

## Isolated Tibial Metastasis from Merkel Cell Carcinoma

Ba D. Nguyen, M.D., and Ann E. McCullough, M.D.

Merkel cell carcinoma is a rare but aggressive neuroendocrine tumor of the skin with high propensity for local, regional and distant soft tissue metastasis not only at initial presentation but also after timely and satisfactory wide-margin surgery. Bone metastases account for 10% of all cases and have been reported involving the calvarium, facial bones and spine related to the head and neck preferential location of this soft tissue malignancy. Appendicular skeletal dissemination is uncommon with only a few cases reported in the radiological literature. We present a case of isolated tibial metastasis from Merkel cell carcinoma occurring 19 months after a technically adequate head and neck tumor resection and lymphadenectomy.

### Introduction

Merkel cell carcinoma is an uncommon but highly malignant skin neoplasm. Also known as trabecular skin carcinoma, murky cell carcinoma, anaplastic skin carcinoma, primary small cell skin carcinoma and neuroendocrine skin carcinoma, this tumor is usually neglected at early stage of the disease due to its indolence and falsely benign appearance. Its diagnosis, confused with squamous cell carcinoma, basal cell carcinoma or melanoma, is frequently delayed resulting in high occurrence of regional

and distant metastasis. Even with an early correct diagnosis and technically impeccable therapy, Merkel cell carcinoma has a high propensity for local and regional recurrence, and systemic dissemination. To illustrate the aggressive behavior of this skin lesion, we present a case of solitary tibial metastasis of Merkel cell carcinoma occurring 19 months after initial skin surgery.

### Case Report

A 69-year-old man presented with a rapidly growing mass at the right cheek. The lesion measured 3 x 4 cm, appeared mildly telangiectatic and was not tender on palpation. Fine needle aspiration suggested Merkel cell carcinoma (MCC). Pre-operative head and neck CT demonstrated a right facial subcutaneous mass without musculoskeletal involvement and adenopathy (Fig. 1). Cross-sectional imaging of the chest, abdomen and pelvis was unremarkable. The patient underwent en-bloc wide resection of the right facial mass along with parotidectomy, and facial and right cervical lymphadenectomy. Pathology confirmed the neuroendocrine nature of the lesion consistent with MCC. The resected right parotid gland, right

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Abbreviations: CT, computed tomography; MCC, Merkel cell carcinoma; MRI, magnetic resonance imaging

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submandibular gland, and facial and jugular nodes were free of metastasis. The post-operative course was uneventful and the patient received adjuvant radiotherapy and VP-16 chemotherapy.

Nineteen months after the initial surgery, close follow-up registered the patient's complain of right knee pain. Right knee radiographs raised the possibility of ill-defined lytic lesion involving the medial tibial plateau (Fig. 2). Bone scintigraphy demonstrated an intense radiotracer uptake at the tibial epiphysis and metaphysis (Fig. 3). Right tibial biopsy showed MCC metastasis. The patient underwent radiotherapy for the right knee metastasis, which was complicated after the first session by a pathologic fracture of the right medial tibial plateau. MR examination confirmed the pathologic fracture and showed an aggressively appearing and poorly defined mass of the medial tibial plateau extending to the tibial metaphysis with adjacent soft tissue involvement (Fig. 4). The patient had tumor resection and kinetic rotating hinge knee prosthetic reconstruction. Pathology confirmed the right knee lesion to be bone and soft tissue metastasis from MCC (Fig. 5).

### Discussion

Merkel cell carcinoma is a rare tumor of the dermis first described by Toker as trabecular cell carcinoma of the skin in 1972 [1]. This cutaneous malignant neoplasm is thought to originate from either Merkel cell, a tactile receptor of the skin, or a totipotential precursor stem cell

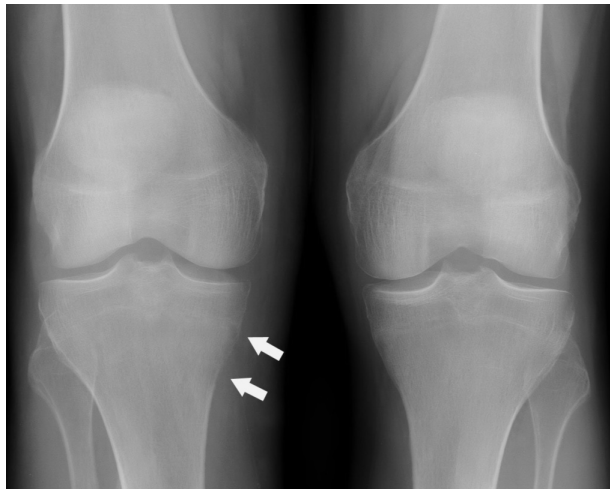


Figure 2. 71-year-old man with Merkel cell carcinoma metastasis. AP radiograph of the knees shows subtle lucent lesion at the medial aspect of the left proximal tibial metaphysis (arrows)

