    - Usually seen in children (rarely seen by ODs as a new lesion)
    - Can consist of fat tissue-hair follicles-teeth

Limbal stem cells

- Source of replenishment of corneal epith
- A highly mitotic & immunologic area
- Explains why the limbal area can be the source of so many disorders
Clinical Identification tips

- Conjunctival lesions
  - Limbal Dermoids
    - Differentiate for Goldenhar's Syndrome
      - Oculoauriculovertebral syndrome
        - Facial asymmetry (FLK): Usually unilateral
        - Scoliosis

So to differentiate, look at the ear as well as the eye!

Clinical Identification tips

- Conjunctival lesions
  - Limbal phlebitis eye
    - Located at the limbus
    - Similar to marginal infiltrate (staph) but no clear zone at the limbus
    - Possible association with TB (if regionally at risk)
    - Very responsive to topical steroids

Clinical Identification tips

- Conjunctival lesions
  - Salzman's nodular degeneration
    - May develop from any chronic surface disease
      - Common after chronic phlebitis eye (UPK - etc.
    - Blush-gray color to avascular lesion
    - Epith intact but thinned
    - Not overly inflamed
    - Often needs graft

Clinical Identification tips

- Conjunctival lesions
  - Bitot's spot
    - Squamous Metaplasia
      - Mucosal tissue change in response to chronic dryness as protection
        - Keratinization
        - Reversible!
    - Leukoplakia
      - White plaque
    - Vitamin-A deficiency
      - ERG to rule out night blindness

Clinical Identification tips

- Conjunctival lesions
  - Conjunctival Intraepithelial Neoplasia (CIN)
    - Was Carcinoma in situ
    - Collective term for ALL Ocular Surface Squamous Neoplasms (OSSN)

Ocular Surface Squamous Neoplasia

- Melanocytic
  - Melanous
  - Malignant Melanomas

- Non-Melanocytic
  - Papilomas
  - Corneal Intraepithelial Neoplasia (CIN)
  - Squamous Cell Carcinoma
Clinical Identification tips

- Conjunctival lesions
  - Conjunctival Intraepithelial Neoplasia (CIN)
  - Once the lesion reaches the limbus, it likes the high mitotic area so it works around the limbus instead of marching across (like a pterygium)
  - Once the lesion breaks through to the underlying conjunctival stroma (invasive), it is termed a Squamous Cell Carcinoma (SCC)
    - One step beyond CIN
  - Basal Cell Carcinoma (BCC) is unheard of in the conjunctiva!
    - On skin think BCC 1st but conj think SCC!

- Conjunctival Gelatinous Polypoid Squamous Cell Carcinoma
  - Will cross the cornea!
  - HPV-16 often found but NOT considered the cause

Clinical Identification tips

- Cystic lesions
  - Epithelial Inclusion Cyst (EIC)
    - Use optic-section beam to "light up" the lesion
  - Formation:
    - Epithelial cells are driven below the surface
Clinical Identification tips

- Cystic lesions
  - EIC Formation Sequence
    - Epithelial cells are designed to separate 2 environments from each other

- Cystic lesions
  - EIC
    - Fornix lesions are cloudy due to mast or goblet cell secretions

- Cystic lesions
  - Lymphangiectasis
    - May be linear or multi-lobular

- Cystic lesions
  - What is it?

Clinical Identification tips

- Lid lesions
  - Transition Areas
    - Generally, in areas where one epithelium transitions from one type to another, is prone to viral induced lesions
      - Lid conj to palpebral conj (Lid Margin)
      - Bulbar conj to cornea (Limbus)

- Lid lesions
  - Molluscum Contagiosum
    - Characteristics:
      - Sessile papillomatous lesion
      - Viral induced
Clinical Identification tips

- Lid lesions
  - Molluscum Contagiosum
    - Characteristics:
      - Sessile papillomatous lesion
      - Viral induced
      - Chronic follicular conjunctivitis
  - Typical manifestation: A small “prick” of the surface to draw a bit of blood may involute the lesion.

- Differentiate from HSK lid lesions

Masquerade Presentations

- Many eyelid tumors spread in a manner that involves different tissue planes at a microscopic level.
- As a result, the process does not present as a discrete lesion and is often misdiagnosed as a benign inflammatory lesion.

