A Clinical Masquerader: Squamous Cell Carcinoma of the Eyelid Previously Diagnosed as an Eye Bump

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Abstract

Malignant eyelid tumors are often difficult to diagnose at an early stage and can be clinically challenging. Due to the high prevalence of periocular skin cancers, clinicians must be very attentive in their assessment of skin lesions. An 83-year-old male with no history of malignancy presented with a non-healing and rapidly growing lesion of the left lower eyelid. After an oculoplastics referral, the patient was diagnosed with squamous cell carcinoma with no metastasis or invasion to deep-layer tissue. Management required exenteration of the left eye socket followed by radiation therapy.

This case illustrates the clinical course and invasive nature of periocular squamous cell carcinoma. While it can present in a variety of different forms, most are painless, hyperkeratotic lesions that progressively change and ulcerate. An extensive history and careful clinical examination are vital to detect malignancy in a timely manner.

KEY WORDS:
eyelid neoplasm, squamous cell carcinoma, metastasis, radiation therapy, oculoplasty
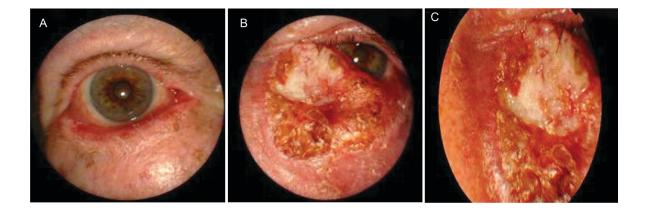
INTRODUCTION

Periocular skin cancers account for over 90% of all ophthalmic tumors.[1,2] Periocular malignant eyelid tumors represent unique challenges to clinicians as they are often difficult to recognize and diagnose in the early stage of presentation.[3] In particular, squamous cell carcinoma (SCC) can present in a variety of different forms, but is mostly seen as painless, hyperkeratotic lesions that progressively change and ulcerate.[3] In the diagnosis of SCC, an indentation or erosion of the eyelid margin, or a scaly nodule, may be observed.[4] Other signs can include madarosis, telangiectasia, ulceration, distortion of the eyelid margin, increasing pigmentation, and secondary ectropion or retraction.[1] These malignant eyelid lesions are more likely to be located on the lower lid than in the upper, medial, or lateral canthal regions.[3] Clinicians must be aware of these clinical indications for SCC since they have the potential for malignant metastasis and are the second-most common eyelid malignancy. They account for 5-10% of all eyelid malignancies, with an incidence of 0.09-2.42 cases per 100,000.[5] Timely diagnosis is imperative as malignant lesions can invade and metastasize quickly by perineural and regional lymph node involvement. Metastasis rates range from 10% to as high as 20-25%.[6] SCC, as a neurotrophic tumor, can infiltrate into the perineural space within the periocular region, defined as perineural invasion (PNI).[2] High densities of motor and sensory nerves are located within this region, which subsequently allow SCC to spread into the orbit and intracranial cavity along branches of the trigeminal, facial, and extraocular motor nerves.[5,7,8]

CASE REPORT

An 83-year-old white male presented to his primary care provider (PCP) with a new non-healing lesion on his left lower eyelid. He described this as an initial bump that progressed and enlarged over several months. The PCP pre-scribed oral antibiotics for suspected ocular cellulitis. After a few days, there was no clinical improvement, and the patient was referred to our eye clinic. His medical history was positive for Myasthenia Gravis (20+ years), hypergly-cemia, chronic osteoarthritis, hypertension, and chronic obstructive lung disease. His ocular history was positive for ocular myasthenia, cicatricial ectropion, and age-related cataracts.

On initial presentation, the patient reported that the eyelid lesion had enlarged over the past few weeks and had begun to drain since he saw his PCP. Clinical examination revealed a mild reduction in best-corrected visual acu-ity (BCVA) to 20/30 OD, and 20/25 OS due to age-related cataracts. Confrontation visual fields were full to finger counting OD, and revealed severe nasal constriction OS. Pupils and extraocular muscles were normal OU. External slit-lamp exam OD showed cicatricial ectropion, but otherwise was normal-for-age (Fig. 1A). External slit-lamp exam OS revealed a large lower-eyelid ulcerating mass (2.0 cm x 2.1 cm) with scant mucoid white discharge and sharp defined borders (Figs. 1 B,C). This mass correlated with the constriction in his field of vision. The conjunctiva was white and quiet OD. The lower puncta OS was not visible, and it was suspected that the lesion had invaded both upper puncta and the lower fornix. Dilated fundus exam was normal-for-age OU.

