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Case Report

Merkel Cell Carcinoma of the Hand in a Young Patient

Matthew LaBarge, BS, * Ross Feller, MD, * Amanda Keene, PA-C *

* Department of Orthopedic Surgery, Maine Medical Center, Portland, ME

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Merkle cell carcinoma (MCC) is a rare, malignant neuroendocrine skin cancer that typically affects patients in the seventh decade of life. Reports of MCC affecting young patients are limited, and there are few mentions of the management of these lesions when they present on the hand and fingers. Hand surgeons must be educated regarding the diagnosis of MCC and the multidisciplinary management required to achieve optimal results. We present the case of a 22-year-old woman with MCC arising on the dorsum of the second digit. Treatment with wide local excision, coverage of the resulting soft tissue defect with a reverse second dorsal metacarpal artery flap, and subsequent radiotherapy resulted in no evidence of disease recurrence or metastasis at 1 year. This case highlights the commonly encountered delay in the diagnosis of this lesion and the necessity for a high index of suspicion when evaluating a patient with an enlarging, solitary hand nodule.

Merkel cell carcinoma (MCC) is a rare and highly aggressive neuroendocrine neoplasm arising from the dermoepidermal junction. First described by Toker in 1972, MCC is a malignant cutaneous neoplasm with high rates of recurrence (25% to 30%), metastasis at the time of presentation (34% to 36%), and mortality (5-year survival rate of 30% to 64%).[1,2] As the name implies, the tumor arises from the Merkel cell, which is a mechanoreceptor—neurotactile cell involved in light touch discrimination of shapes and textures. Merkel cell carcinoma commonly arises in Caucasian men in the seventh decade of life.[1,2] Typically, patients present with a solitary, painless nodule; the sun-exposed areas of the face, chest, and upper extremity are common sites of primary disease.

Hand surgeons should be educated regarding the diagnosis, surgical management, and multidisciplinary involvement required to achieve optimal results with regard to treatment of MCC. Patients may be referred to a hand surgeon instead of a dermatologist or general surgeon for initial consultation, especially if the clinical presentation is a nodule without notable overlying skin changes or appears have a deeper, subcutaneous location on palpation. In addition, when MCC involves the hand or digits, unique anatomical considerations regarding the extensor mechanism, nail, soft tissue coverage requirements, and so forth may prompt involvement of a hand surgeon.

For these reasons, we present a case of MCC of the index finger in a 22-year-old woman treated with wide local excision and soft tissue coverage with a reverse second dorsal metacarpal artery (RDMA) flap, along with sentinel node biopsy and adjuvant radiation therapy. This case highlights the unfortunately common delay in the diagnosis of this condition and the need for hand surgeons to establish MCC on the differential diagnosis to avoid disease progression and the associated marked increase in morbidity and mortality. Also, one must be aware of the bimodal age distribution of MCC, and that this diagnosis is not limited to older patients with a history of sun exposure.

Case Report

A 22-year-old woman presented with a 4-month history of a slowly enlarging mass over the dorsum of the right index finger (Figs. 1, 2). The mass had a pinkish overlying skin discoloration without erosive changes, and on palpation it was minimally tender, firm, nodular, mobile, and consistent with a subcutaneous location. Before presentation, she had undergone incision and debridement of the mass on 2 separate occasions at urgent care for concern of infection. Initial excisional biopsy yielded a 1 × 2-cm mass penetrating down to the extensor mechanism but not involving it. Final pathology demonstrated small blue cells staining positive for CK20,

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Corresponding author: Matthew LaBarge, BS, Department of Orthopedic Surgery, Maine Medical Center, 22 Bramhall Street, Portland, ME 04102.
E-mail address: matthew.labarge@tufts.edu (M. LaBarge).

