

RESIDENT ROUNDS: PART III

Case Report: Metastatic Cutaneous Squamous Cell Carcinoma in an African American Female

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ABSTRACT

Cutaneous squamous cell carcinoma (cSCC) is the most common skin cancer diagnosed in African Americans.[1] Twenty to forty percent of cSCCs reported in African Americans are related to chronic scarring processes or areas of inflammation.[2] Risk factors for developing cSCCs in patients of color include chronic scars resulting from burns, skin ulcers, and radiation sites; and chronic inflammatory diseases such as discoid lupus and hidradenitis suppurativa.[1]

Although skin cancer only accounts for 1% to 2% of cancers diagnosed within African Americans, it is associated with increased morbidity and mortality in this population.[1,3] Significant delays in diagnosis and treatment are largely thought to be responsible for this prognostic incongruity. The rate of metastasis in patients of color is 31%, compared with only 4% in Caucasians.[4,5] Early recognition by physicians and increased awareness resulting in preventative measures by patients may decrease this noted disparity.

J Drugs Dermatol. 2016;16(1):81-84.

CLINICAL PRESENTATION

A 52-year-old African American female with a history of intellectual disability, hypertension, left middle cerebral aneurysm, hyperlipidemia, and a 90-pack-per-year history of smoking presented with a large, painful, fungating, bleeding 9.0 cm x 6.5 cm tumor adherent to her occipital scalp (Figure 1, Panel A) for 4 years.

Biopsy revealed a poorly differentiated squamous cell carcinoma (Figure 1, Panel B). Computed tomography (CT) and whole body positron emission tomography (PET-CT) demonstrated invasion of the occipitalis muscle and subadjacent occipital bone (Figure 1, Panel C, arrow), along with metastatic cervical adenopathy (Figure 1, Panels D and E, arrows).

The patient underwent radical excision of the tumor, including skin and underlying muscle, fascia, and periosteum, which revealed perineural and lymphovascular invasion with positive deep margins. Occipital craniectomy and bilateral posterolateral neck dissection with xenograft placement were also performed, revealing 3 metastatic lymph nodes. After reconstruction, the patient was referred to radiation oncology for adjuvant radiation treatment. Repeat CT after radiation demonstrated gross tumor recurrence in the skull and posterior upper neck vasculature, with increased invasion of the occipital bone with likely dural but no frank parenchymal invasion. Additionally, new metastatic lesions within the lungs were visualized (Figure 2, arrows). At this juncture, the patient has opted for only supportive management.