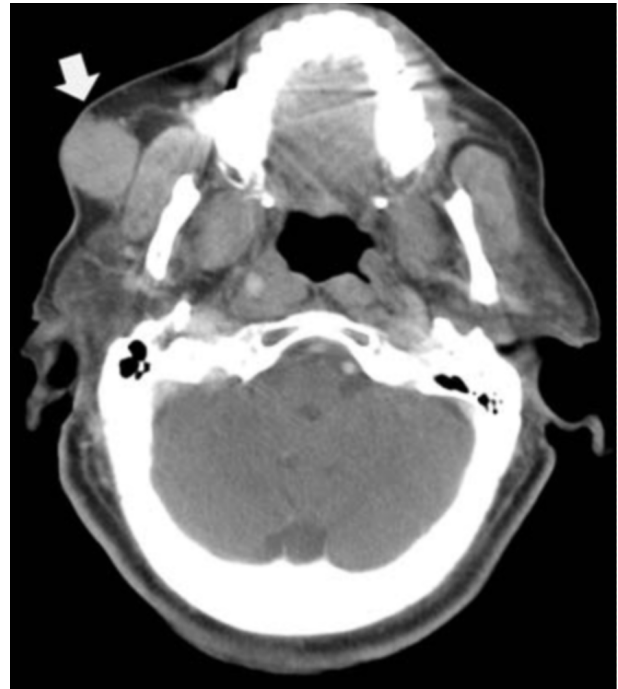


Figure 1. 69-year-old man with Merkel cell carcinoma. CT of the face shows the tumor as a subcutaneous nodular lesion of the right cheek (arrow).

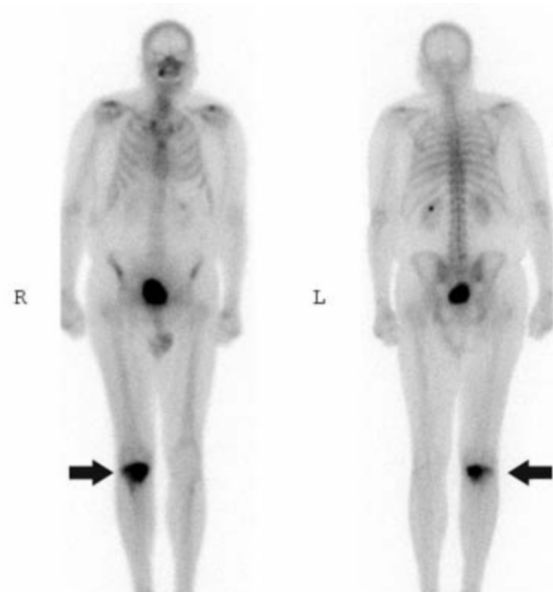


Figure 3. Anterior and posterior views of the technetium-99m MDP whole body bone scintigraphy show abnormal radiotracer uptake at the proximal right tibia predominantly at its medial aspect (arrows).

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Figure 4A. Coronal MRT1-weighted image shows the MCC metastasis within the medial meta-epiphysis of the right proximal tibia (arrows) with pathologic fracture (arrowheads).

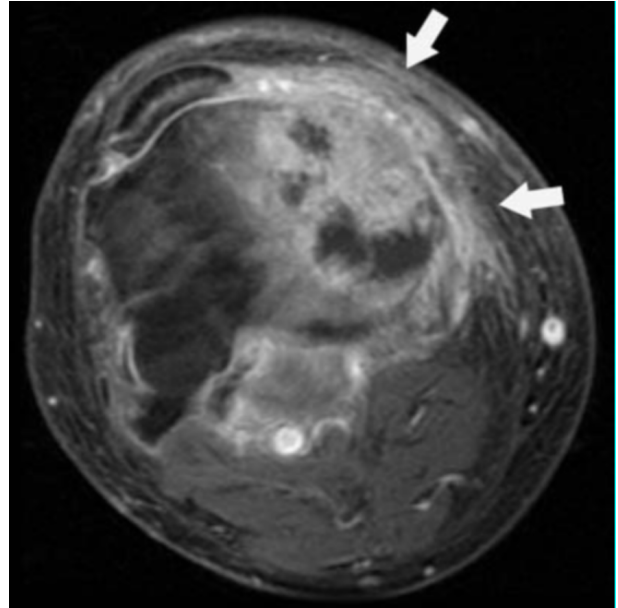


Figure 4B. Enhanced axial MR SPGR image with fat saturation shows the right proximal tibial MCC metastasis. There is soft tissue invasion with increased signal intensity extending beyond the proximal tibial cortex anteromedially and posterolaterally (arrows).

