

Basal Cell Carcinoma in Skin of Color: Diagnosis and Treatment Considerations

BCC may be less common in more darkly pigmented skin, but it occurs, and diagnosis may be delayed. Appropriate treatment is crucial.

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The earliest known cases of skin cancer were discovered in 2,400-year-old mummies in South America.¹ Today skin cancer is the most common type of cancer worldwide, with 3.5 million new non-melanoma skin cancers cases diagnosed yearly in the US alone.² Of those, 80 percent are basal cell carcinomas (BCC). Although the frequency of skin cancer is higher among Caucasians due to lack of photo-protection provided by melanin, skin cancer remains an important occurrence among dark-skinned individuals. The frequency of skin cancer among skin of color has not been well documented but recent reports suggest it accounts for five percent of cancers in Hispanics, two to four percent in Asians, and one to two percent in African Americans. Just as in Caucasians, the most common type of skin cancer in skin of color is BCC.³

CAUSES OF BCC

The etiology of BCC among dark-skinned individuals remains the same as in Caucasians, with a lower emphasis on the effects of ultraviolet (UV) radiation and more on environmental, immunologic, and genetic factors. Risk factors for BCC include scars, physical and thermal trauma, ulcers, nevus sebaceous of Jadassohn, previous radiation treatment, chronic infections, immunosuppression, genetic disorders such as albinism, xeroderma pigmentosum (XP), nevoid basal cell syndrome (NBCCS), basaloid follicular hamartoma (BFH) syndrome, Brooke-Spiegler syndrome, Bazex syndrome, Rombo Syndrome, Cowdens syndrome, and others.

The mechanism of skin cancer formation involves malignant transformation of keratinocytes in a monoclonal fashion. The steps involve damage to the DNA, which, if uncorrected, leads to the initiation of the “weakened cell”:

a cell that already has a mutation in a tumor suppressor gene such as p53 tumor suppressor gene or activation of an oncogene such as ras proto-oncogene. Further exposure to the carcinogen, which may include the same carcinogen as the initiator or a new carcinogen such as a promoter would cause a second “hit” to the weakened cell, and would promote progression into a benign and later malignantly transformed cell. This mechanism is known as the “two or (multiple)-hit theory.”⁴

CLINICAL PRESENTATION

Skin cancer in darker-skinned individuals is usually diagnosed late, leading to more difficult cases and less treatment options.⁵

Case in point, a 33-year-old Peruvian female who had a lesion for more than 10 years on her right medial cheek/orbital rim. It was incompletely removed in Peru and she was told that it was a benign mole. Her biopsy revealed pigmented BCC. She subsequently failed imiquimod 5% cream and mildly improved on vismodegib (Erivedge, Genentech) 100mg BID x four months. Eventually, she required Mohs surgery to extricate the tumor and achieve a definitive cure. (See Figure 1)

BCCs in skin of color individuals can appear as the typical BCC in Caucasians (pearly telangiectatic papule) but more often present as a pigmented, black to brown slightly telangiectatic papules or plaques. They can also appear as nodules, ulcers, indurated or pedunculated tumors and have been reported in Asians to be black and pearly in appearance. The most common locations are similar in both fair skin and skin of color, and include the head and neck (89 percent) with lower frequency on the trunk and extremities and even fewer lesions occurring on the genitals of both males and females.⁶

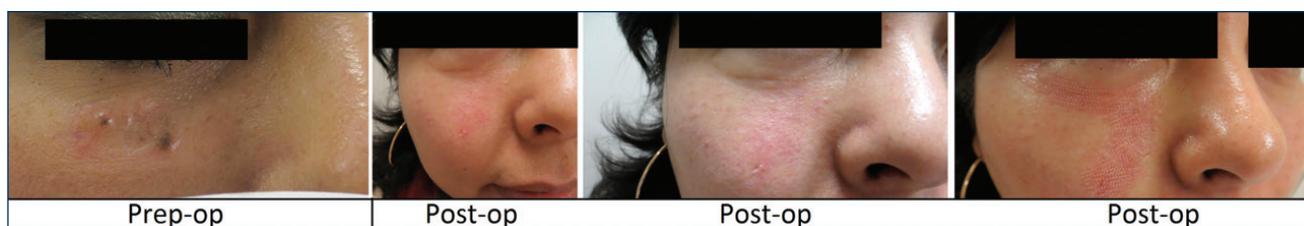


Figure 1

Due to their atypical appearance in patients with skin of color, BCC lesions are often misdiagnosed as seborrheic keratosis, nevus sebaceous, and even malignant melanomas. In the former cases, this leads to false reassurance and a delayed diagnosis, and ultimately a worse prognosis. In the latter case, it can also lead to an aggressive treatment and a worsening scar in an individual prone to developing keloid scars. Therefore, recognizing the unique characteristics of a BCC lesion in an individual with darker skin is vital to prevent the significant morbidity and disfigurement associated with surgery, medications, and the healing process.