- Sebaceous Cell Carcinoma

Chronic Conjunctivitis

- “The patient is non-compliant”
- “I haven’t found the right drop yet”

Chalazion

- Recurrent chalazion, same/multiple locations

Dermatitis

- Allergic dermatitis, chronic eczema, scleroderma

Ectropion

- Cicatricial LL ectropion, LL retraction

Entropion

- Trachoma, OCP

Blepharitis

- Non-compliant patient, poor hygiene
Facial numbness or paralysis
- “It’s just a Bells palsy”

Clinical Identification tips
- Lid lesions
  - Sebaceous Cell Carcinoma
    - Pagetoid spread
      - Can significantly complicate the surgical management of this disease
  - Lash Margin could be best clinical clue
    - Very rare but VERY bad cancer:
      - 8%-25% die from this cancer (even at this early stage)

Clinical Identification tips
- Pink-colored lesions
  - Pyogenic granulomas
    - Neither pyogenic nor granulomatous!
    - Ocular causes:
      - Post-op complication of tissue malpositioning
      - May also occur in response to a retained foreign material
      - May occur if a chalazion/hordeloum ruptures through the tarsus to the conjunctival surface and spontaneously drains
  - Retained suture
Clinical Identification tips

- Pink-colored lesions
  - Pedunculated papillomas
    - Viral induced

Clinical Identification tips

- Pink-colored lesions
  - Sessile papillomas
    - Difficult to differentiate!
    - Note “feeder” vessel(s)
    - Pox virus induced
      - HPV 6 & 11 have been associated

Clinical Identification tips

Viral
- Children/Adolescents
  - Often Bilateral
  - Often Multiple
  - Pedunculated in fornix
  - No inflammation
  - Resolve in 2 yrs

Neoplastic
- Adults
  - Unilateral
  - Solitary
  - Sessile, at limbus
  - Inflammation
  - Do not resolve

Clinical Identification tips

- Pigmented lesions
  - Iris Nevus
    - Melanoma transition & metastasis is rare
    - Management of nevi is photos and monitor for:
      - Growth

Clinical Identification tips

- Pigmented lesions
  - Nevus at the caruncle
    - Caruncle is usually very quiet
    - More suspicious for development of melanoma
Clinical Identification tips

- Pigmented lesions
  - Conjunctival Nevus
    - Focal, movable, congenital hamartoma
    - May darken in puberty
    - Always sample/biopsy if inflamed

- Pigmented lesions
  - Ocular Melanosis
    - Blue, gray or brown pigmentation
    - Does NOT move

- Pigmented lesions
  - Primary Acquired Melanosis (PAM)
    - 35% develop melanoma

Classification of Conjunctival Papillomas

<table>
<thead>
<tr>
<th></th>
<th>Conjunctival Nevus</th>
<th>Congenital Ocular Melanosis</th>
<th>Primary Acquired Melanosis (PAM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Congenital-may darken</td>
<td>Congenital</td>
<td>Acquired-middle age</td>
</tr>
<tr>
<td>Structure</td>
<td>Discrete</td>
<td>Discrete</td>
<td>Discrete</td>
</tr>
<tr>
<td>Color</td>
<td>Brown</td>
<td>Blue/slate gray</td>
<td>Brown</td>
</tr>
<tr>
<td>Cysts</td>
<td>50% of compound</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Pigmentation</td>
<td>Variable</td>
<td>Always</td>
<td>Always</td>
</tr>
<tr>
<td>With conj</td>
<td>Lesions move,</td>
<td>Lesion does NOT move</td>
<td>Lesion moves</td>
</tr>
<tr>
<td>movement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth</td>
<td>Stationary</td>
<td>Stationary</td>
<td>Stationary</td>
</tr>
<tr>
<td>Skin</td>
<td>Not involved</td>
<td>May be involved</td>
<td>Not involved</td>
</tr>
<tr>
<td>Malignant</td>
<td>Conjunctival melanoma</td>
<td>Skin or uveal, rarely</td>
<td>Conjunctival melanoma</td>
</tr>
<tr>
<td>Potential</td>
<td></td>
<td>conjunctival</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Identification tips

- Pigmented lesions
  - Conjunctival Melanoma
    - 10% develop de-novo
    - 20% from pre-existing nevus
    - 60%-70% from spreading PAM
    - Mortality = 25%
      - 40%-44% if from PAM
      - Spreads to PA node or Sub-mandibular nodes