with subsequent malignant transformation [2, 3]. The two best appellations of this tumor are MCC or neuroendocrine carcinoma of the skin based on its postulated Merkel cell origin and immuno-histochemical characteristics. The lesion is encountered in a population of greater than 65 years of age with probable equal gender distribution [4]. MCC is uncommon in blacks and polynesians. The typical MCC lesion appears as a non-tender and indurated skin nodule with red or purple coloration. It may exhibit ulcerative or telangiectatic appearance. MCC is most commonly found in the head and neck especially in the periorcular region [4, 5]. The second most frequent site is at the extremities with truncal involvement uncommon. Risk factors include exposure to ultraviolet and infrared light, past history of radiation therapy and immunosuppressed-immunocompromised status [6]. MCC is an aggressive neoplasm with up to 31% of regional nodal invasion and up to 4% of distant metastases at initial diagnosis, and high rate of local, regional and systemic recurrence even after adequate tumoral resection [7]. MCC may be misdiagnosed as basal cell, squamous cell carcinoma or melanoma. To increase the complexity of its identification, MCC

may co-exist with and be adjacent to other small cell skin neoplasms [8]. Diagnosis is exclusively pathologic relying on immuno-histochemical staining or electronic microscopy [9]. Due to its rarity, a tentative clinical staging has been proposed with three phases: local cutaneous lesion, regional disease with adenopathy and systemic dissemination to lung, liver, bone, skin and central nervous system [4]. Conventional radiography and cross-sectional imaging demonstrate non-specific soft tissue nodules or masses reminiscent of other small cell neoplasm and related metastases [10]. Nuclear medicine provides a more selective assessment at different stages of the disease. Based on the melanoma-like orderly lymphatic progression, lymphoscintigraphy with technetium-99m filtered sulfur colloid is used to locate sentinel nodes draining the MCC sites; it allows a more precise and less aggressive lymphadenectomy to distinguish the local stage from the regional phase of the disease [11]. Somatostatin receptor scintigraphy with Indium-111 octreotide and positron emission tomography with fluoro-deoxyglucose fluorine-18 may facilitate MCC staging and post-therapeutic surveillance: their imaging is based on the neuroendocrine nature and the high glucose-

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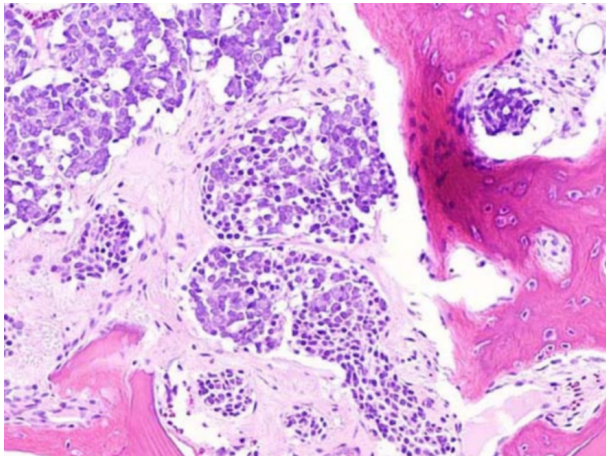


Figure 5. Microphotograph with H&E stain of the right proximal tibial biopsy specimen shows clusters of high grade small blue cells of neuroendocrine carcinoma consistent with metastasis from Merkel cell carcinoma.

related metabolism of MCC respectively [12]. The last two scintigraphic procedures are helpful for timely detection of MCC metastases and recurrence. The prognosis of MCC is guarded due to high rate of local relapse and regional nodal disease after initial treatment, high frequency of systemic dissemination and resulting high mortality rate [4, 9, 12]. Treatment consists of wide-margin resection or Mohs microsurgery combined to locoregional radiation [12]. Chemotherapy has only short-term success [4, 9].

Metastasis to the distal part of the appendicular skeleton especially the knee is usually witnessed at advanced stage of neoplastic diseases. Distant solitary metastasis to the lower extremity is infrequent and may be secondary to a large spectrum of primary malignant tumors. MCC, a rare but very aggressive cutaneous neuroendocrine neoplasm with high frequency of regional and distant dissemination, may exhibit isolated distant metastasis as illustrated by the presented case. It probably involves the soft tissue of the knee by hematogenous dissemination with contiguous invasion of the tibia or small lymph vessels in Haversian canals leading to pathologic fracture. The presented case emphasizes the very aggressive behavior of MCC and the necessity for close post-therapeutic monitoring. Despite a timely and satisfactory treatment of the initial cheek lesion including wide-margin resection and lymphadenectomy, it recurs at a distant site involving the left tibia. Bone metastases, representing 10% of all systemic spread, have been reported in detail targeting different parts of the skull contiguously to the predominant head and neck MCC sites with further

extension to CNS, sacrum and epidural space probably hematogenously or through cerebro-spinal fluid [13-16]. Distant dissemination to appendicular skeleton is rare [17, 18]. Radiological and scintigraphic findings, even though non-specific for MCC without knowledge of the initial diagnosis, are helpful to promptly assess and timely initiate treatment for recurrence and systemic disease.

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