Biomarkers in Sebaceous Gland Carcinomas

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Outline

• Introduction to sebaceous cell carcinoma
• Incidence, demographics, risk factors
• Ocular origins
• Gross pathology
• Microscopic pathology
• Immunohistochemistry
• Management
• Cases

Introduction

• Sebaceous carcinoma (SC) is a malignant neoplasm that arises from the sebaceous glands, most commonly in the perifacial areas.
• Clinical manifestations are often mistaken for benign conditions and thus proper diagnosis and management is delayed.
• Metastases to regional lymph nodes and other sites are common.
Introduction
• Pathologists should be aware of the varied clinical manifestations, histopathological morphology and various biomarkers used for accurate diagnosis.
• Overview of the most important factors in periocular sebaceous carcinomas and biomarkers.

Definitions
• Sebaceous carcinoma (sebaceous gland carcinoma, sebaceous cell carcinoma) is a malignant neoplasm that arises from the sebaceous glands.
• Glands in these areas are named: Meibomian glands (eyelid) Zeis glands (cilia)
• Sebocytes: Foamy cells within the gland Produce sebum to regulate tear evaporation Precursor cell of sebaceous carcinoma

Extraorbital primary locations
• 75% of the cases arise in the ocular adnexae.
• Approximately 25% of sebaceous carcinomas arise from an extraocular region Parotid gland is the most common location.
• These tumors arise from two possible cells: pluripotent cells with capacity for sebaceous differentiation or from ectopic sebaceous cells that developed during embryogenesis

Incidence
• Periocular skin neoplasms account for 5-10% of all skin malignancies in the United States.
• Basal cell carcinoma - 90% of malignant eyelid tumors
• Sebaceous cell carcinoma - 5% of eyelid tumors
• Squamous cell carcinoma - 4% of eyelid tumors
• Melanoma - 1% of eyelid tumors
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Incidence
- Incidence of sebaceous carcinoma is 0.5/million in the Caucasian population older than 20-years-old in the US.
- Reports from China, India and other Asian countries indicate incidence of 31.2% - 39% of eyelid malignancies.

Demographics and Risk Factors
- Age: Mean age at diagnosis has ranged from 57 years to 72 years.
  - Sung details a case of one of the youngest patient on the literature to develop sebaceous carcinoma without syndromic disease at age 32.
- Sex: Approximately 70% of the sebaceous carcinomas occur in females.
- Irradiation: Several reports of patients with prior history of irradiation due to hereditary retinoblastoma treatment, acne, cutaneous hemangioma and eczema.
  - Rundle details a case in which a patient developed sebaceous gland carcinoma after being subject to irradiation for bilateral retinoblastoma.
  - The carcinogenic effects of irradiation are well documented.
  - The irradiation could affect the remaining RB gene and thus predispose the patient for secondary malignancies.
    - Osteosarcoma
    - Cutaneous melanoma
    - Sebaceous gland carcinoma

Ocular origins
- Meibomian glands: Most common origin
  - Upper eyelid is affected in 75%
  - Lower eyelid 22%
  - Conjunctiva 2%
  - Caruncle 2%

SEBACEOUS CARCINOMAS OF THE OCULAR ADNEXA:
A Clinicopathologic Study of 104 Cases, with Five-year Follow-up Data

- Retrospective study of 104 cases of sebaceous carcinoma of the ocular adnexa with at least 5 years’ follow-up
- Various clinicopathologic features that indicate poor prognosis were identified
**TABLE 1. CORRELATION BETWEEN LOCATION AND PROGNOSIS OF SEBACEOUS CARCINOMA**

<table>
<thead>
<tr>
<th>Location*</th>
<th>Fatalities/total</th>
<th>Mortality†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper lid</td>
<td>17/56</td>
<td>26%</td>
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<tr>
<td>Lower lid</td>
<td>0/25</td>
<td>0%</td>
</tr>
<tr>
<td>Upper and lower lid</td>
<td>5/5</td>
<td>83%</td>
</tr>
<tr>
<td>Caruncle</td>
<td>1/7</td>
<td>14%</td>
</tr>
</tbody>
</table>

* Precise location of the tumor in six cases was not specified.
† Difference in mortality between upper and lower lid location significant at $P < 0.05$.