Figure 1: *(A) External adnexa OD showing cicatricial ectropion. (B) External adnexa OS showing an ulcerating mass (2.0 x 2.1 cm) with scant mucoid white discharge and sharp defined borders. (C) Magnified view of the ulcerating mass in (B).*
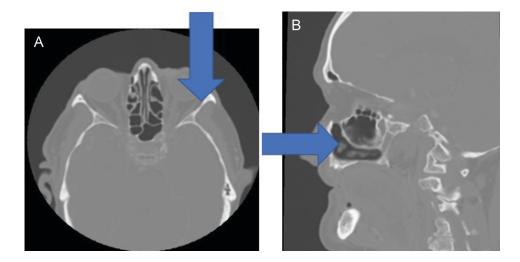

The patient was immediately referred to an oculoplastic surgeon for evaluation. Excisional biopsy and CT of the orbits were ordered for the patient. After a review of the pathology report, the patient was diagnosed with malignant left lower-lid SCC. Furthermore, CT of the orbits showed a large, ill-defined enhancing soft tissue mass arising from the left medial canthus involving the left lower eyelid and extending into the inferior left orbit (Figs. 2 A,B).

The patient and oculoplastic surgeon discussed management options, and it was decided to exenterate the left eye socket followed by radiation therapy (XRT). Surgery was completed successfully. At a follow-up exam 2 weeks after surgery, the left eye was healing well and showed tumor-free margins with no evidence of bone erosion. At a one-month post-operative follow-up, it was determined that the patient maintained tumor-free margins. After a few more routine post-operative follow-up visits, the patient was sent back to our eye clinic as the condition remained stable. As the patient was coping with loss of his left eye, he reported poor depth perception. This led to having difficulty with activities of daily living. He had trouble with near tasks, eating, and loss of sensation on the left side. The patient was then seen in our low-vision clinic and evaluated by our home-based primary care occupational therapist. He was issued hand-held magnifying devices to assist with reading, and issued filters for glare control and contrast enhancement.

At 5 months following surgery, the patient was doing well and adjusted to routine life. He continued to see the oculoplastic specialist every six months, and reported no additional recurrence. External photos were obtained at this time (Figs. 3 A,B), and showed a stable appearance and wound healing. Furthermore, the patient reported increased sensation in his left facial region. Home-based primary care therapy resulted in significant improvements with his ability to perform daily tasks such as grooming and eating. At one-year follow-up, the patient was coping well with his vision loss, and could perform activities of daily living independently. Slit-lamp examination revealed a stable healing socket (Figs. 4 A,B). Additional appointments were co-managed with the oculoplastic specialist. He was advised to use erythromycin ointment as needed. According to the oculoplastic specialist, he will be a candidate for a prosthetic eye in 16 months.

Figure 3: (A) External photo 5 months after exenteration OS. There is a chronic mucoid reaction that has been managed with bacitracin. (B) OS orbital socket, showing the mucoid reaction.
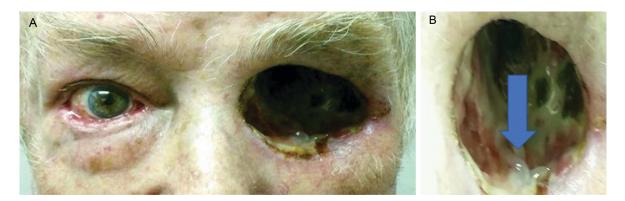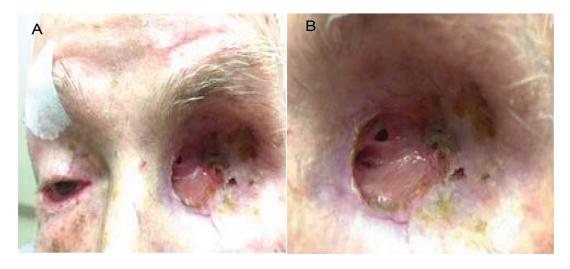
Figure 4: *(A) External photo 12 months after exenteration OS. (B) Magnified view of the well-healed orbital socket post-exenteration.*

DISCUSSION

Case comparison to the literature

As previously mentioned, our patient experienced a progressive eyelid lesion with obstruction of the visual axis and ulcerative bleeding. Initially, the lesion was scabby and ulcerative, and measured 2.0 x 2.2 cm. After microscopic and histopathological analyses from the left inferior-medial orbital and eyelid biopsy, an infiltrating SCC mass was confirmed. It was apparent from these results that the tumor was diffuse and deep, and would require exenteration for complete removal. Exenteration of the left eye socket, followed by radiation therapy (XRT) was performed. The patient was tumor-free after treatment and is currently being monitored closely for recurrence.

