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Clinical-Pathological Correlation of Common Periocular Lesions

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System for Eye Pathology Diagnosis

• Identify the tissue
• Identify the abnormal process
  – Hyperplasia vs Hypoplasia
  – Degenerative vs Dystrophy
  – Chronic vs Acute Inflammation
  – Dysplasia vs Benign Process
• Develop a differential diagnosis
• Make diagnosis

55 yo man with eye lesion

Diagnosis?

spheroidal degeneration

• Spheroidal Degeneration is also known as Labrador keratopathy, Bietti nodular hyaline bandshaped keratopathy, climatic droplet keratopathy, proteinaceous corneal degeneration, elastotic degeneration, Fisherman’s keratopathy, and Eskimo’s corneal degeneration.
• Amorphous mauve colored globules are seen in the superficial corneal stroma or substantia propria close to the limbus in hematoxylin and eosin sections.

10 yo girl with pigmented lesion
10 yo girl with pigmented lesion

Diagnosis?

conjunctival nevus

- Bland pigmented nevus cells in nests.
- Conjunctival nevus cells feature. intranuclear cytoplasmic inclusions.
- Cysts are very common.
- Very rarely may lead to melanoma.

35 yo hispanic with eye pigment

Diagnosis?

35 yo hispanic with eye pigment

benign melanosis of the conjunctiva

- Pigmentation of the basal layer of the epithelium without a proliferation of melanocytes.
- Benign melanosis is a normal phenomenon in heavily pigmented individuals and statistical data suggest that pigmentation may be protective from UV exposure (i.e. dramatically lower incidence of PAM with atypia and conjunctival melanoma).
- There is increased pigmentation in the cells of the basal layer, i.e. squamous epithelium.

50 yo white man with pigmentation
primary acquired melanosis

- PAM is a term used to describe increased brown pigmentation of the conjunctiva, usually flat and speckled, associated histologically with an increased number of melanocytes in the epithelium.
- Most common in middle-aged persons.
- PAM without atypia is a histologic term denoting increased pigmentation within the epithelium with hyperplasia of the basal melanocytes lacking cytologic atypia.
- PAM with atypia denotes atypical melanocytes which may involve or replace the epithelium with spindle or epithelioid cells.

50 yo white man with pigmentation

40 yo woman with pigmented lesion

70 yo with conjunctival lesion

conjunctival melanoma

- Malignant tumor of melanocytes originating in the conjunctiva.
- The cause of conjunctival melanoma is largely debated but is strongly correlated with the presence of PAM, or acquired conjunctival lesions (manifested as detectable pigmentation), with atypia seen in these lesions.
- Conjunctival melanomas feature infiltration of the substantia propria by atypical pigmented cells with prominent nucleoli and abundant cytoplasm containing brown granular pigment. The tumor may show pagetoid infiltration of the epithelium and there is often accompanying primary acquired melanosis or a nevus.

40 yo woman with pigmented lesion

Diagnosis?
70 yo with conjunctival lesion

Diagnosis?

70 yo with conjunctival lesion

Diagnosis?

dysplasia of squamous epithelium of the conjunctiva (OSSN)

• Dysplasia of the corneal epithelium refers to abnormal maturation of the epithelium as it differentiates from the basal layer in the superficial layers.
• At low magnification the epithelium shows acanthosis, cellular crowding and altered cellular polarity without maturation. There is nuclear enlargement, dyskeratosis, and often mitotic figures above the basal layer of the epithelium. There may be pleomorphism and abnormal mitoses.

75 yo man with leukoplakic lesion on the eye

Diagnosis?

75 yo man with leukoplakic lesion on the eye

Diagnosis?

squamous carcinoma of the conjunctiva

• malignant neoplasm of conjunctiva characterized by invasion of the substantia propria and squamous differentiation
• Squamous carcinoma is strongly correlated to overexposure of the conjunctiva to ultraviolet light. The appearance of dysplasia has also been found to result from human papillomavirus type 16 (HPV 16).
Allergic conjunctivitis

- Allergic keratoconjunctivitis is a group of distinctive clinical disorders that are largely IgE-mediated hypersensitivity reactions but have quite similar histopathology. These disorders include Hay Fever Conjunctivitis, Vernal keratoconjunctivitis (VKC), and Atopic Keratoconjunctivitis.