**TABLE 6. CORRELATION OF DEGREE OF DIFFERENTIATION WITH MORTALITY OF SEBACEOUS CARCINOMA**

<table>
<thead>
<tr>
<th>Differentiation</th>
<th>Fatalities/Total</th>
<th>Mortality*</th>
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<tbody>
<tr>
<td>Well differentiated</td>
<td>5/54</td>
<td>9%</td>
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<tr>
<td>Moderately differentiated</td>
<td>12/40</td>
<td>30%</td>
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<tr>
<td>Poorly differentiated</td>
<td>6/10</td>
<td>60%</td>
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</table>

* Change in mortality with degree of differentiation significant at $P < 0.001$.

**Ocular origins**

- Zeis glands: Glands associated with cilia: 10% of SC of the eyelid.
- Caruncle: 5-10% of all SC (abundant sebaceous glands).
- Conjunctiva: SC of the conjunctiva with no involvement of the nearby skin structures (rare).

**Clinical Features**

- Commonly can masquerade as a benign condition, blepharitis/chalazion (“masquerade syndrome”).
  - Resulting in a delay in diagnosis.

- Increases the chance of local recurrence, metastasis, and death.

**Clinical Presentation**

- **Solitary nodule**
- Diffuse pseudoinflammatory pattern
- Pedunculated lesion
- Caruncular mass
Clinical Features

- Solitary eyelid nodule: Most common clinical manifestation.
- Painless, firm, sessile to round, subcutaneous nodule in the eyelid.
- Yellow color due to the presence of lipid.
- Loss of cilia (madarosis).

Clinical Presentation

- Solitary nodule
- Diffuse pseudo-inflammatory pattern
- Pedunculated lesion
- Caruncular mass

Clinical Features

- Diffuse pseudo-inflammatory pattern: The second most common presentation.
- Diffuse unilateral thickening of the eyelid.
- Most likely to extend to the epithelium.
- SC must be ruled out in an older patient with unilateral blepharitis that does not respond to standard treatment.

Clinical Presentation

- Solitary nodule
- Diffuse pseudo-inflammatory pattern
- Pedunculated lesion
- Caruncular mass

Clinical Features

- Pedunculated lesion: SC may become pedunculated with keratinization and possess a cutaneous horn appearance.
- Most common ocular location is the eyelid margin, from the gland of Zeis.

Clinical Presentation

- Solitary nodule
- Diffuse pseudo-inflammatory pattern
- Pedunculated lesion
- Caruncular mass
Clinical Features
Caruncular mass: Irregular, yellow mass in the medial canthal lesion. May replace the entire eyelid and involve the orbit.

Gross Pathology
- Yellow color due to the lipid deposition.
- Specimens may show origin in the tarsal plate.

Microscopic Pathology
- Cells with finely vacuolated, frothy cytoplasm
- Pleomorphism and high nuclear mitotic rate are frequent features
- Tumor cells often have hyperchromatic, atypical nuclei with foamy cytoplasm
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Microscopic Pathology
• A characteristic feature of SC is its ability to exhibit intraepithelial spread into conjunctival, eyelid and corneal epithelium, this occurs in 44-80% of the cases (pagetoid spread).

Microscopic Pathology
• Lobular pattern: Occurs more frequently and looks like a normal sebaceous gland with undifferentiated cells in the periphery and well-differentiated lipid producing cells centrally.

Microscopic Pathology
• Comedocarcinoma: Lobules show large necrotic central core with peripheral viable cells.

Microscopic Pathology
• Papillary: Occurs in conjunctival SC, with papillary projections and sebaceous differentiation.

Microscopic Pathology
• Papillary: Occurs in conjunctival SC, with papillary projections and sebaceous differentiation.
Methods of Spread

- Epithelial involvement: SC has been shown to exhibit flat, superficial involvement of the eyelid or conjunctival epithelium.
- Pagetoid spread because of the morphological similarity of pagetoid spread of intraductal breast carcinoma.

**Pagetoid spread**

Methods of Spread

- Regional metastasis: Most common route of metastasis is via lymphatic channels to regional lymph nodes.
  - SC of the upper eyelid tends to invade the preauricular and parotid nodes.
  - SC of the lower eyelid tends to metastasize to the submandibular and cervical nodes.
- Distant metastasis: Organs most commonly involved are lung, liver, bone, and brain.

