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Pigmented Basal Cell Carcinoma: An Argument for Sub-Classification

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ABSTRACT

Basal cell carcinoma (BCC) has several subclassifications, including pigmented basal cell carcinoma. In our clinical experience, we have found that pigmented basal cell carcinoma itself has multiple subtypes which can overlap with traditional basal cell carcinoma subclassifications. In this letter, we argue for the subclassification of pigmented basal cell carcinoma, as either superficial, nodular, or morpheaform. We believe further subclassification of pigmented BCCs may reveal important therapeutic and prognostic differences which could make an impact on the morbidity and mortality of this condition for those affected, many of whom are skin of color patients that are already disproportionately affected by health disparities related to skin cancer.

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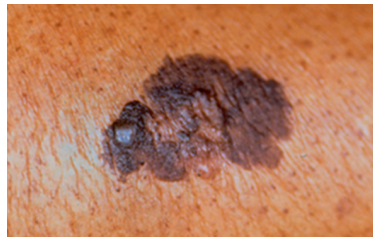
INTRODUCTION

Basal cell carcinoma (BCC) is the most common skin malignancy among Caucasians, Asians, and Hispanics and the second most common amongst African-Americans.[1] There are several recognized subtypes of BCC, including superficial, nodular, and morpheaform.[1] Additional subtypes occasionally discussed in the literature include pigmented, red-dot, fibroepithelial, infundibulocystic, and infiltrative.[1] The clinical features and prevalence of BCC subtypes can differ by race, ethnicity, and Fitzpatrick phototype as well as age, gender, and anatomic location.[1-4] Nodular BCC followed by superficial BCC is the most common subtype overall, while pigmented BCC is the most common subtype within skin of color (SOC) populations.[1] Amongst African Americans, roughly 50% of BCCs are pigmented, compared to only 5-6% amongst Caucasians.[1] Pigmented BCCs are twice as likely amongst Hispanics than Caucasians.[1] The classification system for BCC, however, is inconsistent, with some reports failing to include pigmented BCC as a subtype. Additionally, there is a paucity of literature discussing the various clinical features of pigmented BCC outside of its relation to SOC.

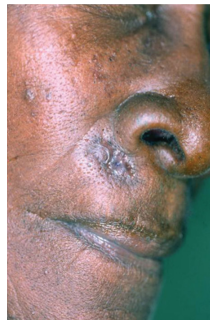
In our clinical experience, pigmented BCCs may present with varied morphologies that overlap with the recognized subtypes of BCC, specifically superficial, nodular, and morpheaform. These recognized BCC subtypes are reported to vary not only in clinical presentation, but prognosis and treatment as well. Similar differences likely exist amongst the various morphologies of pigmented BCC. Such differences, however, remain unexplored due to lack of subcategorization as well as limited investigation on diseases primarily affecting patients with SOC. We, therefore, propose a sub-classification system specific to pigmented BCC. Based upon morphology, we suggest pigmented BCCs be precisely categorized as pigmented-superficial (Figure 1), pigmented-nodular, or pigmented-morpheaform BCC (Figure 2). This additional

FIGURE 1. A superficial pigmented basal cell carcinoma along the lower extremity of an African American male represented by a brown plaque with irregular borders.



Source: Kelly A, Taylor SC, Lim HW, et al eds. *Taylor and Kelly's Dermatology for Skin of Color.* 2nd ed. New York: McGraw-Hill Education. 2016. All rights reserved.

FIGURE 2. Pigmented basal cell carcinoma on the right upper cutaneous lip of an African American female representing a morpheaform presentation of pigmented BCC.



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stratification will not only help differentiate the various clinical presentations of pigmented BCC but will provide incentive and opportunity to further investigate these potential differences in presentation, disease course, and therapeutics.

A study conducted by Scrivener et al highlights the remarkable variations between BCC subtypes in relation to patient demographics and its association with treatment.[2] Scrivener et al, along with several others, discuss how BCC subtype, age, gender, and/or anatomic location may predict presentation, etiology, prognosis, and treatment.[2-4] As an example, superficial BCCs are more prevalent on the trunk. When stratified by gender, however, Scrivener et al found that superficial BCCs may be more likely to affect the head and neck of women, but the trunk of men.[2] Additionally, age of excision differed by location and gender, with head and neck lesions excised later in women and trunk lesions excised later in men, regardless of BCC subtype.[2] It is possible the various morphologies of pigmented BCC have similar and other differences when subcategorized and stratified by age, gender, and/or anatomic location. Differences between BCC subtypes extend beyond patient age and gender, however, and exist within the context of race as well. A study by Lobl et al is the first study to compare mutational differences in BCC amongst individuals of color and suggests genetic variations between different races.[5]

Using targeted gene sequencing, Lobl et al found significant mutational differences in BCC between Asians, Caucasians, and Hispanics.[5] The most common mutations reported for BCC throughout the literature are TP53 and KDR, however, a majority of previous studies and clinical trials pertaining to BCC were comprised of majority Caucasian participants.[5] Lobl et al found the GATA3 mutation, which may serve as a predictor of metastasis, invasions, and high tumor grade for head and neck BCCs, to be the most common mutation amongst Hispanic participants and TP53 amongst Asian and Caucasian participants.[5] Type of mutation also differed by race/ethnicity, with frameshift mutations more common amongst Hispanic patients and missense mutations amongst Asian and Caucasian patients.[5] Although the clinical associations of these findings are unclear at this time, certain studies suggest frameshift mutations to be more immunogenic and thus more susceptible to immunotherapies.[5] Lobl et al's findings suggest that patient race/ethnicity may be associated with specific mutational differences that may ultimately translate into differences in prognosis and treatment. Larger, more racially and ethnically inclusive studies investigating potential mutational differences amongst the histological subtypes of BCC are needed, as there are currently no known specific mutations unique to any particular BCC subtype.

The classification of BCC subtypes along with additional subcategorizations for pigmented BCC, specifically, is critical to improved patient care. Implementation of this sub-classification system requires improved physician education and research pertaining to pigmented BCC. Educational resources, including textbooks, kodachromes, and lectures on pigmented BCC will aid diagnosis and evaluation as well as allow dermatologists to appreciate the nuances of these pigmented lesions, especially in darker skin types. Finally, larger investigational studies analyzing this classification system and how subcategorizations of pigmented BCC may vary by race, ethnicity, age, gender, and location in relation to genetics, clinical presentation, diagnosis, prognosis, and therapeutics are needed to continue to improve our understanding of conditions that disproportionately occur in SOC.

DISCLOSURES

The authors have no conflicts of interest to disclose. All manuscripts contributed substantially to this manuscript and have been listed accordingly.

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