- As seen in the photograph the epithelium is thickened and spongiotic (intercellular edema or separation of epithelial cells). There is dramatic hyperemia in the substantia propria and a chronic inflammatory infiltrate with numerous eosinophils. However, most important is the exocytosis of eosinophils within the epithelium.
oncocytoma of the caruncle

- Oncocytomas are benign tumors that arise most commonly in the caruncle or canthal conjunctiva but may also occur in the lacrimal glands (including accessory glands) and lacrimal sac.
- Oncocytomas are characterized by large eosinophilic cells that form glandular or ductular spaces. Between the ducts there are solid trabeculae of cells. The abundant eosinophilic cytoplasm and the relatively small round to oval nuclei that are located in the middle of the epithelial cell are key features.

50 yo woman with poor vision

Diagnosis?

Fuch's Corneal Endothelial Dystrophy

- Fuchs corneal endothelial dystrophy features loss of endothelial cells controlling proper endothelial pump function; thus, malfunction permits marked edema.
- The hallmark of Fuchs dystrophy is of course the guttata that can be seen clinically within Descemet's membrane.

25 yo woman with eye pain

25 yo woman with eye pain
25 yo woman with eye pain

Acanthamoeba keratitis

- Acanthamoeba protozoa most commonly cause infection in soft contact lens wearers who do not take appropriate precautions in cleaning and sterilizing their lenses.
- In most cases sections show a background of necrotizing keratitis with an interlamellar necrotic infiltrate. However, there may be little inflammation. The organisms have a double walled cyst in microscopic sections that is characteristic.

35 yo woman with eye pain

Diagnosis?

Herpes simplex virus stromal keratitis

- Herpes simplex virus keratitis is a viral infection of the cornea caused by Herpes simplex.
- One of the most frequent causes of corneal blindness in the United States.
- The inflammation is often granulomatous. The finding of giant cells and histiocytes on Descemet’s membrane or between Descemet’s membrane and the stroma should invoke a careful search for inclusions of Herpes keratitis.
Young contact lens wearer with loss of vision.

Another contact lens wearer with vision loss.

Third contact lens patient with eye pain.

21 yo man with eyelid lump

fungal Keratitis

- The incidence is less than 5% of corneal infections in the U.S. The most common organisms include Aspergillus, Candida, and Fusarium.
- Aspergillus and Fusarium are more common in the southern U.S. Candida makes up a greater percentage of fungal keratitis in the northern U.S.
- The hallmark of fungal keratitis is the necrotizing keratitis that in general is associated with both an acute and granulomatous inflammatory infiltrate.
- Aspergillus has septae and 45 degree branching.
- Candida exhibit budding yeast.
- Fusarium is usually distinguished by its thin hyphae with very rare septae and a right angle branching pattern.
**21 yo man with eyelid lump**

**Diagnosis?**

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**chalazion**

- Localized lipogranulomatous inflammatory condition that involves sebaceous glands of the eyelid presumably due to duct obstruction.
- The lesion features lipogranulomatous inflammation, the proper diagnosis given by pathologists for this lesion. Chalazion is a clinical diagnosis.

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**70 yo woman with an eyelid lesion**

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**70 yo woman with a second eyelid lesion**

**Diagnosis?**
seborrheic keratosis

- Benign neoplasm of the epidermis in which keratinocytes in G1 arrest are accumulated. The epithelial proliferation of the skin characterized by a stuck on appearance clinically and acanthosis and papillomatosis pathologically.
- The criteria used in the diagnosis are hyperkeratosis, acanthosis, and some degree of papillomatosis.

30 yo woman with lid lesion

Diagnosis?

Intradermal nevus

- Nests of nevocytes may be present at the epidermal-dermal junction (hence junctional nevus), confined to the dermis (intradermal) or both (compound). The nevus shown in the image is an intradermal nevus. Nests are composed of uniform cells with bland nuclei and variable amount of cytoplasmic pigmentation.

30 yo woman with lid lesion

Diagnosis?

Boy with fast growing lesion

Diagnosis?
molluscum contagiosum

- A viral infection, poxvirus, that produces one or multiple eyelid nodules.
- At low magnification the "domed papule" is divided into pear shaped nodules of proliferating epidermis which on the surface appear as volcanic micro craters separated by the epidermal lips of the crater. The characteristic and key feature is the presence of molluscum bodies also known as Henderson-Patterson bodies in the depths of the "volcanos".