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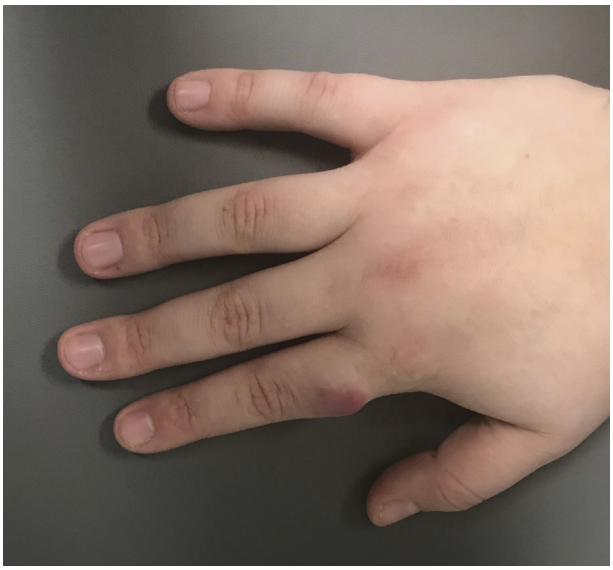

Figure 1. Preoperative presentation of MCC on radial aspect of dorsal second finger.

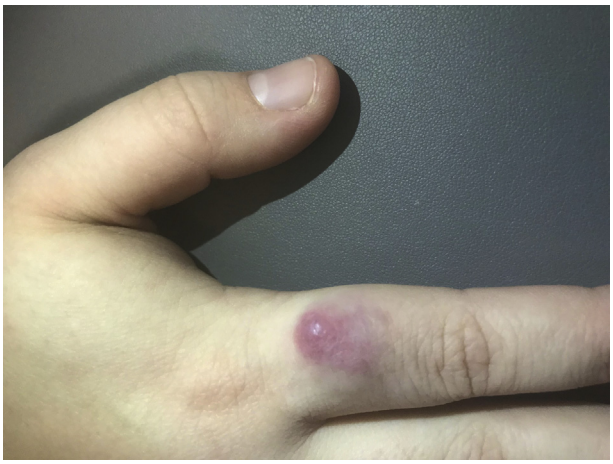

Figure 2. Clinical presentation of MCC of the finger. The mass had a pinkish overlying skin discoloration without erosive changes. On palpation, it was minimally tender, firm, nodular, and mobile and consistent with a subcutaneous location.

chromogranin, and synaptophysin, consistent with MCC (Figs. 3–5). The patient was presented at our institution's skin cancer tumor board, and a plan for wide local excision (WLE), sentinel lymph node biopsy (SLNB), and adjuvant radiation therapy was formulated. Preoperative computed tomography scan of the chest and abdomen demonstrated no evidence of metastasis. Subsequent WLE (2-cm margin) and coverage using an RDMA flap was performed (Figs. 6, 7), along with SLNB by general surgery. Pathology demonstrated clear margins without involvement of the extensor mechanism, and nodal pathology was free of disease. Three months after surgery, the patient underwent adjuvant radiation therapy (5000 cGy in 200-cGY fractions daily). Surveillance positron emission tomography–computed tomography as well as targeted ultrasound evaluation of the ipsilateral axillary lymph nodes performed at 6 months and 1 year confirmed no evidence of recurrence. Figures 8 through 10 show functional and cosmetic results. The patient is satisfied with the outcome.

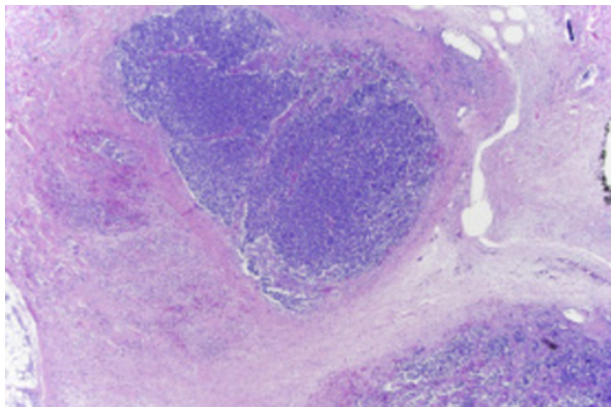

Figure 3. Typical histopathologic appearance of MCC. Large nodular collections crowded with basaloid cells in the dermis and subcutis with foci of necrosis (hematoxylin-eosin, magnification ×40).[1]