TREATMENT

The most difficult aspect of managing BCC in dark-skinned individuals is accurate diagnosis. Therapy selection and implementation does not differ greatly than protocols for fair-skinned individuals, however it bears mentioning that certain options may lead to an undesirable cosmetic effect in darker skin. A wide array of treatment modalities is available, but these therapies differ in their proven efficacies. They also differ in the clinical and logistical challenges they present, including comorbidities, adverse effects, and patient compliance.

Surgery. Surgery is regarded as the most definitive treatment of BCC and within this option are three types of procedures. Mohs surgery is the most precise and carries the highest chance of a complete cure.

Mohs Surgery. Due to its microscopic precision, Mohs surgery carries a 99 percent success rate when performed by an experienced and fellowship trained MS surgeon.⁷ The value of Mohs surgery lies firstly in its highest accuracy of margin control, whereby it provides a complete edge (sides and depth) evaluation of a continuously spreading tumor. Secondly, Mohs surgery results in a smaller defect size and thus a smaller resulting scar. The downside is the duration of the procedure, which often requires the patient to take an entire day off from work to have the tumor removed and reconstructed.

Suture Surgery. Suture Surgery is a surgical procedure in which the physician uses clinical judgment to conclude the size and depth of a BCC lesion, and then excises it with a scalpel. The resulting defect is closed with sutures in a way that achieves optimal healing and the best possible cosmetic effect. Due to the lack of immediate margin control when using simple excision, the surgeon evaluates the tumor with the naked eye and typically removes about a 5mm margin of what appears to be normal skin in order to assure the excision will be free of the tumor. This method has a range of 93 to 98 percent⁸ cure rate depending on the location, with lower cure rates on the face (due to tumor tracking in embryonic fusion plains and the likely tighter margins removed in cosmetically sensitive areas by the surgeon) and higher cure rates on the trunk and extremities.

ED&C. In ED&C, the physician uses a curette to remove the BCC lesion. The curette is a loop-like instrument used to spoon and then scrape the tumor out from the normal skin. This works for most BCCs, with the exception of morpheaform (scar like BCCs) due to the usually soft jelly-like mucin secreted by and nesting these BCCs. Cure rates vary just as with suture surgery to between 97-98 percent on the trunk and 90 percent on the face, but the overall reported success rate is 96 percent.⁹ The wound area is then cauterized with an electro-cautery device. Debris is then scraped out from the wound with the curette and this process is repeated three to five times. The more times it is repeated, the larger the scar becomes and the higher the reported cure rate. ED&C is a subjective method that depends on the physician's ability to discern the difference in fill of the soft BCC versus the hard healthy skin at the margins.

Radiation Therapy. BCCs can be treated very successfully using either Grenz Rays or electron beam radiation. The cure rate is approximately 93 percent for BCC.¹⁰ This treatment option is recommended for patients who cannot or do not wish to undergo any type of surgery. It is typically

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reserved for lesions in an individual older than 55 years of age, due to the possible risk of developing an SCC in the radiation area approximately 20 years or more after the treatment.¹¹

Cryotherapy. Success rates for cryotherapy vary (perhaps due to differences in technique) but generally hover percent.¹² The most common agent used in cryotherapy is liquid nitrogen and it is sprayed directly onto a lesion such as a BCC. The proper technique for cryotherapy requires inserting the probe into the tumor to confirm that a temperature of -50C is reached at the base of the tumor. Although it is effective in treating the cancer, this option is not advised for persons with darker skin due to its tendency to cause permanent loss of pigment. After the treatment, a blister is formed and the wound is allowed to heal by the process of secondary intention healing.¹³

Photodynamic Therapy. BCC can be treated with a combination of the photosensitizer medication Levulan (aminolevulinic acid) and a light source, usually blue (shallowest penetration ~2mm) or red (deeper ~3mm). Alternatively, an Nd:YAG laser can be used, which has deeper penetration but less optimal results. In the presence of oxygen, the reaction between the Levulan and light leads to the formation of reactive oxygen species, which generate free radicals, which in turn cause tissue toxicity and death of the cancer cells. Because malignant tumors have a higher degree of vascularity and faster rate of angiogenesis, they absorb the Levulan preferentially. This selective mechanism allows for sparing of healthy cells. The protocol and incubation periods vary as does the pain associated with this procedure. Likewise, the downtime from the redness and skin sloughing that usually follows the treatment varies from patient to patient and is related to the photosensitivity that usually lingers for 48 hours until the photosensitizer in the tissue is completely spent. This therapy has an approximate cure rate of 80 to 90

percent (depending on the depth of the BCC and the protocol used) but has the adverse effect of causing the skin around the lesion to be very sensitive to sunlight and heat for a few days to rarely a few weeks.¹⁴ It is not an FDA approved treatment.