70 yo woman with lid lesions

xanthelasma

- Xanthomatous inflammation of the eyelid.
- Sections show collections of histiocytes with microvesicular foamy cytoplasm clustered around vessels and adnexal structures within the dermis without significant numbers of accompanying lymphocytes or other inflammatory cells.

Diagnosis?
Syringoma

• Syringoma is considered a benign neoplasm of the eccrine ducts in the skin.
• Lesion features ductular structures and more solid appearing nests and strands that are present within the dermis. Occasionally the ducts have solid extensions that have been likened to a comma in shape.

60 yo man with lid lump

Diagnosis?

Eccrine hidrocystoma or ductal cyst

• Benign cystic lesion of the eyelid characterized by cuboidal epithelium and fluid content.
• The classic description features a cystic cavity with lightly eosinophilic staining material in the center. There is perhaps eosinophilic proteinaceous contents here although it is poorly defined. Eccrine hidrocystoma is lined by a double layer of cuboidal cells.
60 yo man with lid lesion

Diagnosis?

basal cell carcinoma

- Malignant neoplasm of the skin.
- The nests and strands exhibit peripheral palisading. Usually single cells ring the nests with their long axis oriented radially from the center of the nest creating a picket fence arrangement.
- Tumor nests exhibit retraction artifact where there is a cleft created from processing between the nests and the surrounding stroma.

77 yo woman with lid lesion.

Diagnosis?

Osmicate the tissues with osmium tetroxide. This can be done on formalin fixed material. One micron plastic sections are stained with toluidine blue.

77 yo woman with lid lesion.

Sebaceous carcinoma

- Sebaceous carcinoma is a malignant neoplasm arising in sebaceous glands that is characterized by extensive lipid production.
- Sebaceous carcinoma is considered the second most common malignant neoplasm of the eyelid accounting for about 5% of all primary eyelid malignancies (basal cell carcinoma 91%, squamous carcinoma 4% and malignant melanoma 1%).
- The demonstration of lipid within the cytoplasm of tumor cells by special stains is a prerequisite for the diagnosis: osmiate the tissues with osmium tetroxide (formalin fixed tissue) or oil red O or Sudan black staining (frozen sections).
30 yo man with glaucoma

angle recession

- Usually the result of blunt trauma to the eye.
- There is tearing of the ciliary body between the external longitudinal muscle fibers and the internal circular and oblique fibers.

70 yo woman with orbital mass

MALT Lymphoma

- MALT refers to mucosal associated lymphoid tissues. The MALT lymphoma is a proliferation of monocytoid B cells.
- By far this is the most common lymphomas of the conjunctiva and orbit.
- MALT Lymphoma is characterized by poorly defined follicular appearing areas that are composed of monocytoid B cells that feature enlarged nuclei.

2 yo boy with intraocular tumor
**retinoblastoma**

- Most common primary intraocular tumor in children.
- Chromosome 13
- Histologically, cells are blue, hyperchromatic, and surrounded by necrosis (i.e., blue cells in a sea of necrosis).
- Calcification can be seen in areas of necrosis.
- Flexner-Wintersteiner rosettes are characteristic of retinoblastoma; however, Homer Wright rosettes with the central neurofibrillary tangle can be seen in other neuroblastic tumors.

**70 yo man with metamorphopsias**

70 yo man with metamorphopsias

Diagnosis?

**Drusen**

- This is a photo of hard drusen featuring PAS-positive material located between the RPE and Bruch's membrane.

**50 yo man with intraocular tumor**

50 yo man with intraocular tumor

Diagnosis?

**choroidal melanoma**

- Intraocular tumor of melanocytic cells featuring spindle A, spindle B, epithelioid cells, or mixed cell types.
- HMB-45 and S-100 positive.
- Some tumors may not have much pigment.
- Look for spindle and epithelioid cells.
70 yo man with vision loss.

Diagnosis?

**giant cell arteritis**

- Granulomatous inflammation of small to medium sized arteries.
- Destruction of the internal elastic lamina.
- Giant cells can be seen associated with marked inflammation of the wall of the artery.

Thank you for your attention.