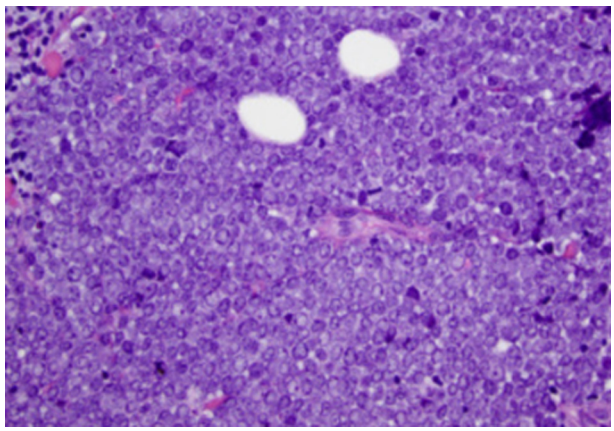

Figure 4. Cytomorphology of MCC showing round nuclei, scant cytoplasm, salt and pepper chromatin: indistinct nuclei (hematoxylin-eosin, original magnification ×200).[14]

Discussion

There is a scarcity of literature regarding primary MCC of the hand and fingers. The vast majority of case reports detail the classic clinical presentation of a subcutaneous nodule appearing in sun-exposed areas in the seventh or eighth decade of life.[3–7] However, there has been a rise in case reports with the growing rates of diagnosis. The incidence of MCC has been increasing dramatically; reports demonstrate a 95% rise in cases since 2000. By comparison, this greatly outweighs the observed increase in the rate of melanoma (57%).[8] Only 4% of MCC is diagnosed in patients aged less than 50 years, and Caucasians account for 95% of all cases.[1,2] Merkle cell carcinoma has a high rate of local recurrence (25% to 30%), regional lymph node involvement (52% to 59%), and metastasis (34% to 36%) and a 5-year disease-specific survival rate of 30% to 64%.[2,9] This neoplasm has a predilection for early lymphovascular invasion and metastasis.[10] A published cohort of 1,100 patients with MCC reported metastasis rates after 1, 2, and 5 years of 49%, 80%, and 99%, respectively.[11,12] Primary sites of metastasis were distant lymph nodes (41%), liver (23%), bone (21%), pancreas (8%), and lung (7%).[11,12] Distant skin or body wall metastases were more common in patients with an upper-extremity primary site than any other primary site.[11,13]

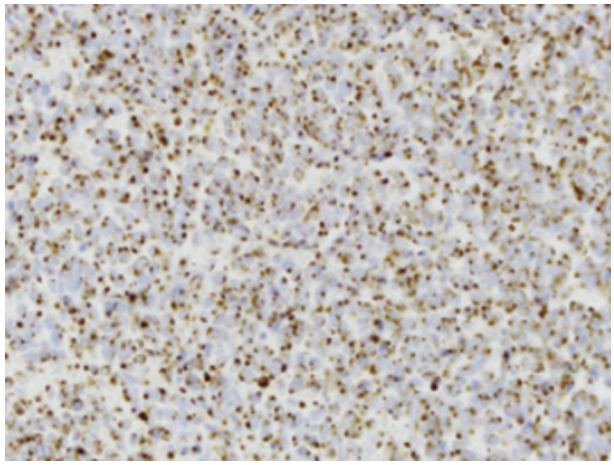

Figure 5. Cytokeratin-20 immunohistochemical staining in MCC showing a paranuclear dot pattern (immunohistochemical, original magnification ×200).[1]