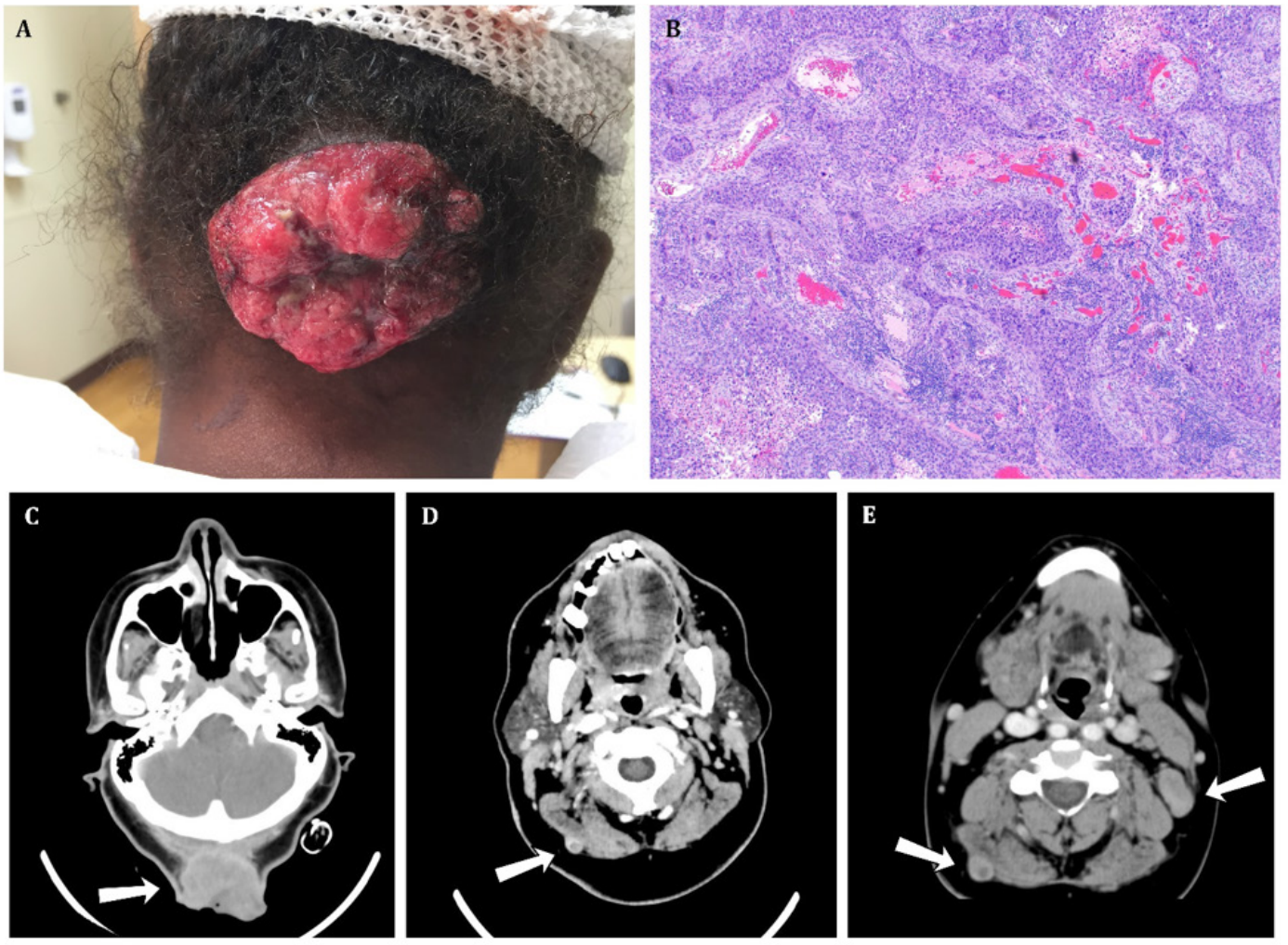
DISCUSSION

An estimated 700,000 cases of cutaneous squamous cell carcinoma (cSCC) are diagnosed annually.[6] While the overall majority of cSCCs are low-risk tumors with a favorable prognosis, a subset of tumors is considered "high-risk" cSCC (HRcSCC), demonstrating the need for a more aggressive clinical course, with a potential for local recurrence or metastasis. The annual incidence of metastasis is approximately 4%, though this is likely to be an underestimation as epidemiological analysis is hindered by the lack of a national cancer registry for cSCC.[7,8]

The 5-year overall survival of a patient is reduced by 50% with the presence of metastasis, making both early identification of this subset and prompt initiation of aggressive management of paramount importance.[5] Multiple staging algorithms have been published in an attempt to help risk stratify cSCCs based on proposed tumor characteristics thought to predict risk of metastasis, though no official guidelines have been formally validated.[8]

As defined by the American Joint Committee on Cancer (AJCC) in 2002, the intended purpose of cancer staging is to distinctly

FIGURE 1. (A) Large, painful, fungating, bleeding tumor adherent to occipital scalp; (B) Histopathology demonstrating poorly differentiated squamous cell carcinoma; H&E 4x; (C) CT head demonstrating SCC invasion into occipitalis muscle and subadjacent occipital bone; (D and E) CT neck demonstrating metastatic cervical adenopathy.



identify and divide patients into separate stages based on similar or different projected outcomes.[6] Initially, the AJCCs staging system classified the majority of cases as T1 or T2, with a requirement of bone invasion to be classified as a higher stage T3 or T4. As a result, the majority of tumors with poor outcomes were similarly grouped with indolent tumors into the low grade T2 stages, making the AJCC classification system of limited prognostic use in distinguishing between the T2 cases with good versus poor outcomes.[6,9]