- Pigmented lesions
  - Lid Melanoma

Case:
Ah... those suspicious lumps & bumps

HG
- 67 yowf
- CC: Raised limbal lesion OS
- MHx: Neg (Smoker!)
- OHx: Neg
- Meds: None
- FHx: Neg
- VA<sub>sc</sub>: 20/20 OU

HG
- Pupils: PERRL - APD
- EOM: full range of motion
- Tapp: 15 OU
- SLE: - OD: WNL
  - OS: Temporal raised gelatinous vascularized lesion X 6+ months
- DFE: c/d 0.3 OU Mac/vessels/periph WNL
**Diagnosis:**
- Pterygium
- Pinguecula
- Corneal intraepithelial neoplasm (CIN)
- Squamous cell carcinoma (SCC)
- I don’t know, that is why I called YOU!

**Management:**
- Topical antibiotics
- Mitomycin-C 0.002% (MMC)
- Surgery
- No treatment necessary
  - Monitor

**Lesion was biopsy positive SCC and referred to us for a second opinion:**
- Enucleate
  - Other options
- No association with HPV
- No evidence of AC invasion, TM involvement or cataract.

**What is the most identifying characteristic of these lesions?**
- Gelatinous appearance
- Location on the cornea
- Vascularization
- Raised lesion
- Persistence &/or changes over time
Management:
- Option #1:
  - Lamellar keratectomy with conjunctivectomy and sclerectomy
  - Cryo of the margins
- Option #2:
  - Topical Mitomycin-C 0.002% (MMC)
  - Head and Neck oncologists start systemic chemo of Fluorouracil and Cisplatin (X two cycles)

Is it reasonable to monitor CIN?
- Not all will need MMC!

A newer biopsy technique
- Impression Cytology
  - Non-invasive technique that allows ID of cell types to classify a lesion

Impression Cytology Procedure
- Instructions for patient specimen collection:
  - The Biopore membrane device (Millipore CM 0.4 µm PSCM 02550, Millipore Corp, Bedford, MA, USA) comes in a sealed sterile package
  - The filter disc is 8 mm in diameter and is attached to a small plastic tube which is seal storage collection of the specimen
  - Before collecting a sample, three protruding plastic legs must be snapped off from the base of the tube with a pair of Spencer-Wells forceps
  - Topical proparacaine 0.5% eye drops are then instilled onto the ocular surface/lower fornix
  - Cytology specimens are obtained from the conjunctiva or cornea
  - The membrane device is firmly pressed against the area to be sampled for 10-20 seconds until the membrane becomes translucent
  - Lastly, the device is immediately transferred into a 10 ml container of 95% ethanol without air drying
  - Be sure to fully immerse the membrane in the solution

MMC Tx example
- 6/21/00 6/28/00 7/17/00 12/13/00

Impression Cytology Procedure
- Instructions for patient specimen collection:
  - We use the Univ. of Colorado Denver Dept. of Anatomic Pathology/Cytology Lab at The Anschutz Center
  - There are national labs that accept overnight delivery for assessment
Impression Cytology

Procedure

- Codes:
  - Benign Neoplasm of eye = 224.00
    - Conjunctiva = 224.30
    - Cornea = 224.40
    - Eye lid = 216.10
  - Carcinomas (in situ) = 234.00
    - General code for eye
      - cornea or conjunctiva
    - Excludes lid
    - Eye lid = 232.10

Limitations & Disadvantages

- Tissue Biopsy and Surgical Excision
  - Can cause disorganization of the specimen during
  - Can often miss tumor margins in the tissue collection
  - Longer recovery time
  - More invasive procedure for the patient
  - Recurrence rate near 52%
  - Can cause scarring
  - Removes limbal stem cells with each surgical procedure

- Impression Cytology
  - Sample depth is only first few superficial layers
  - Inconsistent reliably to distinguish invasive SCC or epithelium carcinoma in situ from minimally invasive disease
  - Keratinizing dysplasias may yield no or few atypical cells on impression cytology

OSSN lesions have been routinely ID’ed by surgical biopsy
- P/op stem cell deficiency concerns
- Impression cytology is a less invasive diagnostic option

What is that bump?

- OSSN lesions have been routinely ID’ed by surgical biopsy
- P/op stem cell deficiency concerns
- Impression cytology is a less invasive diagnostic option

References

1. Yanoff M, Duker J. Ophthalmology. 2nd ed. St. Louis, MO Mosby; 535-541