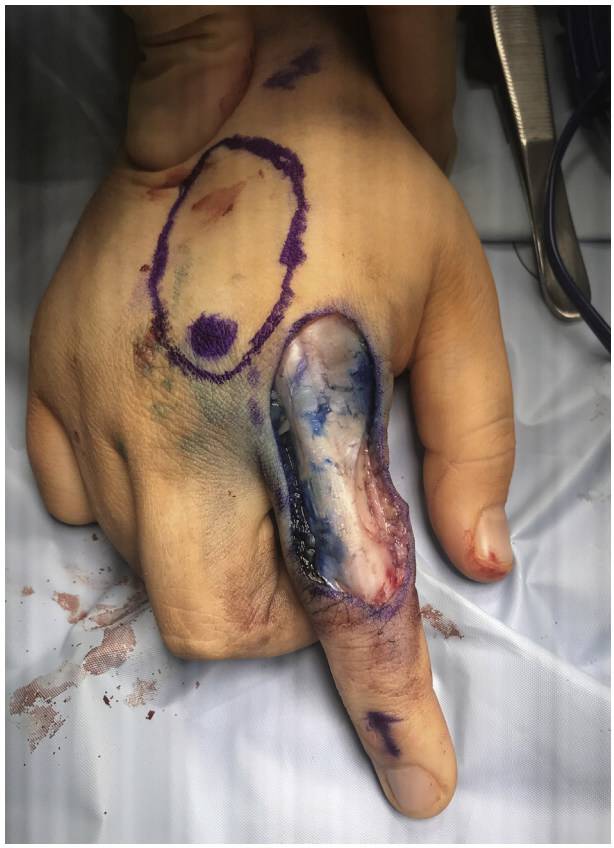

Figure 6. Intraoperative depiction of WLE with dissection down to the extensor mechanism but not including it. Surgical pen markings outline the RDMA flap before mobilization, with the dark circle marking the vascular pedicle.

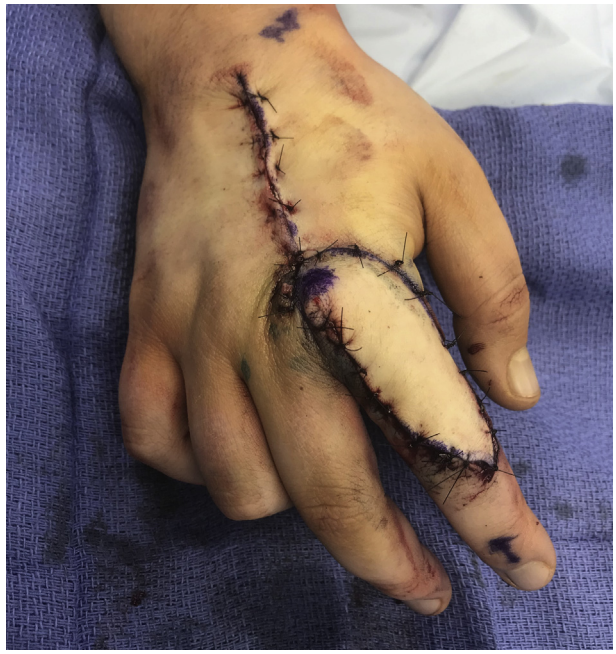

Figure 7. Reconstruction of the dorsal radial skin defect of the second digit using the RDMA flap.

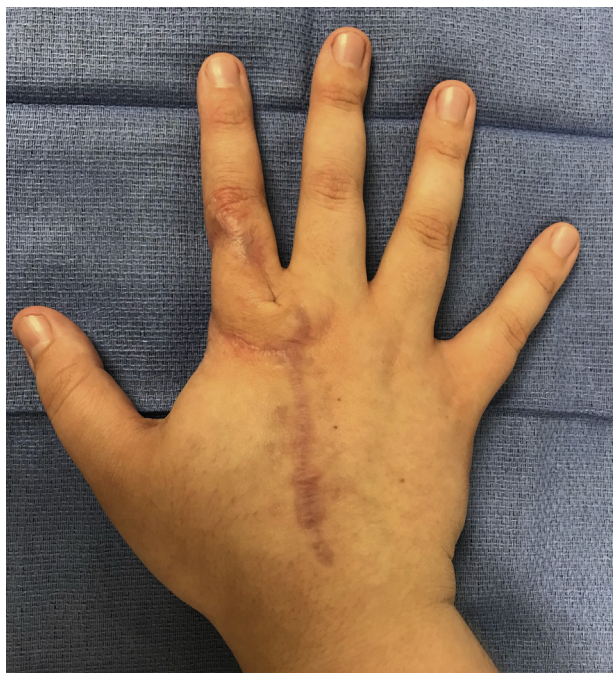

Figure 8. One-year postoperative follow-up demonstrating wound healing and flap tissue preservation (dorsal view).