In 2010, the 7th edition of the AJCC tumor staging system was revised to better stratify T1 and T2 lesions by using several "high-risk" factors that were felt to be of more prognostic utility. These features include tumor depth greater than 2 mm, Clark level > IV, perineural involvement, primary site located on the ear or non-hair-bearing lip, and poorly differentiated tumors. Unlike the

FIGURE 2. Repeat CT chest demonstrating new metastatic disease within the lungs.

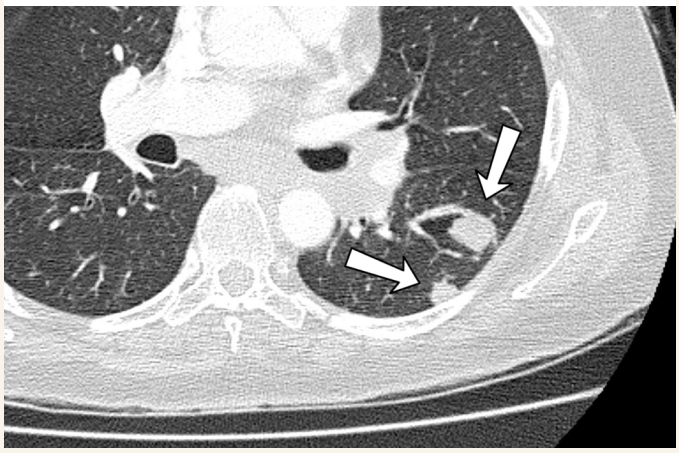


TABLE 1.

Brigham and Women's Hospital (BWH) Tumor Staging System	
Designation	**Description**
T1	0 high-risk factors
T2a	1 high-risk factor
T2b	2-3 high-risk factors
T3*	4 or more high-risk factors or bone invasion

High-risk factors include tumor diameter ≥ 2 cm, poorly differentiated, perineural invasion of ≥ 0.1 mm, or tumor invasion beyond fat (excluding bone invasion, which upgrades tumor to stage T3). Our patient's stage is denoted by *.

National Comprehensive Cancer Network (NCCN) guidelines, this updated AJCC staging system does not take into account host factors such as immunosuppression and tumor recurrence, which many believe correspond to increased risk of metastasis.[7]

A study in 2012 compared the 2 systems and found that neither was reliable in predicting the estimated risk of metastasis.[10] In 2013, an alternative system, now known as the Brigham and Women's Hospital (BWH) tumor staging system, further attempted to stratify T2 stage tumors by subdividing this group into T2a and T2b based on specific defined high-risk factors found to correlate with outcome.[6,7,9] These 4 risk factors include tumor diameter ≥ 2 cm, poorly differentiated histologic characteristics, perineural invasion > 0.1 mm, and tumor invasion beyond subcutaneous fat (excluding invasion of bone, which automatically upgrades a tumor to stage T3) (Table 1).[9] T1 and T2a are generally considered low stage, whereas T2b and T3 are high-stage tumors.

While further validating studies are needed, a multivariate analysis by Karia and colleagues compared the AJCC, UICC (International Union Against Cancer), and BWH staging systems. This study revealed superiority in the BWH staging system in terms of dividing patients with good prognosis (97% 10-year cure rate) into the 2 lower stages (BWH T1 and T2a), while appropriately upstaging the tumors with poor outcomes into the higher-risk stages (T2b and T3).[6]

TABLE 2.

