**Slide diagnosis/topic:** Periocular sebaceous carcinoma

**Case number:** MTT 5

**Name of Question writer:** Michael Tetzlaff MD PhD

**Image link:**

**Case vignette:** 72 year old man with a 6 month history of ‘blepharitis’ of the right lower eyelid, now also involving the upper eyelid. The tumor cells are are positive with antibodies for Cytokeratin 7, but negative with antibodies for Sox-10.

**Discussion of slide diagnosis:** Sections reveal eyelid with an intraepithelial proliferation of cytologically atypical epithelioid cells with voluminous cytoplasm and conspicuous intracytoplasmic vacuoles—many of which indent or scallop the nucleus. The tumor cell nuclei are enlarged, irregular and hyperchromatic. Nests of tumor cells also invade the underlying dermis/submucosa with an associated lymphohistiocytic inflammatory response.

Ocular adnexal sebaceous carcinoma (OASC) is an uncommon but aggressive carcinoma of the eyelid and ocular adnexa and accounts for ~5% of malignant epithelial eyelid tumors. OASC has a high propensity for multifocal intraepithelial and locally infiltrative growth that each contribute to frequent local recurrence, and metastases are estimated to occur in 10-20% of cases. Historically, up to 20% of patients with OASC die due to disease, although this incidence is currently lower. OASC often presents a clinical diagnostic difficulty because it mimics other more common inflammatory conditions of the eyelid, like blepharitis. Histopathologically, OASC may also present a diagnostic challenge as it also mimics other locally invasive carcinomas of the eyelid—notably, squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). As such, immunohistochemical (IHC) studies are central to an accurate diagnosis. Two important IHC markers that delineate sebaceous lineage (in the appropriate histopathologic context) are Adipophilin and Factor XIIa (AC-1A1 clone). Adipophilin is a protein expressed in lipid droplets in many normal cells (including sebocytes) and is frequently detected in sebaceous neoplasms, including OASC with a sensitivity of 97% and specificity of 95%. Factor XIIa (AC-1A1 clone) represents an additionally informative marker of sebaceous differentiation with a reported sensitivity between 73-100% and a specificity of 88-98%.(1-4)

**Question 1:** The best diagnosis is:

A. Basal cell carcinoma  
B. Squamous cell carcinoma  
C. Invasive melanoma  
D. Ocular adnexal sebaceous carcinoma  
E. Endocrine mucin-producing sweat gland carcinoma
Question 1: The best diagnosis is:

A. **Basal cell carcinoma**—Incorrect. Basal cell carcinoma does not show epithelial growth/pagetoid extension, and instead of nests of basaloid cells (with peripheral palisading of the basaloid cells) infiltrating the underlying dermis with a characteristic mucinous stromal reaction and retraction artifact.

B. **Squamous cell carcinoma**—Incorrect. Although squamous cell carcinoma (SCC) may exhibit cytoplasmic clearing, the tumor cells of SCC do not typically contain intracytoplasmic vacuoles that scallop the nucleus as seen in the current case.

C. **Invasive melanoma**—Incorrect. Melanoma may show a similar pattern of intraepithelial extension with pagetoid extension and invasion as seen in the current case, but intracytoplasmic vacuoles that scallop the nucleus are not typical of melanoma. Further negativity for Sox-10 excludes melanoma as a likely diagnosis.

D. **Ocular adnexal sebaceous carcinoma**—Correct. Sections reveal eyelid with an intraepithelial proliferation of cytologically atypical epithelioid cells with voluminous cytoplasm and conspicuous intracytoplasmic vacuoles—many of which indent or scallop the nucleus. The tumor cell nuclei are enlarged, irregular and hyperchromatic. Nests of tumor cells also invade the underlying dermis/submucosa with an associated lymphohistiocytic inflammatory response.

E. **Endocrine mucin-producing sweat gland carcinoma**—Incorrect. Endocrine mucin-producing sweat gland carcinoma (EMPSGC) typically consists of a dermal based proliferation of basaloid cells arranged as expansile multinodular nests with pushing borders usually with adjacent small pools of mucin within which variably sized nests of tumor cells usually are floating. In contrast to the current case, the tumor cells of EMPSGC are usually cytologically bland with round-oval nuclei with finely granular stippled chromatin and variable amounts of pale eosinophilic cytoplasm.

References: