Basal Cell Carcinoma: A Series of Cases Optometry Should Not Miss

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Abstract

Basal cell carcinoma (BCC) is a highly prevalent non-melanoma skin cancer that exhibits potentially lethal behavior when left untreated. Since the number of cases is rising each year secondary to ultraviolet light exposure, eye care clinicians can expect to encounter many cases of BCC throughout their professional careers. Because the lids and periocular adnexa are considered to be at high risk due to sun-exposure, optometrists are well-positioned to recognize and refer patients for treatment prior to the development of significant cosmetic and life-threatening damage. This report describes three cases that were suspected to be BCC in varying facial locations and presents a review of clinical features and appropriate treatment options.

KEYWORDS:

skin cancer, eyelid, basal cell carcinoma, ultraviolet radiation, Mohs micrographic surgery, dermatology, optometry

INTRODUCTION

Basal cell carcinoma (BCC) is one of the most common malignancies in the world with a lifetime risk of 20% and more than four million new cases annually in the United States alone.[1] Despite these significant numbers, it is likely that BCC is even more prevalent: reliable statistics are limited because many national and international cancer registries exclude non-melanoma skin neoplasms (NMSN) from their records.[2] It is estimated that BCC has risen in prevalence by 20 to 80% over the past 50 years and these numbers are expected to continue rising as a result of prolonged life expectancy and heightened exposure to ultraviolet (UV) radiation secondary to sun-seeking behaviors, such as tanning.[3, 4] Although BCC is slow-growing and rarely metastasizes, undiagnosed lesions have a propensity to become highly infiltrative and create significant structural and cosmetic damage.[5] Primary eye care providers, including optometrists, are ideally positioned to identify suspicious skin lesions in the high-risk facial area, and should be well-versed in the identification and treatment of BCC to ensure the proper care of affected patients. The following is a brief case series consisting of a basal cell masquerader followed by two presentations of basal cell carcinoma of increasing severity, and a review of clinical features and various treatment options for BCC.

CASE SERIES

Case 1

A 78-year-old white female presented to the clinic seeking treatment for a persistent stye that had developed approximately one month previously. The patient stated that this lesion had grown in size over the past month and noted that it now felt tender to the touch. The patient's family history was significant for basal cell carcinoma of the face, though the patient was unable to confidently recall the exact familial relation. At the time of the exam, the patient's pinhole visual acuity was 20/20 in the right eye (OD) and 20/25 in the left eye (OS). All further examination components were unremarkable, except that slit lamp examination was significant for an unevenly pigmented pearly lesion with central vascularization/umbilication on the upper left lid (Figure 1). The patient was referred to an oculoplastic specialist for an excisional biopsy. The lesion was surgically excised with 2 mm margins without complication and then sent to the pathology lab.

The diagnostic report from the pathology lab described "an oriented white-tan skin excision which measures 1.0 x 0.6 cm and is excised to a depth of 0.1

cm with a raised nodular 0.6 x 0.2 cm lesion in the central portion of the specimen." Following microscopic evaluation, the pathology report noted that the findings were suggestive of verrucous keratosis or irritated seborrheic keratosis, and were not cancerous in nature.

Figure 1: *Benign verrucous keratosis/irritated seborrheic keratosis with features resembling BCC.*

Case 2

A 97-year-old white male presented to the eye clinic for a comprehensive exam. The patient's medical history was remarkable for osteoarthritis and gastroesophageal reflux disease, but there was no prior history of skin cancer. Systemic medications at the time of the appointment included cholecalciferol and omeprazole. The patient's ocular history was remarkable for bilateral moderate-stage primary open angle glaucoma and intermediate-stage dry age-related macular degeneration (ARMD). Treatment for glaucoma was timolol maleate 0.25% twice daily and latanoprost 0.005% nightly in each eye. The ARMD was treated with an AREDS 2 supplement containing lutein, zeaxanthin, and other antioxidants. The patient was pseudophakic with well-positioned posterior chamber intraocular lens implants. The patient's best corrected visual acuity (BCVA) was 20/20-1 OD and 20/50 OS, and the reduced vision in the left eye was secondary to the ARMD. On slit lamp and dilated fundus examination, ocular findings appeared to be stable compared to the prior visit, and no significant progression of the glaucoma or ARMD was noted on clinical examination. Gross observation of the patient's face and skin revealed a large indurated lesion on the left side of the patient's nose (Figure 2). The patient stated that the lesion had been present for at least five months without improvement despite self-treatment with multiple over-the-counter topical antibiotic gels and creams. The lesion was not itchy or painful, but did occasionally bleed. The patient was referred to dermatology for shave biopsy. Pathology described the lesion as a "white-tan unoriented shave of skin which measures 1.5 x 1.2 x 0.4 cm". The diagnosis was nodular/morpheaform-type basal cell carcinoma. Treatment consisted of electrodesiccation and curettage (EDC) combined with cryotherapy (Figure 3). Following successful removal and skin healing, the patient was instructed to use 5-fluorouracil cream once per day for two to three weeks to minimize the potential of recurrence.

Figure 2: *Basal cell carcinoma at presentation; present for approximately 5 months without resolution, significant ulcerated region that bleeds on occasion.*
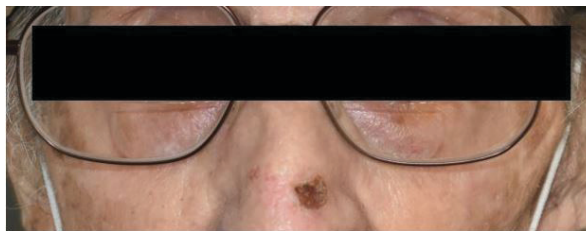

Figure 3: *Appearance of lesion immediately following removal of basal cell carcinoma with EDC + cryotherapy.*

Case 3

A 74-year-old white male presented for a comprehensive eye exam. The medical history was remarkable for seborrheic keratosis, hypertension, and type 2 diabetes mellitus. The patient had no known drug/medication allergies and no known family history of ocular or orbital conditions. BCVA was 20/20 OD and 20/25+1 OS. Slit lamp findings were remarkable for a 1.5mm nasal pterygium in the left eye and bilateral pseudophakia. Dilated fundus examination revealed bilateral mild non-proliferative diabetic retinopathy and grade 1 hypertensive retinopathy. Gross examination of the patient's face and adnexa revealed an isolated 1.1 cm ulcerated nodular lesion on the right upper cheek with internal scabbing (Figure 4). The patient stated that the lesion had been present for a few months and occasionally bled with only minor contact. A dermatology consultation was arranged. The dermatologist performed a shave biopsy which resulted in a diagnosis of nodular and focally infiltrative basal cell carcinoma. Dermatology suggested a Mohs micrographic procedure to remove the lesion. Post procedure, the tumor dimensions were 1.4cm x 1.5xcm with a total cutaneous defect of 2.5cm x 2.0 cm. Following tumor removal, the wound was repaired with a full-thickness skin graft from the postauricular neck (Figures 5 and 6).

Figure 4: *Basal cell carcinoma at presentation; ulcerated with adjacent nodule.*

Figure 5: *Status post removal of basal cell carcinoma immediately following excision and repair with autologous skin graft.*

Figure 6: *Status post removal of basal cell carcinoma at 5 weeks post-op.*

DISCUSSION

Although a significant majority of eyelid and adnexal lesions are benign, some have the potential to be highly destructive.[6] For this reason, it is vital that clinicians become adept at recognizing lesions with the potential to become infiltrative, structurally damaging, and metastatic. Of these, the most commonly described non-melanoma malignant skin lesion is basal cell carcinoma.[7]

Basal cell carcinoma (BCC) is the most prevalent carcinoma among humans, with an overall incidence that is increasing by 1 to 3% each year.[6,8] The most important risk factor for the development of BCC is a history of chronically sun-exposed skin resulting in damage from ultraviolet (UV) radiation. Although UV-A radiation has been noted to contribute, UV-B radiation has the most significant impact, with an estimated 15- to 20-year delay between primary pathological exposure and development of the skin lesion. UV-A radiation has been shown to cause indirect damage to DNA by creating free radicals that inflict both localized and systemic damage, whereas UV-B radiation alters the genetic code.[7] The altered gene most frequently associated with BCC, found in nearly 70% of patients, is *PTCH1*. Mutations in tumor suppressing gene *p53* are also highly associated with BCC.[9] Both UV-A and UV-B radiation play a role in the development of BCC by suppressing the cutaneous immune system on and around the lesion, leading to an inability to properly repair damage and reduced immune surveillance of suspicious tissues.[7] Due to the strong correlation between UV exposure and the diagnosis of BCC, patients who work outdoors and/or live in more equatorial regions tend to show the highest risk for the development of BCC.[6,10] Further risk factors include male sex, increased age, frequent use of tanning beds, fair complexion, positive family history of skin cancer, significant participation in recreational outdoor activities such as swimming and surfing, as well as a history of sunburns, especially blistering. The duration and intensity of sun exposure particularly during adolescence plays an additional role in the development of risk.[9] Although there is a proven direct relationship between the amount of UV exposure and the development of BCC, up to 20% of cases have been found on skin that is not commonly exposed to sunlight. In these instances, BCC is believed to arise from exposure to arsenic or ionizing radiation, or in patients who have a history of immunosuppression and genetic alterations, most notably those who have been diagnosed with rare diseases including xeroderma pigmentosum, Gorlin syndrome, Bazex-Dupre-Christol syndrome, and Rombo syndrome.[6,7,11]

Basal cell carcinoma has a low mortality rate and a very low risk of metastasis. Mortality is associated primarily with severe immunocompromise, in addition to less significant factors such as male sex, increased age, and Caucasian ethnicity.[9] On very rare occasions, BCC can metastasize to regions such as the lymph nodes, bone, lungs, and neighboring skin.[12]

Subtypes of BCC include nodular, superficial, and morpheaform variations, and the nodular variation is the most frequently encountered presentation.

Nodular BCC is histologically identified by a central island of basaloid cells with a surrounding nest of basaloid cells elevated around it. This creates the characteristic ulceration that is often present in larger lesions. Further identifiable clinical characteristics include a "pearly" pink or flesh-colored lesion in the early stages of presentation that later enlarges to create a rodent ulcer, which refers to the fact that the lesion's ragged borders and central ulceration create a presentation similar to that of a rodent bite.[12-14] The micronodular variant, which is often distinguished by the small size of the lesion and lack of peripheral elevation that is evident in the nodular variety, has a similar histological appearance.[13] The superficial variant is most often recognized by a red or pink macule that often contains telangiectatic vessels, and is similar in appearance to eczema or psoriasis. Superficial variant lesions are composed of basaloid cells that are attached between the epidermis and dermis layer of the skin, sometimes with a small band of fibrous stroma surrounding the lesion.[13] Pigmented BCC may be found in all subtypes and is not specific to one variant. These lesions are more commonly seen in Asian or African American patients and rarely present in Caucasians. Lesions that exhibit a "spoke wheel" pattern of pigmentation or that contain several spherical blue-gray specks are highly indicative of BCC.[13] The morpheaform variant is a smooth, indurated lesion that is usually white or flesh-colored in appearance.[13,15] Morpheaform lesions are the most infiltrative and have the highest potential for extensive tissue destruction. They are histologically classified by islands of neoplastic cells with surrounding sclerotic collagenous stroma.[13] Basosquamous BCC is a rare but highly aggressive subtype that is composed of basaloid cells, squamous cells, and intermediate cells. This subtype is believed to be representative of BCC that is undergoing squamous differentiation and is not frequently encountered due to the highly specific behavioral pattern of the involved cells.[13]

Basal cell carcinoma lesions most often develop on the head and neck. In 2019, Kasumagic-Halilovic et al. showed that, in a population of 442 participants who had been clinically diagnosed with BCC, 33.5% of lesions were located on the nose, 25.4% on the cheeks, 12% on the forehead, and 7.1% on the ear/preauricular region. In this study, 59.2% of participants had the nodular variant, 16.1% had the superficial variant, 15.2% had pigmented variants, and 9.5% had a morpheaform variant.[13,16]

The diagnosis of basal cell carcinoma requires a skin biopsy of the lesion, with punch and shave biopsies providing the most accurate results.[1] Treatment options vary depending on the size and location of the lesion, the patient's age and sex, and most importantly, the variant of BCC. More infiltrative lesions are addressed differently than less destructive lesions, and although multiple treatment modalities are available depending on the anatomical location of the lesions, only certain methods are used to treat facial BCC, including Mohs micrographic surgery, standard surgical excision, electrodesiccation and curettage (EDC), radiation therapy, and topical therapy.[17,18] Mohs micrographic surgery is considered to be the standard of care due to its low recurrence rate of only 1.0%, while other treatment modalities have recurrence rates ranging from 7.5% to 10.1%.[9] Further, Mohs procedures improve the histologic accuracy and allow a more favorable post-treatment cosmetic appearance.[19] The high success and low recurrence rates associated with Mohs are a result of the layer-by-layer removal of the lesion. This guarantees complete histologic clearance of the cancerous cells with excision of the least amount of tissue, promoting total resolution with minimal risk of future proliferation.[18] For this reason, Mohs is a highly favorable option for facial BCCs as it minimizes the potential need for future surgeries. In comparison to standard excision, Mohs is more time-consuming and expensive in the short term; however, it is thought to be more cost-efficient in the long-term as the recurrence rates are so low that future procedures are generally not required.[13] Mohs is the method of choice for tumors with the following characteristics: facial lesions (particularly around the eyes, nose, mouth, and ears), lesions larger than two centimeters, recurrent lesions, lesions that lack well-defined margins, and lesions classified as morpheaform, infiltrative, micronodular, or basosquamous.[13,18,19]

EDC, as was performed in Case 2, is more commonly used for treating lower-risk BCCs. In this procedure, the superficial tumor is removed with a curette and the base is cauterized to help seal the wound and destroy any remaining underlying tumor. This method is thought to be the quickest and most cost-effective option; however, it can result in significant scarring and poor cosmetic results.[13] Lesions treated with EDC also have a higher risk of recurrence, ranging from 7.7 to 19% at 5 years post-procedure.

Cryotherapy is also a quick and efficient procedure that uses liquid nitrogen to destroy cancerous tissues. Similar to EDC, cryotherapy tends to be more favorable in lower-risk lesions due to a higher recurrence rate when used as the sole treatment method. The combination of EDC and cryotherapy has been shown to offer much higher success rates and lower recurrence rates than either procedure performed alone.[13,14]

Non-surgical treatment options include radiotherapy, photodynamic therapy (PDT), topical imiquimod, and topical 5-fluorouracil. Radiotherapy uses X-ray and electron beams to ablate the tumor and has been proven to be nearly 90% effective in treating both primary nodular and superficial lesions. Radiotherapy is generally used in instances where surgery may be more difficult due to poor access or the potential for tissue damage: this includes many facial lesions such as those involving the lower eyelid and inner canthus.[20] It is important to note that radiotherapy of the upper eyelid is contraindicated due to reports of conjunctival keratinization. Radiotherapy can also cause long-term scarring and telangiectasia, resulting in a poor cosmetic outcome. However, the cosmetic result is often superior to that following standard excision, and the recurrence rate is only 6.6% higher. The most significant drawback to radiotherapy is that this is the most expensive form of treatment, at nearly four times the cost of Mohs micrographic surgery.[18]

PDT is a process by which a photosensitizing agent that is preferentially absorbed by tumor cells is exposed to a specific wavelength of light, creating reactive oxygen species that destroy the neoplasm. This process is also believed to stimulate the immune system and release cytokines to further combat neoplastic cells. PDT is effective, with an 82% clearance rate in superficial BCC and a 67% clearance rate in nodular BCC 2 years post-treatment.[18] Although recurrence rates are higher, PDT is much less damaging and more cosmetically appealing compared to other methods. For this reason, it has been a desirable method for primary facial lesions that are not significantly infiltrative.[17]

Topical imiquimod cream is an immunomodulator that selectively promotes apoptosis in neoplastic cells.[20] This cream has been studied extensively on lesions throughout the body with a high rate of success: when applied to the lesion five to seven times per week, imiquimod has been shown to be 79 to 82% effective following three months of consistent use. Treatment with imiquimod results in a low recurrence rate, with a clearance of 69% at 5 years.[18] Facial BCCs treated with imiquimod have not been studied as intensively, as this treatment tends to cause temporary side effects such as redness, swelling, and moderate to severe erosions and ulcerations. However, one study showed that imiquimod was an effective treatment option for facial BCC when the patient is able to tolerate the cream, noting that most side effects subside following discontinuation of treatment and the final cosmetic appearance is highly favorable.[21] For this reason, imiquimod may be a preferable option for patients with primary periocular BCC where surgical methods of treatment are technically difficult or will result in significant tissue destruction.

Topical 5-fluorouracil cream (5-FU) is a pyrimidine analogue that disrupts DNA synthesis in tumor cells.[20] Though still relatively novel and not as extensively studied, 5-FU shows significant potential as an adjuvant therapy for any of the above treatment options, with the exception of topical imiquimod. This treatment, however, only shows 70% long-term clearance rates as a singular modality and therefore is not often used as the sole method for treating facial BCCs.[18,20]

The prognosis of BCC is often favorable, as there is a low risk for metastasis. However, the rate of recurrence is highly variable and dependent upon factors such as histology and location of the lesion. Lesions that are found on the nose and ears have a higher risk of recurrence than lesions found on the forehead, cheeks, and neck. Lesions with the best prognosis are those found in a low-risk area, nodular, and between one and two centimeters in diameter, whereas recurrent and morpheaform lesions are associated with a poorer prognosis. [11,14]

CONCLUSION

Optometrists are trained in the diagnosis and management of several ocular conditions: it is particularly important to incorporate an evaluation of the patient's head, neck, face, and scalp with that of the ocular adnexa. With nearly 78% of basal cell carcinomas presenting in these regions and an estimated incidence of 88 to 164 cases per 100,000 individuals, it is highly likely that optometrists will encounter many undiagnosed cases of BCC during their careers.[6,11] As the prognosis of the condition improves with early diagnosis, it is crucial that optometrists are well-versed in the risk factors and presenting features of these lesions to facilitate appropriate referrals and catalyze more expeditious, effective, and less invasive treatment plans. ●

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