Clinically, MCC presents as a rapidly growing, firm, painless, pink or flesh-colored nodule. The mnemonic AEIOU (Asymptomatic, Expanding rapidly, Immunosuppressed, Older than age 50, UV-exposed area) is an often-used clinical tool for diagnosis for which 3 of 5 findings are present in 89% of patients.[13] Factors associated with a poorer prognosis include male sex, primary location of the head or neck, metastasis at the time of presentation, and recurrence.[13] Diagnosis is confirmed by histology and immunohistochemistry. Hematoxylin-eosin staining shows neuroendocrine morphology of poorly differentiated small round blue cells with large nuclei, scant cytoplasm, and high mitotic bodies. Expression of cytokeratin-20 is present in a punctate

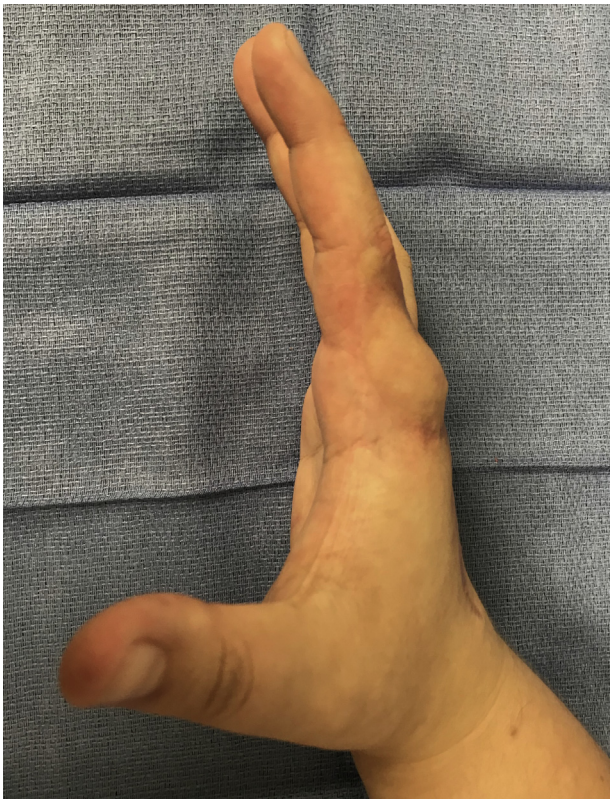

Figure 9. One-year postoperative follow-up demonstrating wound healing and flap tissue preservation (lateral view).

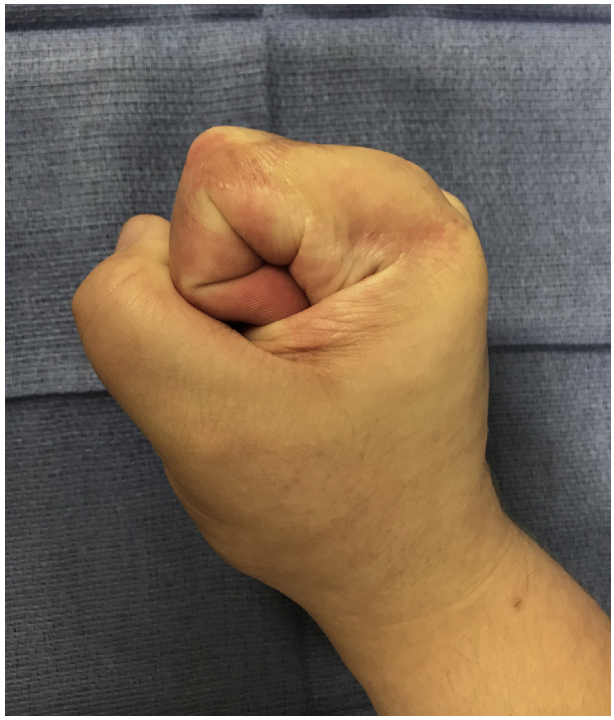

Figure 10. One-year postoperative follow-up depicting full range of motion of the second digit after flap healing.

pattern, and neuroendocrine cell markers (synaptophysin, neuron-specific enolase, and chromogranin A) are seen on immunohistochemistry.[1,2,14]

