

Clinics in Dermatology

# Eyelid and ocular surface carcinoma: Diagnosis and management



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**Abstract** Eyelid cancers account for 5% to 10% of all cutaneous malignancies. The incidence of eyelid cancer is approximately 15 cases per 100,000 individuals per year. Basal cell carcinoma is by far the most common cutaneous malignancy in the periocular area; other cutaneous malignancies that occur in this area include, in decreasing order of frequency, squamous cell carcinoma, sebaceous carcinoma, melanoma, and Merkel cell carcinoma. The most common treatment for eyelid carcinomas is surgical resection with frozen section examination for margin control, but exenteration may be needed when there is orbital invasion. Adjuvant radiotherapy may be needed in patients at high risk for local recurrence; sentinel lymph node biopsy may be considered in patients at high risk for lymph node metastasis. Primary or residual *in situ* disease of the conjunctiva can be treated with topical chemotherapy, such as mitomycin C, 5-fluorouracil, or interferon alpha-2 b. For patients with metastatic or locally advanced basal cell or squamous cell carcinoma not amenable to surgical excision or radiotherapy, targeted therapy against the hedgehog pathway (for basal cell carcinoma) or epidermal growth factor receptor (for squamous cell carcinoma) has been shown to be effective in preventing disease progression. Patients with eyelid and ocular surface malignancies need to be monitored with careful clinical examination for at least 5 years after surgical treatment, and additional investigations may be warranted in some cases.

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#### Introduction

Reported age-adjusted incidences of eyelid malignancies range from 5.1 cases per 100,000 individuals per year in Singapore<sup>1</sup> and 6.5 cases per 100,000 individuals per year in Taiwan<sup>2</sup> to 15.7 cases per 100,000 individuals per year in the United States.<sup>3</sup> Basal cell carcinoma (BCC) is by far the most common of all eyelid malignancies, accounting for 86% to 96% of all cases; squamous cell carcinoma (SCC) accounts for 3.4% to 12.6% of cases, sebaceous carcinoma (SebCa) for 0.6% to 10.2%, and melanoma and Merkel cell carcinoma (MCC) for less than 1% each.<sup>1–6</sup> SebCa is more common in Asia than in other parts of the world, and in some regions of Asia, SebCa is actually more common than SCC.<sup>2</sup>

Eyelid malignancies require different considerations from other cutaneous malignancies of the same cell type due to the unique anatomic considerations in the periocular region and the functional impact of surgical resection and reconstruction on ocular protection and visual function. The management of

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eyelid malignancies is dependent on histopathologic type and disease stage according to the American Joint Committee on Cancer (AJCC) staging system. The standard treatment is surgical excision with negative margins. In patients at high risk for local recurrence, adjuvant radiotherapy may be needed; and in patients at high risk for lymph node metastasis, sentinel lymph node (SLN) biopsy may be considered. In some instances, topical chemotherapy may be considered. Therapy needs to be tailored in each case.

#### Basal cell carcinoma

The incidence of BCC is approximately 14.35 cases per 100,000 individuals per year, age and gender adjusted, according to an epidemiologic study in Olmsted County, Minnesota, published in 1999.<sup>3</sup> BCC typically appears at presentation as a nodule with pearly edges, central ulceration, and telangiectatic vessels (Figure 1). Risk factors for BCC include sun exposure, advanced age, immunosuppression, fair skin, and smoking in women<sup>7</sup>; the incidence of BCC is also increased in patients with xeroderma pigmentosum and Gorlin-Goltz syndrome.<sup>8</sup>

Histopathologically, the nodular subtype is the most common subtype of BCC, accounting for 43% to 77% of cases, and is classically described as consisting of nests of basophilic cells with peripheral pallisading.<sup>9–11</sup> The infundibulocystic subtype of BCC is more common in patients with Gorlin-Goltz syndrome, basal cell nevus syndrome, or HIV.<sup>12,13</sup> The sites of periocular involvement with BCC, from most to least common, are the lower lid, medial canthus, upper lid, and lateral canthus.<sup>10,11</sup> The morpheaform subtype and medial canthus location are associated with a higher rate of incomplete resection, which is associated with a higher likelihood of local recurrence.<sup>10</sup> Medial canthal



**Fig. 1** Large basal cell carcinoma involving the left medial canthus, nasal bridge, and glabella showing extensive ulceration and elevated pearly edges (arrow).

location is also associated with a higher risk of orbital involvement and, thus, a higher likelihood that orbital exenteration will be needed.<sup>11,14,15</sup>

After complete resection of BCC with negative margins, the rate of local recurrence is less than 1% at 5 years of follow-up; however, with incomplete excision, the local recurrence rate can be as high as 38% at 5 years.<sup>16–18</sup> Recurrence is more common with the morpheaform subtype: The 5-year recurrence rate is reported to be as high as 3.8%, even after resection with negative surgical margins.<sup>9</sup> The rate of metastasis of BCC is extremely low, .03%, and the disease most commonly metastasizes to the regional lymph nodes.<sup>19</sup> Perineural invasion is found in 19% of patients with orbital invasion by BCC.<sup>15</sup>

#### Squamous cell carcinoma

SCC arises from abnormal keratinocyte proliferation. SCC most commonly appears in the sixth or seventh decade of life. SCC may often appear at presentation as a raised nodule or plaque with overlying scaling, induration, keratinization, or ulceration (Figure 2, Figure 3B).

Men are affected two or three times as often as women. The most common periocular sites of SCC involvement are the lower eyelid and medial canthus; however, tumors often span more than one periocular skin zone.<sup>20</sup> Risk factors for SCC include fair skin, exposure to ultraviolet light, immunosuppression, exposure to radiation, a high-fat diet, exposure to chemicals (such as hydrocarbons and arsenic), and infection with human papillomavirus.<sup>21,22</sup>

SCC may arise *de novo* or from areas of preexisting actinic or solar keratosis and is characterized by invasion by atypical keratinocytes. The degree of keratinocyte dysplasia can range from partial-thickness keratosis to full-thickness



**Fig. 2** Squamous cell carcinoma of the right medial lower eyelid in an 84-year-old Caucasian man that showed slow growth over at least 1 year. The plaque-like tumor is associated with overlying scaling and keratinization.

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