Comparing Staging Systems' Definitions of High-Risk Cutaneous Squamous Cell Carcinoma Features		
National Comprehensive Cancer Network High Risk Factors[13]	**American Joint Committee on Cancer Staging[15]**	**Brigham and Women's Hospital Staging[6]**
Clinical features:	**Depth/Invasion:**	Diameter > 2 cm
Location/size*	2 mm thickness	Perineural invasion of nerve > 0.1 mm in diameter
Area L ≥ 20 mm	Clark level > IV	
Area M ≥ 10 mm	Perineural invasion	Invasion beyond fat (excluding bone invasion which upgrades tumor to BWH stage T3)
Area H (independent of size)	**Anatomic location:**	
Poorly defined borders	Primary site ear	Poor histologic differentiation
Recurrent nature	Primary site non-hair-bearing lip	
Rapid growth	**Differentiation:**	
Neurologic symptoms	Poorly differentiated	
Immunosuppressed patient		
Prior radiation to site		
Area of chronic inflammatory process		
Pathologic features:		
Depth > 2 mm; Clark level IV/V		
Poor histologic differentiation		
Acantholytic, adenosquamous, desmoplastic, or metaplastic subtypes		
Perineural invasion		
Lymphovascular invasion		

*Area H = "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermillion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet
Area M = cheeks, forehead, scalp, neck, and pretibia
Area L = trunk and extremities (excluding pretibial, hands, feet, nail units, and ankles)

Currently, there is no universally validated tumor staging system, and each system selects distinctive "high-risk" factors considered to be predictive of a more aggressive clinical course (Table 2). Irrespective of the staging system used, physicians should be aware of the multiple tumor features widely discussed in the literature as enhancing metastatic potential: tumor diameter, depth of invasion, poorly differentiated tumors, histologic features, location (head/neck, lip, ear), perineural or lymphovascular involvement, tumor recurrence, incomplete excision, multiple tumors, patient characteristics, and genetic or molecular markers.[7-9,11] Our patient was found to have a poorly differentiated tumor, with perineural and bone invasion, as well as lymph node and lung metastases; all of which portend a grim prognosis.

Once a HRcSCC has been identified, there remains an absence of established protocol regarding additional indicated work-up. Lymph node involvement by SCC increases morbidity and mortality, highlighting the importance of lymph node evaluation in HRcSCCs. An estimated 80% of cSCC metastasis predictably spreads to a single regional lymph node first, making sentinel lymph node biopsies (SLNB) a potentially very useful aid in early identification of subclinical nodal metastasis.[12] According to a meta-analysis by Schmitt and colleagues, SLNBs were positive in 29.4% of T2b and 50% of T3 tumors, compared with only 7% of BWH T2a tumors.[12] This data suggests that SLNB should be considered in T2b and T3 patients.

Radiographic imaging should also be considered in HRcSCCs. The NCCN recommends imaging of tumors presenting with extensive disease, including involvement of deep structures (ie, bone), perineural disease, deep soft tissue involvement, or lymphovascular invasion.[13] These general guidelines, likely due to a paucity of data, do not clearly delineate which patients should undergo imaging.

A recent study by Ruiz and colleagues evaluated the impact of imaging on the management of HRcSCC and revealed only 46% of high-stage tumors (BWH T2b/T3) underwent imaging, of which 33% had management altered due to imaging results. Furthermore, those that received imaging had a lower risk of nodal metastasis and an increased 5-year disease-free survival (73%) compared with those in the non-imaging group (51%).[14]

In the case of our patient, imaging did in fact alter the course of the initial plan. After discovering invasive and metastatic involvement, a more aggressive and appropriate treatment plan was pursued rather than proceeding with Mohs micrographic surgery as initially planned. She was instead treated with radical excision, craniectomy, and lymph node dissection followed by adjuvant radiation therapy. Despite these aggressive measures, the tumor recurred along with new distant metastases.

CONCLUSION

Early identification of the subset of cSCCs with high-risk of local recurrence or metastasis is of principal importance as it guides optimal management and triggers prompt treatment. Following the diagnosis and treatment of a HRcSCC, the risk of locoregional recurrence or distant metastasis is highest within the first several years, with a risk of 75% within the first 2 years and 95% within the first 5 years.[11] As such, it is imperative that physicians ensure close long-term follow up in these patients. Physicians should also be alerted to the importance of vigilant screening in patients of all skin types, including those of color.

DISCLOSURES

The authors have no conflicts of interest to declare.

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