Methods of Spread

- Corneal invasion: Sebaceous carcinoma with pagetoid spread from the bulbar conjunctiva to the corneal epithelium and stroma.
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Methods of Spread

- Perineural invasion

AJCC Cancer Staging

- Pathological classification
  - Tumor type
  - Differentiation (grade)
- Completeness of tumor removal
- Greatest tumor dimension
- Tumor margins

AJCC Cancer Staging - 8th edition

- Size < 10 mm, 20 mm
- Tarsal plate
- Eyelid margin
- Invasion of ocular or orbital structures

AJCC Staging - 8th edition

Definition of Regional Lymph Nodes (N)

- N0: No regional lymph node involvement
- N1: Single lymph node involvement
- N2: Multiple lymph node involvement

Definition of Distant Metastasis (M)

- M0: No distant metastasis
- M1: Distant metastasis

AJCC Prognostic Stage Groups

<table>
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<th>N Category</th>
<th>M Category</th>
<th>Stage Group</th>
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Grading

Grade IV

Recommended Approach

- Microscopic examination raises the prospect of SC
- Immunostaining for both EMA and p53
- If either EMA or p53 is positive then confirm with adipophilin staining
- A negative androgen receptor result can be used to rule out SC in a poorly differentiated tumor

Biomarkers in Sebaceous Gland Carcinomas

- A large variation of biomarkers exists with questionable utility.
- Experienced pathologists can usually confirm the diagnosis using morphology and immunohistochemistry is not necessary.

Immunohistochemistry

- Plaza et al. studied 27 cases of SC
  - Tissue microarray technique.
- Compared IHC results to 21 control cases of basal cell carcinoma (BCC) and 22 control cases of squamous cell carcinoma (SCC).

- EMA
- CK7
- Ber-EP4
- Factor VIII
- Androgen receptor
- p53
- Adipophilin
- Progesterone receptor membrane component 1 (PGRMC1)
- Squalene synthase (SQS)
- Alpha/beta hydrolase domain-containing protein 5 (ABHD5)

Epithelial membrane antigen

- EMA – Glycoprotein with extensive O-linked glycosylation of its extracellular domain.
  - Product of MUC1 gene
- Overexpression of the MUC1 gene is often associated with colon, breast, ovarian, lung and pancreatic cancers.
- Membrane staining

EMA

- Commonly used as a marker to evaluate:
  - Epithelial carcinomas
  - Meningioma
  - Paget disease
  - Systemic anaplastic large cell lymphoma vs cutaneous anaplastic large cell lymphoma

EMA in Sebaceous Carcinoma

- In the series by Plaza et al., 27/27 SCs were EMA-positive (100%).
- In 4 cases of SC, EMA was only focally and irregularly positive because these cases represented poorly differentiated lesions.
- All cases of BCC (21/21, 100%) were negative.
- SCC expressed EMA in 16/22 (72.72%) of cases.
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EMA in Sebaceous Carcinoma

- EMA is useful in differentiating SC from BCC.
  - EMA alone is not useful in differentiating SC from SCC.

CK7 in Sebaceous Carcinoma

- Plaza et al. found that
  - 24/27 (88.8%) of cases of SC
  - 2/22 (9%) of SCC
  - 6/21 (28.5%) of BCC expressed CK7.

- May be valuable in differentiating SC from SCC in most instances.

- CK7 is not a reliable marker to separate SC from BCC.

CK7 - SC

- Cytokeratin 7 is an intermediate filament protein
  - Low molecular cytokeratin (54 kDa)
  - Found in breast, lung, ovary, and urothelium but usually not in the GI tract or in stratified squamous epithelium
  - It is often used in conjunction with cytokeratin 20 in distinguishing ovarian, pulmonary, and breast carcinomas (CK7+) from colon carcinomas (CK7-).
  - Cytokeratin 7 shows cytoplasmic positivity in epithelial cell nests in a Brenner tumor.
Biomarkers in Sebaceous Gland Carcinomas

CK7 - BCC

CK7 - SCC

Ber-EP4

- EpCam (CD326) is a transmembrane epithelial adhesion molecule present on all non-squamous epithelial cells.
- Ber-EP4 targets EpCam

Ber-EP4

- Membranous staining
- Sensitive and specific for lung adenocarcinoma (positive) vs. mesothelioma (negative)
- Distinguishes metastatic adenocarcinoma to liver or cholangiocarcinoma (positive) from hepatocellular carcinoma (usually negative)


Ber-EP4 in Sebaceous Carcinoma

- Plaza et al. showed:
  - 7/27 (25.9%) of SC expressed Ber-EP4
  - 21/21 (100%) of BCC cases are positive (diffusely and strongly positive)
  - 22/22 (100%) of SCC are negative
- This suggests that Ber-EP4 is a reliable marker in differentiating SC (EMA+/Ber-EP4 +/) from BCC (EMA-/Ber-EP4+) and SCC (EMA+/Ber-EP4-)
- When used with other markers.