Arora et al. reported a case of SCC of the lower eyelid, where they found a 6.0 x 5.0 cm ulcerated and exophytic lesion.[3] The lesion, which was initially very small, progressed into an ulcerative lesion over two years before it was finally evaluated. After incisional biopsy and histopathological analysis, SCC was confirmed. Since the lesion engulfed the globe and retrobulbar contents as evidenced on CT, local excision and orbital exenteration were performed. Postsurgical lesion histopathology confirmed tumor-free surgical margins.[3]

Vrcek et al. described a non-resolving eyelid mass that enlarged over the course of six weeks.[8] The mass was initially diagnosed as a chalazion that did not improve under a 10-day course of oral trimethoprim and sulfamethoxazole. It was then referred for further evaluation. The mass measured 2.0 x 2.3 cm with mucoid discharge and thinning of the overlying skin.[8] The mass was then treated by the intralesional injection of 0.5 ml of 10 mg/ml triamcinolone acetonide injectable. Although it decreased in size, the lesion remained and was subsequently biopsied. Histopathological results revealed cutaneous SCC with deep invasion, hyperkeratosis, and parakeratosis with all margins positive for tumor. The patient's medical metastatic workup was negative. The patient underwent Mohs surgery with oculoplastic repair. At the conclusion of Mohs surgery, the surgical margins were negative for tumor and the defect measured 3.0 x 1.5 cm.[8]

The management in our case was very similar to that described by Arora et al. in that both cases required orbital exenteration to ensure tumor-free surgical margins. This was due to the advanced nature of the tumor. Meanwhile, Vreck et al. required Mohs surgery with oculoplastic repair, and achieved tumor-free margins. Despite the differences in the management of these cases, both treatment modalities were successful options to ensure tumor-free margins.

Spread and metastasis

SCC has the potential to be a life-threatening disease. The lesion must be removed before perineural invasion and metastasis can occur. Although periocular SCC is less prevalent than basal cell carcinoma (BCC), it has a higher potential for orbital invasion. Orbital invasion has been documented and diagnosed in up to 5.9% of all cases. Meanwhile, BCC has an orbital invasion rate of 1.6-2.5%.[5,9-13] Risk factors associated with orbital invasion include, but are not limited to, neglected untreated ulcerated lesions, an ulcerated lesion with extraocular muscle restriction, epiphora, dysesthesia, a history of recurrent lesions, and radiotherapy treatment.[5,13] Outside the clinical presentation of SCC of the eyelid with orbital involvement, the clinician must also rule out paranasal sinus involvement, which is also a common cause of orbital invasion from SCC.[5,9-13]

Another way SCC could metastasize is through perineural spread, which is tumor growth in and around a nerve. When present, the prognosis is poor, with a high mortality rate. As previously discussed, SCC is a neurotrophic tumor and can infiltrate the orbit and intracranial cavity along branches of the trigeminal, facial, and extraocular motor nerves.[5,14] A major reason to diagnose and assess all anomalous eyelid lesions is that patients with SCC and PNI are asymptomatic 60-70% of the time. Others may have symptoms of anesthesia, dysesthesia or paresthesia, and pain or facial weakness causing debilatation.[2,14,15] If left untreated, the natural course of periocular SCC with PNI is spread along the supraorbital and infraorbital nerves to the orbital apex. This could then result in ptosis, ophthalmoplegia, and vision loss.[5,16-19] Once spreading occurs past the orbital apex, there is a high fatality rate if it invades the cavernous sinus, meninges, or middle or posterior cranial fossa. Despite the potential for periocular SCC tumors to cause orbital and intracranial spread, this can also be caused by other cutaneous lesions in the head and neck, or sometimes the primary lesion is never found. If PNI is suspected, aggressive adjunctive therapy with radiation is recommended.[5,16-18] Late-stage SCC spread and metastasis occurs through the regional lymph nodes to distant sites through the lymphatic system and bloodstream. The rates of metastasis with SCC can vary within a wide range.[5] If metastasis occurs through the lymphatic and hematogenous systems, there is a worse prognosis and higher mortality rate.

Tumor removal
After the initial diagnosis of SCC, a tactical management plan should be established for the patient. Since various options are available for eradication of the lesion, risk factors regarding the lesion should be evaluated to ensure the best method of removal. Tumor characteristics that must be considered include location, grade, histological subtype, PNI, and metastasis. Other considerations when developing a proper treatment plan is to consider the best technique to completely eradicate the lesion, while preserving tissue function and cosmesis.[5] In the presence of high-risk tumors or those with metastasis and perineural invasion, aggressive treatment should be initiated. There should be less concern for function and cosmesis in these cases, as these risk factors have a higher rate of mortality.[5,20] Also, once the tumor is removed, long-term follow-up for a minimum of five years is advised, since 95% of local recurrence and metastasis will develop within this time frame.[5,21]

