# Clinical and dermoscopic features of combined cutaneous squamous cell carcinoma (SCC)/ neuroendocrine [Merkel cell] carcinoma (MCC)

Andrea Luísa Suárez, MD, PhD,[a] Peter Louis, MD,[b] Jasmine Kitts, BS,[b] Klaus Busam, MD,[b] Patricia L. Myskowski, MD,[c] Richard J. Wong, MD,[d] Chih-Shan Jason Chen, MD, PhD,[c] Philip Spencer, MD,[c] Mario Lacouture, MD,[c] and Melissa P. Pulitzer, MD[b]
*New York, New York*

***Background:*** Merkel cell carcinoma (MCC) is a neuroendocrine carcinoma, associated with Merkel cell polyomavirus. MCC admixed with squamous cell carcinoma (SCC) is unassociated with polyomavirus, and is genetically distinct.

***Objective:*** We sought to distinguish clinically and dermoscopically between MCC and SCC/MCC.

***Methods:*** We compared patient data for SCC/MCC (n = 26) and MCC (n = 20), and reviewed clinical and dermoscopic images (n = 9) of SCC/MCC.

***Results:*** Patients with SCC/MCC were older (median 76.5 vs 69 years) and more often male (77% vs 60%), and had more nonmelanoma skin cancer (85% vs 25%), malignant extracutaneous tumors (25% vs 5%), lymphoproliferative disorders (23% vs 10%), and immunodeficient/proinflammatory states (77% vs 35%). In all, 58% of SCC/MCC versus 10% of MCC were clinically diagnosed nonmelanoma skin cancer. Patients with SCC/MCC had more metastases (77% vs 40%), more treatment failures (53% vs 45%), shorter survival (41 vs 54 months), and more death from disease (50% vs 40%). SCC/MCC demonstrated marked scale (7/9), and telangiectasia (1/9). Dermoscopically, small dotted and short linear irregular peripheral vessels and central milky-red areas with large-diameter arborizing vessels were seen.

***Limitations:*** The rarity of SCC/MCC limits available data.

***Conclusions:*** SCC/MCC is aggressive, arising within elderly patients' chronically ultraviolet-exposed skin, often in the setting of immunosuppression or inflammation. Dermoscopically, polymorphous vessels in lesions suspicious for nonmelanoma skin cancer are suggestive. (J Am Acad Dermatol 2015;73:968-75.)

***Key words:*** biphenotypic; dermoscopy; Merkel cell; neuroendocrine carcinoma; polyomavirus; ultraviolet signature.

Merkel cell carcinoma (MCC) is a rare cutaneous neuroendocrine carcinoma that typically arises in the background of a clonally integrated virus, the Merkel cell polyomavirus (MCV). MCC has an estimated annual incidence of 0.6 per 100,000 persons. The disease exhibits an aggressive course and there is no definitive cure; mortality for MCC exceeds that of melanoma, with the 5-year disease-specific survival estimated at 30% to 64%.[1] Histologically, MCC co-occurring with

From the Department of Dermatology, New York-Presbyterian Hospital/Weill Cornell Medical Center[a]; and Department of Pathology,[b] Dermatology Service, Department of Medicine,[c] and Department of Surgery,[d] Memorial Sloan Kettering Cancer Center.

Funding sources: None.

Disclosures: Dr Lacouture has consultant roles with Bayer, Boehringer Ingelheim, Galderma, Pfizer, Merck, Genentech, Bristol Myers Squibb, Novartis, Helsinn, EMD Serono, Glaxo SmithKlein, and Advancell. He is on the advisory board and/or board of directors for Amgen, Genentech, and GSK. Drs Suárez, Louis, Busam, Myskowski, Wong, Chen, Spencer, Pulitzer and Ms Kitts have no conflicts of interest to declare.

Accepted for publication August 20, 2015.

Reprint requests: Melissa P. Pulitzer, MD, Department of Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10021. E-mail: pulitzem@mskcc.org.

Published online September 30, 2015.