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- When used with other markers.
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Ber-EP4

Factor XIIIa

- Component of the final stages of the clotting cascade.
- Acts on fibrin to form cross links between fibrin molecules to form an insoluble clot.

Factor XIIIa

- Nuclear staining
- Positive staining in:
  - Soft tissue: benign fibrous histiocytoma and variants, malignant fibrous histiocytoma
  - Calcinifying fibrous tumor
  - Verruciform xanthoma
  - Atypical fibroxanthoma, hemangiopericytoma, myofibroblastoma in lymph nodes, pleomorphic hyalinizing angiectatic tumor, storiform collagenoma
  - Cervix: angiomyxoma
  - CNS: Erdheim-Chester disease

Clark et al. found consistent, strong nuclear staining in normal, hyperplastic and neoplastic sebocytes
He concluded: Useful marker to differentiate sebaceous from squamous carcinoma analyzing staining pattern.

Nuclear factor XIIIa staining (clone AC-1A1 mouse monoclonal) is a highly sensitive marker of sebaceous differentiation in normal and neoplastic sebocytes

Factor XIIIa
Factor XIIIA

- Plaza et al. found that none of the SC (0/27), BCC (0/21), or SCC (0/22) expressed Factor XIIIA.
- Discrepancy in these findings may be attributed to the clone or dilution of the antibody used.

Androgen Receptor

- The androgen receptor dimer binds to a specific sequence of DNA.
- Results in up- or down-regulation of specific gene transcription.
- Insulin-like growth factor I receptor (IGF-1R).

Androgen Receptor on Sebaceous Carcinoma

- Plaza et al. found different results compared to other studies:
  - 9/27 (33.3%) of the SC cases were positive.
  - 3/21 (14.2%) of BCC cases were positive.
  - 0/22 (0%) of SCC were positive.
- They concluded that nuclear expression of androgen receptor can be seen in BCC cases in a similar percentage.
  - Not a valuable marker to differentiate SC from BCC.

- Sensitive marker for sebaceous carcinoma:
  - AR positive in 19/19 (100%) cases of SC.
  - AR positive in 6/18 (33.3%) cases of BCC.
  - AR positive in 0/18 (0%) cases of squamous cell carcinoma.
- Along with other markers and morphology, AR can be helpful in the differentiation of SC from SCC and BCC.
p53 as a marker

- Tumor suppressor gene
- Induces cell cycle arrest
  - DNA repair or to force the cell to undergo apoptosis.
- Differentiate malignant conditions (p53+)
  - Carcinoma in situ
  - Invasive carcinoma
  - Others
- Reactive and metaplastic conditions (p53-)

p53 in Sebaceous Carcinoma

- Plaza et al. found that:
  - SC cases 12/27 (44.4%) expressed p53
  - BCC cases 4/21 (19%) expressed p53
  - SCC cases 3/22 (13.6%) expressed p53
- Not a recommended diagnostic marker in the differential diagnosis of SC, BCC, and SCC.

Adipophilin

- Assists with the storage of neutral lipids within the lipid droplet
- Expressed in sebocytes and sebaceous lesions
- Membranous labeling of intracytoplasmic lipid globules
- Also expressed in:
  - Lactating mammary epithelium
  - Adrenal cortex
  - Steatotic hepatocytes in alcoholic cirrhosis
  - Renal cell carcinoma
  - Hepatocellular carcinomas
  - Pancreatic carcinomas
  - Prostatic carcinomas
  - Liposarcomas

- Plaza et al. found adipophilin expression in:
  - 27/27 (100%) in cases of SC
  - BCC 16/21 (76.19%)
  - SCC 11/22 (50%) showed a granular uptake in the cytoplasm.
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Adipophilin

- The pattern of adipophilin expression can be useful in distinguishing SC from other periocular neoplasms.
- No cases of BCC or SCC showed membranous labeling of intracytoplasmic lipid globules.

