Four-Eyelid Sebaceous Cell Carcinoma Following Irradiation

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Background: Sebaceous cell carcinoma is a distinctive tumor of the eyelid associated with a high rate of metastasis and mortality. Involvement of both upper and lower lids has been described; however, involvement of all 4 eyelids is extremely rare.

Objective: To describe the evaluation and diagnosis of the clinicopathologic features in a 74-year-old patient with 4-eyelid sebaceous carcinoma and a history of whole face irradiation for eczema.

Methods: Bilateral eyelid, conjunctiva, map, and fine needle biopsy of enlarged, submandibular lymph node specimens were stained with hematoxylin-eosin and oil-red-O for light microscopy and fresh-frozen sections were evaluated by electron microscopy.

Results: The biopsy specimens from the eyelids and conjunctiva showed sebaceous carcinoma cells in the meibomian glands and scattered within the conjunctival epithelium. The cells were moderately well differentiated. Similar cells stained with oil-red-O were found in the submandibular lymph nodes.

Conclusions: The appearance of bilateral sebaceous carcinoma supports the concept of simultaneous occurrence of multiple primaries in specific patients, especially after radiation therapy. Patients with a history of facial irradiation and atypical eyelid lesions should be evaluated for malignant tumors such as sebaceous carcinoma.


Sebaceous cell carcinoma is an uncommon eyelid malignancy, with a rate of incidence from 0.2% to 0.7% of all eyelid tumors and 1% to 5.5% of eyelid malignancies in the Western literature. Simultaneous involvement of both eyelids on one side occurs in 6% to 8% of the patients. In most cases it is probably due to intraepithelial spreading. This is the first report, to our knowledge, of a diagnostically challenging, 4-eyelid sebaceous cell carcinoma with a pertinent history of facial irradiation.

Report of a Case

A 74-year-old white woman complained of bilateral ocular irritation, tearing, and redness for 4 years. She had been treated for presumptive blepharoconjunctivitis and later was also suspected of having ocular cicatricial pemphigoid. The patient’s history was notable for juvenile facial eczema, treated with irradiation in the 1940s. Subsequently, she developed multiple facial basal and squamous cell carcinomas, mixed, low-grade, parotid tumor, and breast carcinoma. The medical history was otherwise unremarkable and there was no family history of malignancy.

The patient’s best-corrected visual acuity was 20/30 OD and 20/400 OS. Intraocular pressure was 17 mm Hg OU. Marked actinic changes of the face, irregular thickenings of all 4 eyelids, and madarosis were noted (Figure 1). A 3-mm, yellowish nodule was present on the left upper eyelid. Symblephara and conjunctival hyperemia were noted in both eyes. A diffuse, grayish, dull tint of the corneal epithelium was accompanied by a peripheral vascularized pannus covering 360° of the left cornea. Findings from regional lymph node examination revealed enlarged submandibular lymph nodes on the left side.

Computed tomographic scan of the head with contrast medium showed diffuse thickening of the left upper eyelid. Computed tomographic scan of the neck revealed enlargement of the submandibular, posterior triangle, and sternocleidomastoid lymph nodes on the left side. A bone and computed tomographic scan of the chest and abdomen showed no abnormalities.
The diagnosis of sebaceous cell carcinoma with pagetoid spread throughout the conjunctiva in both eyes was made following examination of full-thickness, bilateral eyelid and conjunctival map biopsy specimens. A fine needle biopsy of the enlarged submandibular lymph nodes, stained positively with oil-red-O, revealed tumor cells. The patient declined a total exenteration with radical neck lymph node dissection on the left side and radiation palliative treatment to the right side.

**HISTOLOGIC FINDINGS**

**LIGHT MICROSCOPY**

The sections from the eyelids demonstrated the tumor in the meibomian glands (Figure 2). The tumor cells contained vacuolated, pale-stained cytoplasm, hyperchromatic nuclei, and mitotic figures (Figure 3). The cytoplasm of these cells stained positively with oil-red-O. The conjunctival epithelium contained both normal appearing cells as well as atypical cells with large pleomorphic nuclei and frothy, vacuolated cytoplasm (Figure 4). The atypical nuclei appeared smudged in areas and elsewhere were indented by the cytoplasmic lipid packets. These cells were consistent with moderately well-differentiated sebaceous cell carcinoma. Spread of the tumor cells along the epithelium together with prominent mitotic figures was noted. Immunocytochemistry indicated that many tumor cells were reactive to anti-S100 antibody. Sebaceous carcinoma cells stained with oil-red-O were found in the cervical lymph node specimen (Figure 5).

**ELECTRON MICROSCOPY**

Both normal squamous cells with tonofilaments and tumor cells with lipidized cytoplasm were noted in the epithelial conjunctival layers. The abnormal pale cells were large and electronlucent compared with the usual dark epithelial cells (Figure 6). Numerous cytoplasmatic vacuoles containing lipids were seen in the pale cells. Free ribosomes, scattered tonofilaments, occasional desmosomes, and some cells that contained myelinlike figures were also noted. The nuclei were often lobulated and indented, and were more vesicular than those of the surrounding dark epithelial cells.

**COMMENT**

Simultaneous appearance of upper and lower eyelid sebaceous carcinoma occurs in 6% to 8% of patients. When it occurs, both upper and lower eyelids of the same eye are involved and the tumor is rarely bi-
In most cases, malignant epithelial cells in the conjunctiva (oncorrhea) can be explained by intraepithelial con-
junctional spreading, spontaneous development of multiple primaries, or even implantation of tear-floating,
nonocular malignancies.8,9 Our patient had multiple basal and squa-
mous cell carcinomas and a parotid gland tumor in the irradiated area.

The prognosis of 4-eyelid seba-
ceous cell carcinoma is worse than for carcinoma of 1 or 2 eyelids. The pres-
ence of tumor cells in the conjunctival epithelium is associated with an even poorer prognosis.10 The treat-
ment of choice for this tumor is a complete excision, usually by exen-
teration; however, when all eyelids and cervical lymph nodes are in-
volved, the disease is incurable. As an alternative to observation, a pallia-
tive treatment may be performed by exenteration with radical neck dis-
section of the more involved side and radiation therapy of the opposite side.

Sebaceous cell carcinoma can masquerade as an inflammatory con-
dition such as blepharitis, blepha-
roconjunctivitis, meibomianitis, ocu-
lar cicatricial pemphigoid, and recurrent chalazion.1 Malignancy should be suspected for any atypi-
cal unilateral inflammatory eyelid disorder unresponsive to medical therapy. When it is bilateral, accurate diagnosis is more challenging. Eyelid irregularities and thickening on palpation followed by contour irregularities and obvious masses may be the earliest clues for a correct diagnosis of meibomian gland carcinoma. We suggest that any unusual inflammatory eyelid dis-
order in an elderly patient, whether bilateral or unilateral, should be evaluated as a potential malignant condition, especially if the patient has a history of irradiation. A prompt, full-thickness, eyelid biopsy for frozen sections and lipid stains should be obtained.

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