Standard removal
Due to the aggressive nature of SCC, frozen microscopically controlled section or Mohs micrographic surgery (MMS) surgical excision is the treatment of choice in most cases, as it has the highest cure rate and lowest 5-year recurrence rate (1.9-3.9%).[5,22,23] These techniques detect and excise tumor cells beyond the clinical margins and examine close to 100% of the peripheral and deep tumor margins.[5] These techniques are supported by a study by Brodland and Zitelli in which they found that surgical excision with 4-mm margins was required to achieve greater than 95% of tumor clearance.[24] In larger lesions, i.e., greater than or equal to 20 mm, or those with higher risk, surgical excision with 6-millimeter margins is recommended.[5,24] When margin control is not considered in SCC removal, there is a higher rate of 5-year recurrence, ranging from 5% to 18.7% for primary tumors in all locations.[5,25,26] In addition, standard frozen sections with broadleaf sectioning only examine less than 1% of these peripheral and deep margins.[5,26]

In the presence of perineural invasion, MMS is recommended as the initial treatment of choice. Post-operative radiotherapy or chemotherapy is then recommended to improve the effectiveness of the overall treatment and to reduce recurrence.[5,18] Once orbital invasion occurs, treatment options are limited due to the severity and advanced stage of the condition. At this point, exenteration with microscopic analysis of peripheral and deep margins is recommended, since orbital invasion has a higher risk for morality. Due to rare recurrence after exenteration, this procedure increases the rate of survival of patients at this stage of SCC.[27]

Other modalities and limitations
Radiotherapy, when performed as monotherapy, has a 5-year recurrence rate of 12.5% for eyelid SCC, and up to 50% for recurrent or advanced lesions.[26] It lacks histological control compared to MMS, and has a higher rate of periocular complications after treatment. In addition to post-operative periocular complications, radiotherapy has carcinogenic potential and must be used with caution in young patients.[2,27] Radiotherapy is most useful as adjunctive therapy in high-risk tumors, or those with perineural involvement and metastasis.[5, 28] It is used when local and regional control are needed, which can reduce the mortality rate, or in palliative control of advanced tumors.[5,29]

Chemotherapeutic agents have been shown to be very effective as adjunctive therapy in advanced cases, but can also be used as the primary treatment in patients where surgery cannot be tolerated.[5,30,31] Studies have shown an increased survival rate with chemoradiation. Chemotherapeutic agents are most useful in treating advanced head and neck SCC.[30,31] Cryotherapy, curettage, cautery, and various systemic retinoids are often used to remove small, low-risk lesions, but provide minimal benefit for high-risk aggressive SCC periocular lesions due to their suboptimal cure rate.[5,32]

Eyelid reconstruction and cosmesis

A detailed overview of eyelid reconstruction is beyond the scope of this manuscript. Instead, we will provide only a very brief explanation of eyelid reconstruction. Once an invasive periocular tumor is removed, the orbital architecture could be left dismantled, or completely removed through exenteration. This can present the reconstructive surgeon with several challenges in restoring eyelid function and cosmesis.[1] Small eyelid defects are closed directly and left to heal, with satisfactory results. Larger defects usually require reconstruction of the lamellae with a skin graft or flap.[1] Flaps are preferred over grafts because the former have better blood supply, contract less, provide better cosmetic color, do not allow violation of the distant donor site, and thickness can vary.[1] When exenteration takes place, referral for an ocular prosthesis will provide the patient with proper cosmetic results.

CONCLUSION

SCC is an aggressive skin cancer with a high mortality rate if perineural invasion, metastasis, and/or lymphatic involvement occurs. Timely diagnosis and biopsy are imperative for improved prognosis and a lower mortality rate. Because SCC can masquerade as other skin neoplasms, the practitioner must be aware of early signs associated with SCC. These include a painless, hyperkeratotic lesion that progressively transforms and ulcerates. The clinician must also be aware of other signs, including madarosis, telangiectasia, ulceration, distortion of eyelid margin, increasing pigmentation, and secondary ectropion or retraction. The gold standard for treatment is frozen microscopically controlled section or Mohs micrographic surgical excision. If an advanced tumor is suspected, orbital exenteration is recommended. In support of this protocol, our case involved orbital exenteration followed by adjunctive radiation therapy, Arora et al. reported local excision followed by orbital exenteration, and Vrcek et al. reported MMS with oculoplastic repair. All three of these cases resulted in a favorable prognosis and a low mortality rate, as all patients were tumor-free after treatment. Lastly, regardless of which treatment modality is used, clinicians must monitor the patient for recurrence for a minimum of five years, especially when MMS and orbital exenteration are not performed. ●

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