Results - SC

- Significantly stronger adipophilin expression, a greater number of intracytoplasmic vacuoles, and larger vacuoles.
- The specificity and sensitivity of adipophilin immunostaining were both 100% when more than 5% of the staining occurred in vacuoles (>95% granular staining).
- Conclusions:
  - Histology remains the gold standard for diagnosis of sebaceous carcinoma.
  - Immunohistochemical assessment for adipophilin is a helpful diagnostic adjunct in the assessment of ocular adnexal neoplasms presumed to be sebaceous carcinoma.

Other lipid droplet proteins

- Alpha/beta hydrolase domain-containing protein 5 (ABHDC5)
  - The protein encoded by this gene belongs to a large family of proteins defined by an alpha/beta hydrolase fold
- PGRMC1: Protein which co-purifies with progesterone binding proteins in the liver and ovary.
- Squalene synthase (SQS) or farnesyl-diphosphate: farnesyl-diphosphate farnesyl transferase
  - Enzyme localized to the membrane of the endoplasmic reticulum.

Diagnostic Utility of Adipophilin Immunostain in Periocular Carcinomas

- Retrospective, histopathologic study
- Evaluated the efficacy of adipophilin immunohistochemistry in the diagnosis of sebaceous cell carcinoma of the ocular adnexal region
- 25 patients with sebaceous carcinoma, 21 with basal cell carcinoma, 22 with conjunctival squamous cell carcinoma, 9 with cutaneous squamous cell carcinoma, and 5 with conjunctival mucoepidermoid carcinoma.

Results: SC

- Plaza et al. found:
  - PGRMC1 was expressed in 22/27 (81.4%) of SC
  - SQS in 14/27 (51.8%) of SC
  - ABHDC5 in 19/27 (70.3%) of SC.
- BCC 0/21 (0%) or SCC 0/22 (0%) expressed none of these markers.
- PGRMC1, SQS, and ABHDC5 are therefore very specific but not very sensitive markers for the diagnosis of SC.
• Perforin stained strongly in 9/11 (81%) of the sebaceous neoplasms
  • 7/9 (77.7%) of the SC
  • 2/2 (100%) of sebaceous adenoma
  • The specificity of perforin in identifying sebaceous neoplasms versus SCC and BCC was 100% (95% CI 69–100).
  • Perforin better highlighted the intraepithelial spread of SC than EMA.
• The expression pattern of perforin in sebaceous neoplasms allows the use of perforin as a new immunohistochemical marker for sebaceous neoplasms.

Biomarkers in Sebaceous Gland Carcinomas

Summary of Immunohistochemistry

• Jakobiec et al - EMA, p53, adipophilin, androgen receptor are useful adjuncts for diagnosis of SC
• Plaza et al – adipophilin, ABHD5, PGRMC1, and SQS are novel markers specific for SC
  • Adipophilin is the most sensitive
• Millman et al - pattern and intensity of adipophilin immunostaining are helpful in distinguishing sebaceous carcinoma from other neoplasms with overlapping histology.

Differential Diagnosis

• Chalazion: Painful, tender, circumscribed nodule, without diffuse involvement that has similar appearance to SC.
  • Any patient with recurrent chalazia, especially in older individuals must undergo biopsy to rule out SC.

http://www.emedicinehealth.com/chalazion_lump_in_eyelid/page4_em.htm

http://eyepath.org.uk/atlas/chalazion/

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Differential Diagnosis

• Blepharitis: Common; diffuse inflammation of the eyelids
  • Often SC is misdiagnosed as blepharitis.
  • No madarosis

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Differential Diagnosis

• Conjunctivitis: Diffuse SC involvement of the palpebral, fornical and bulbar conjunctiva can appear as a conjunctivitis. Bilateral conjunctivitis is less likely to be SC.
Differential Diagnosis

- Keratoconjunctivitis: As SC progresses it may involve the corneal epithelium. It causes reactive inflammation around the neoplasms and thus it may resemble keratoconjunctivitis.

Differential Diagnosis:

- Basal cell carcinoma: Nodular form of BCC presents as a solitary nodule. Generally white, with vascular elevated margins with likely ulceration.
- Most commonly involves the lower eyelid.

Differential Diagnosis:

- Squamous cell carcinoma: Most common in upper lid. Associated with actinic keratosis. Conjunctival intraepithelial neoplasia (CIN) can be similar to diffuse epithelial invasion of SC.

Differential Diagnosis:

- Melanoma: Nodular or diffuse growth pattern. Generally pigmented with brown appearance, rather than the characteristic SC yellow. Amelanotic melanoma may resemble SC.
Differential Diagnosis:

- Merkel cell carcinoma: Solitary subcutaneous nodule in the upper eyelid of older individuals, with red or red-blue color.

**Biomarkers in Sebaceous Gland Carcinomas**

Merkel cell carcinoma: Solitary subcutaneous nodule in the upper eyelid of older individuals, with red or red-blue color.

http://www.pathologyoutlines.com/topic/skintumornonmelanocyticmerkelcell.html
http://webeye.ophth.uiowa.edu/eyeforum/cases/217-Merkel-Cell-Carcinoma-Eyelid.htm

Lymphoma: More common than SC. In the eyelid area, it is usually deep to the epidermis and the skin moves freely over the lesion. Conjunctival lymphoma has characteristic “salmon patch” with no inflammatory signs that are present in SC.

http://www.pathologyoutlines.com/caseofweek/case281.htm

Muir-Torre Syndrome

- Variant of autosomal dominant hereditary nonpolyposis colorectal cancer (HNPCC) syndrome or Lynch syndrome.
- Incidence: HNPCC occurs in about 1/350 individuals in the general population
  - Muir-Torre syndrome is evident in 9.2% of the cases and in 28% of families with HNPCC.

- Muir-Torre Syndrome
  - MMR genes:
    - Mutator S Homologue (MSH)2
    - Mutator L Homologue (MLH)1
    - MSH6
    - Postmeiotic Segregation Increased (PMS)2

- To diagnose Muir-Torre:
  - One characteristic from Group A and B or
  - Three characteristics from Group C

- Muir-Torre Syndrome: Sebaceous Adenoma
  - Benign growth that presents as a small, usually less than 0.5 cm in diameter (2-4 mm), smooth, yellow, spiculated papules with central umbilication on the skin of the face or scalp over several months.
  - Most common cutaneous manifestation of Muir-Torre (68%).
  - Multilobulated tumor sharply demarcated from the surrounding tissue. Central cells contain frothy and vacuolated cytoplasm.
**Sebaceous Adenoma vs. Sebaceous Carcinoma**
- 94 sebaceous tumors from 92 patients
- Tumors with strong p53 staining were significantly associated with the diagnosis of sebaceous carcinoma vs benign sebaceous lesions
- Nuclear mismatch repair protein expression was intact in all lesions showing p53 alterations
- Suggests p53 dysfunction may represent a divergent pathway in these tumors


**Signalling**
- Beta-catenin: coordination of cell-cell adhesion and gene transcription WNT-catenin overexpression is associated with increased tumor size invasion and metastasis
- P53: overexpression associated with tumor type and location
- P21: cyclin dependent kinase inhibitor; down regulation has association with lymph node metastasis
- Shh ABCG2: maintenance of stem cells in adult tissues; sonic hedgehog pathway; overexpression associated with aggressiveness and metastasis

**Sebaceous hyperplasia**
- A papule is an area of abnormal skin tissue that is less than 1 cm around.
- Usually a papule has distinct borders, and it can appear in a variety of shapes
- No malignant potential
- Risk factors: Sun exposure and old age

**Androgen receptor**
- Regulation of gene expression; increased activity inhibits p53 expression
- E-cadherin: suppressor of invasion and growth of epithelial cancers
- Lower expression-poor differentiation, high proliferation rate
- Promoter methylation-reduced survival, size >2 cm, lymph node mets, poor differentiation

**Signalling**
- Androgen receptor: regulation of gene expression; increased activity inhibits p53 expression
- E-cadherin: suppressor of invasion and growth of epithelial cancers
- Lower expression-poor differentiation, high proliferation rate
- Promoter methylation-reduced survival, size >2 cm, lymph node mets, poor differentiation
Management
• The first step is to establish the diagnosis and determine the extent of the disease
  • Skin
  • Conjunctiva
  • Cornea
  • Caruncle
  • Periocular tissue

• Palpation of head and neck nodes is advisable.

• Management options include: surgical excision, surgical excision combined with cryotherapy, topical chemotherapy, radiotherapy, amniotic membrane grafting and other techniques.