Because of the rare nature of MCC, there is currently no standard treatment. According to the National Comprehensive Cancer Network (NCCN), WLE with 1 to 2 cm margins is the treatment of choice for local primary tumors, and Mohs surgical technique may be useful in areas where tissue sparing is important.[15] Large retrospective analyses have demonstrated sentinel lymph node (SLN) positivity in 30% to 38% of patients, which warrants SLNB in initial tumor evaluation.[15] The prognostic value of SLN status is currently under debate. Some studies link SLN negativity to a lower risk for recurrence and improved rates of survival, whereas others show no correlation of SLN status and improved clinical outcomes.[15] The NCCN recommends that patients with a positive SLNB receive baseline imaging, if not already completed, to screen for and quantify both regional and distant metastasis.[15] Recently published meta-analyses report that adjuvant radiotherapy (RTX) is associated with reduced rates of local recurrence and increased rates of overall survival and disease-free survival compared with surgery alone. The NCCN recommends using adjuvant RTX to the draining lymph node basin after lymph node dissection if multiple nodes are involved and/or if extracapsular extension is detected.[15] When adjuvant RTX is used to treat the primary site, doses should be delivered in 2-Gy/d standard fractionation and wide margins (5 cm) around the site should be used when feasible.[15] In instances of unresectable or known metastatic disease, systemic chemotherapy and immunotherapy are recommended. A variety of regimens have been described and often include a platinum agent, cyclophosphamide with fluorouracil, and methotrexate (combined with vincristine or doxorubicin). Overall response rates are reported to be 40% to 60%.[15] There are reports of patient response to checkpoint immunotherapy agents, and current phase I and II clinical trials are investigating avelumab (programmed death-ligand 1) and pembrolizumab—nivolumab (programmed cell death protein 1) for use in MCC.[15]

The surgical approach for the patient in the current report, in accordance with NCCN guidelines and recommendations from our institution's tumor board, was WLE of the primary tumor site with 2-cm margins. Excision of skin and subcutaneous tissue was performed down to the extensor mechanism, preserving the paratenon. Axillary SLNB demonstrated no nodal involvement. Postoperative RTX to the primary site was performed given the high rates of local recurrence.

Although the decision was made to perform an RDMA flap, several other options might have been considered for coverage of the resulting soft tissue defect after WLE in this patient. This list includes split-thickness skin grafting, full-thickness skin grafting, dermal substitute with subsequent skin grafting, and a local random pattern rotational flap. We decided to proceed with an RDMA flap for multiple reasons. There is minimal donor site morbidity with primary wound closure possible.[16] The tissue harvested is thin, pliable, and similar in thickness to the area requiring coverage. The flap is vascularized and results in reliable healing rates with less tissue contracture and pigmentation changes compared with skin grafting options.[16] Like any distally based reverse flow flap, venous congestion is the major complication that can be encountered. However, the flap has been well-studied with a reliable and consistent vascular pattern.[16] Its ease of harvest and versatility make it an ideal candidate for coverage of dorsal digital defects. There is a concern that the RDMA flap could mask clinical diagnosis of local tumor recurrence that would otherwise be detected in a thinner skin graft. There is also the potential of tumor seeding along underlying planes of the flap. We considered these when determining the best method for defect closure and concluded that the functional and cosmetic benefits of the RDMA flap outweighed those risks. We will monitor the area with

frequent and regular follow-up and have a low threshold to pursue imaging for a suspected subcutaneous nodule or secondary flap defect, especially within the first 2 years.

After surgery, the patient was placed in a radial gutter intrinsic plus orthosis and physical therapy was initiated after 1 week.

Merkle cell carcinoma is a rare yet aggressive neuroendocrine cancer that has seen a dramatic increase in incidence. It commonly presents on the skin of the hand and upper arm. As such, hand surgeons should be aware of its presentation and management. Current guidelines focus on a multidisciplinary treatment approach, including surgical excision and soft tissue coverage, histopathological assessment, radiotherapy, and potential systemic therapy. Multiple options are available for soft tissue coverage; however, the reverse dorsal metacarpal artery flap is a reliable option with excellent cosmetic and functional outcomes. Merkle cell carcinoma is not limited to elderly patients with a history of excessive sun exposure and must be considered as a differential diagnosis in younger patients presenting with a solitary, painless, pink or flesh-colored nodule.

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