Laser Treatment. BCC can also be treated with either the pulsed dye laser or the alexandrite laser. This treatment targets the blood supply of the tumor, in effect “choking the tumor”. The limitation of this treatment is the laser beam’s depth of penetration of about 2-3mm, making it ineffective for deeper tumors. In darker-skinned individuals, laser treatment of BCC may have less efficacy because of the difficulty of penetrating the skin through the melanin pigment. This is because melanin absorbs the particular wavelength of light emitted by the alexandrite laser, allowing less of it to reach the tumor cells. Laser treatment has an approximate cure rate of 75 percent but reported results vary.¹⁵ This is not an FDA approved treatment.

Imiquimod. Imiquimod is a topical medication that can be applied by the patient at home directly to the BCC. Imiquimod is an immune modifier which upregulates the body’s own immune system to attack and destroy the BCC. This treatment carries an 80 percent success rate and is FDA approved only for superficial BCC on the trunk.¹⁶ As with any treatment that is self-administered, an imiquimod regimen requires strong patient compliance to ensure proper application and timely follow-ups. Although protocols vary, we tend to apply it daily for six weeks. The reaction, if it occurs, is usually brisk, beginning two weeks after the application of the cream and becoming more intense. We observe crusting, redness, and oozing that usually fades to leave behind mild redness and eventually no permanent sequelae. Although, we have observed some permanent hypo or hyper pigmentation in Fitzpatrick skin types V & VI.

Tazarotene. Tazarotene has shown some efficacy in treating BCC. Tazarotene comes in a topical gel formulation and is used for the treatment of acne and psoriasis. When used in conjunction with imiquimod, tazarotene may have an additive effect on the destruction of cancer cells. This is an off-label use of tazarotene and has been reported to have a largely various degree of success. Some clinical trials using tazarotene alone demonstrate over 50 percent regression while others only six percent.^{17,18} In our practice, we concomitantly use tazarotene with imiquimod 5% cream and have had about 90 percent cure rate, but with more resultant scarring and dyspigmentation (hypo

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or hyper-pigmentation). This is not an FDA approved treatment.

Vismodegib. Vismodegib is the first drug FDA approved to treat local as well as metastatic BCC. It carries a 40 to 50 percent success rate and comes in the form of a 150 mg pill taken once daily.¹⁹ When the drug is successful, the results begin to be noticeable in one to two months and continue to improve. If I see no improvement for four months from the beginning of treatment I usually discuss with the patient other treatment modalities. Vismodegib is a good treatment option for BCC that cannot be treated with surgery or radiation because of its location or comorbidities. The most common side effects of this drug are muscle cramps, which may be reduced by supplementing potassium. This can be followed by loss or reduced taste and hair thinning of the scalp. All these side effects are reversible when the medication is stopped. The problem with the use of the medication is that once the treatment is discontinued the skin cancers slowly recur. To reduce the risk of recurrence, we had some patients start a six-week treatment with imiquimod one month after the initiation of the vismodegib and saw that roughly 90 percent of those cancers that the vismodegib worked on did not return following the discontinuation of the drugs. This is based on our personal observations and the case reports have not yet been published.

Isotretinoin. Isotretinoin is indicated for the treatment of severe, recalcitrant acne, but has also shown a slight degree of efficacy in treating BCC. This medication can help shrink and slow the formation of new BCCs but the skin cancers usually return rapidly as soon as the oral retinoid is discontinued and thus this method must be used in conjunction with other methods to achieve lasting results. As with all retinoid medications, the

physician must be sure that the patient is not pregnant and has no medical contraindications that could precipitate severe adverse reactions. In all patients on isotretinoin, regular blood tests should be performed, especially to follow liver function and other indices as indicated by the individual case.

CONCLUSION

Although treatment is crucial, our goal as medical professionals should always be to educate our patients on preventive methods as well as healthy lifestyle behaviors that include daily sun protection and monthly self-exams for early detection. As global warming continues and the ozone layer thins, it is paramount that we become more aware of our susceptibilities and adopt measures to reduce the epidemic of skin cancer worldwide among both light and dark skinned individuals. ■

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