Management
• Primary excisional biopsy
  • It is generally preferred to perform a complete surgical excision of the lesion when the diagnosis is suspected.

• Cosmetic appearance is an issue to consider if the diagnosis is unclear
  • Incisional biopsy to confirm
  • Excisional biopsy afterward

Management
• Full-thickness, pentagonal, eyelid resection is favorable.
  • Margins are 5.0 mm on the nasal and temporal sides.

Map Biopsy
• Determines extent of disease.
  • Usually 10-15 biopsies are taken.
  • The most common method involves:
    • Eversion of the eyelids and taking four specimens from the palpebral conjunctiva
    • Six specimens from the bulbar conjunctiva.

Management
• Cryotherapy
  • Useful in cases of SC with pagetoid spread to the conjunctival surface.
  • It is used during map biopsies and during definitive surgical excision.

• Topical chemotherapy
  • Has been used in select cases of pagetoid spread involving the conjunctival epithelium.

Orbital Exenteration
• Widely believed to be the best option for SC that diffusely involves the conjunctiva and with invasion into the orbit.
  • Lid-sparing exenteration is an option that must be considered if the eyelid contains no tumor
  • Faster healing
  • Better fitting prosthesis
An 87-year-old female presented for evaluation of left eyelid redness for a couple of weeks.

**Case 1**

<table>
<thead>
<tr>
<th>Incisional Biopsy</th>
<th>Incisional Biopsy</th>
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</table>

**Basic Eye Exam**

- **Visual Acuity (Snellen - Linear):**
  - Right: 20/40E
  - Left: 20/20E

- **Pupils:**
  - Right: PERIL, RL.AYO
  - Left: PERIL, RL.AYO

- **Tonometry (Tono-pen, 1.35 PM):**
  - Right: Normal
  - Left: Normal

- **Pressure:**
  - Right: 15mmHg
  - Left: 10mmHg

1. Lacrimal system: normal
2. Conjunctiva: normal
3. Cornea: clear
4. Anterior Chamber: deep and quiet
5. Iris: round and flat
6. Lenses: posterior chamber irisscopic lens
7. Posterior Chamber: irisscopic lens

**Examination:**

- **External Exam:**
  - No lymphadenopathy
  - No lymphadenopathy

- **SLP Exam:**
  - No lymphadenopathy
  - No lymphadenopathy
Pathology report:

- M. Infiltrating basaloid neoplasm, conjunctival: infiltrating basaloid neoplasm in conjunctiva with pagetoid spread of sebaceous carcinoma (Site: nasal).
- N. Superficial spreading: sebaceous carcinoma with pagetoid spread of sebaceous carcinoma (Site: nasal).
- O. Infiltrating basaloid neoplasm, conjunctival: sebaceous carcinoma with pagetoid spread of sebaceous carcinoma (Site: nasal).
- P. Superficial spreading, conjunctival: sebaceous carcinoma with pagetoid spread of sebaceous carcinoma (Site: nasal).
- Q. Ciliary, right upper: Sebaceous carcinoma with extension to multiple margins of incision.
Case 2

- 74-year-old female who presents with recurrent chalazion of the left eye.

Map Biopsy
• Sebaceous carcinoma on the eyelids, palpebral conjunctiva, fornical conjunctival and corneal epithelium
• Marked amount of pagetoid spread.
Biomarkers in Sebaceous Gland Carcinomas

- CK7
- Ber-EP4 – stains epithelium
- p53
Biomarkers in Sebaceous Gland Carcinomas

Androgen Receptor

Factor XIIIA

Summary

- Sebaceous cell carcinoma has high morbidity/mortality and may be misdiagnosed as squamous cell and basal cell carcinoma
- Morphology remains most important for the diagnosis of sebaceous cell carcinoma
- Immunohistochemical stains including EMA, p53, adipophilin, and perforin; as well as CEA may be useful adjuncts in diagnosis

IHC Summary

<table>
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<tr>
<th>IHC</th>
<th>Result</th>
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<tbody>
<tr>
<td>EMA</td>
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<tr>
<td>CK7</td>
<td>++</td>
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<td>Ber-EP4</td>
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<tr>
<td>Androgen Receptor</td>
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<td>Factor XIIIA</td>
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<td>p53</td>
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The Online CME/Evaluations/SAMs claim process will only be available on the USCAP website until September 30, 2017.

No claims can be processed after that date!

After September 30, 2017 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.

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**References**