0190-9622/$36.00



http://dx.doi.org/10.1016/j.jaad.2015.08.041

non-MCC tumors, particularly squamous cell carcinoma (SCC), comprise 5% to 14% of all MCC.[2] Combined tumors are increasingly thought to represent a distinct disease process from MCC, with reproducibly absent MCV,[2-4] and a more aggressive course.

We report clinical findings and long-term follow-up data from a series of cutaneous SCC/MCC in comparison with pure MCC. This report highlights the more aggressive nature of combined tumors compared with pure MCC. The clinical examination and dermoscopic findings reported here for SCC/MCC might aid clinicians in identifying this tumor type, potentially reducing delays in diagnosis and appropriate treatment.

**CAPSULE SUMMARY**

- Combined squamous cell carcinoma (SCC)/Merkel cell carcinoma (MCC) is molecularly distinct from pure MCC.
- SCC/MCC favors ultraviolet-damaged skin of elderly patients with immunosuppressive or inflammatory comorbidities. Dermoscopically, SCC/MCC demonstrates scaly nodules/plaques, centrally located milky-red areas, and polymorphous/large-diameter arborizing vessels.
- Recognizing clinical/dermoscopic features of SCC/MCC should prompt deeper biopsies, enabling correct diagnosis/management.

## METHODS

### Patient selection

The study was performed with an approved application for exemption from review by the institutional review board/privacy board of Memorial Sloan Kettering Cancer Center. The pathology department archive was searched for patients with a diagnosis of MCC, with or without the key words "squamous cell." Cases for which slides were available for histopathologic and immunohistochemical confirmation of combined SCC/MCC or pure MCC were reviewed. Specifically, combined tumors showing SCC with a distinct neuroendocrine component (Fig 1) that was typically immunoreactive for CK20 with areas of paranuclear dotlike staining, and/or CAM5.2[3] positivity were accepted as SCC/MCC. In these cases thyroid transcription factor-1 and S100 were generally negative, as was the marker for the large T antigen of integrated Merkel cell polyomavirus, CM2B4.[3]

### Clinical data

The main clinical characteristics of patients were retrospectively assessed by patient chart review. Dates of tumor diagnosis and recurrence, along with clinical features, medical history, treatments pursued, and patient outcomes at follow-up were obtained from the patient's medical records.

### Clinical and dermoscopic image data

Cases for which only high-quality clinical photographs and dermoscopic images were available were examined. Features assessed included appearance of background skin, lesion size and shape, presence or absence of surface scale, pigment alteration/structures, and presence, quality, and location of vascular structures.

## RESULTS

### Clinical features of SCC/MCC tumors: photographic review

Clinical features of the tumors from 9 patients with available clinical ± dermoscopic images are presented in Table I. Six of the 9 tumors presented as firm, dome-shaped, smooth pink to red, sharply demarcated nodules with overlying thick adherent scale (Figs 2 and 3). One such tumor was present as multiple nodules, and another case presented as a papule arising in a surgical scar (Fig 4). Two cases were sufficiently violaceous in color that the clinical suspicion was melanoma (case 5) or hemangioma (case 8). All lesions occurred on sun-exposed sites. The face/scalp was involved in 6 cases, and the neck, back of wrist (Fig 5), and upper aspect of chest (Fig 6) in 1 case each. All patients had significant dermatoheliosis with actinic keratoses, solar lentigines, and telangiectasia in the skin away from the neoplastic growths. Basal cell carcinoma (BCC) (6/9) or SCC (3/9) were the most commonly suspected diagnoses at the time of biopsy. Intraoperative photographs from 2 patients with hyperkeratotic nodules demonstrated well-circumscribed, fleshy dermal nodules deep to and separate from the underlying crust (Figs 2 and 3). Lesions were asymptomatic in all 9 cases.

### Dermoscopic features of SCC/MCC tumors

High-quality dermoscopic images were reviewed (Figs 6 and 7). Tumors had surface scale and demonstrated small dotted vessels and short linear irregular vessels at the periphery. In some cases there also were milky-red areas located centrally with large-diameter arborizing vessels. None had white structureless areas, pigment, or a blue-gray veil.