Merkel cell carcinoma with concurrent squamous cell carcinoma of the lower lip treated with Mohs micrographic surgery: A case report

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INTRODUCTION

Merkel cell carcinoma (MCC) is a rare skin cancer with a high potential for metastasis and recurrence that commonly involves the head and neck.[1] While MCC typically presents as a solitary, fast-growing, shiny, asymptomatic, and pink nodule, MCC remains a diagnostic challenge given its non-specific and overlapping features with other dermatologic entities.[1] Although MCC management varies by disease stage, standard treatments include wide local excision (WLE) with sentinel lymph node (SLN) dissection, radiation, chemotherapy, and immunotherapy.[1] Mohs micrographic surgery (MMS) has also shown to be effective for early-stage disease and is included in the National Comprehensive Cancer Network guidelines.[2,3] Concurrent MCC with squamous cell carcinoma (SCC) is rarer and considered to be more aggressive than MCC alone.[4] Here, we present a unique case of a MCC associated with SCC of the left lower vermilion lip that was treated definitively with MMS.

Abbreviations used:

MCC:	Merkel cell carcinoma
MMS:	Mohs micrographic surgery
SCC:	squamous cell carcinoma
SLN:	sentinel lymph node
WLE:	wide local excision

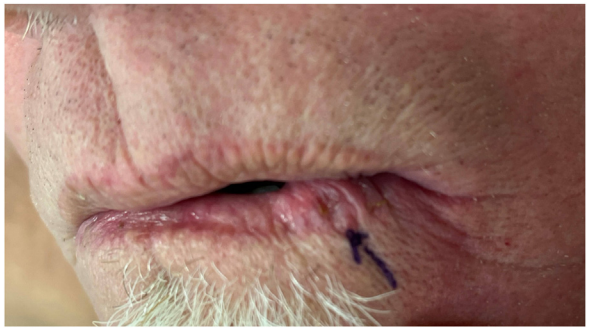

Fig 1. Non-healing, bleeding papule on the left lower vermilion lip, before shave biopsy. Biopsy revealed a combined Merkel cell carcinoma and squamous cell carcinoma.

CASE

A 69-year-old man with a history of non-melanoma skin cancers including a poorly-differentiated SCC of the right calf status post MMS and adjuvant radiation, presented to the dermatology clinic with a non-healing, bleeding papule on the left lower vermilion lip (Fig 1). The lesion measured 0.9 cm x 0.9 cm clinically on the day of surgery. Histologic examination showed an ulcerated basaloid tumor, with nuclear molding in the basaloid cells and concurrent atypical keratinocyte aggregates (Fig 2). The MCC portion of the tumor was strongly positive for neuroendocrine marker insulinoma-associated protein 1 and synaptophysin, whereas neurofilament

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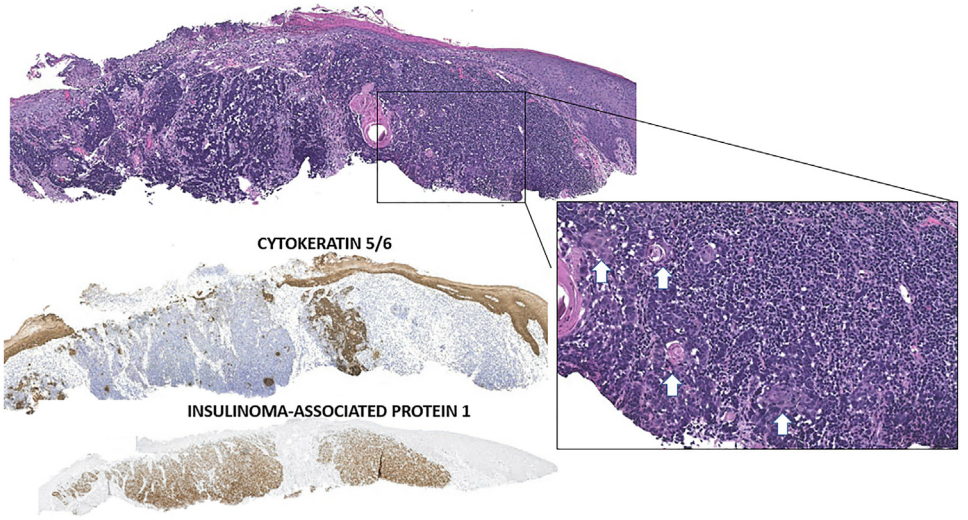

Fig 2. Ulcerated atypical basaloid tumor with sheets of crowded, hyperchromatic cells (*upper left*, hematoxylin and eosin stain, 20× magnification) labeling with insulinoma-associated protein 1 antibody defining Merkel cell carcinoma. Concurrent atypical keratinocytes and squamous pearls (*Bottom right insert*, *white arrows*; hematoxylin and eosin stain, 200× magnification), best highlight with cytokeratin 5/6 immunostain (20× magnification), defining concurrent squamous cell carcinoma.

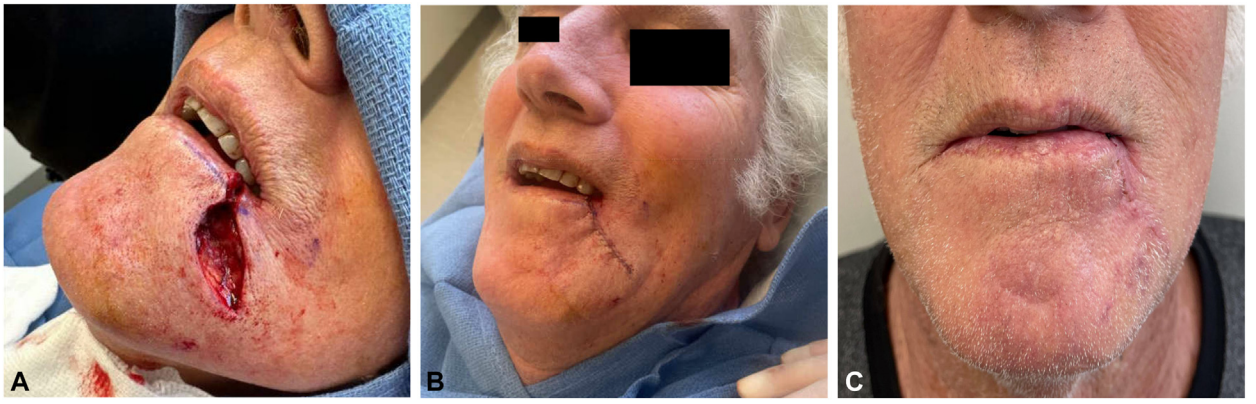

Fig 3. A, Post-surgical defect after tumor was removed with initial debulking followed by 2 Mohs micrographic surgery stages. **B,** Status post full thickness lip defect repair. **C,** Well-healed surgical scar at 1 week follow-up.

showed focal immunolabeling, and thyroid transcription factor 1, chromogranin, and special AT-rich sequencing-binding protein 2 were collectively negative. Additionally, p63 and cytokeratin 5/6 were positive in the component of SCC (Fig 2).

The patient underwent positron emission tomography/computed tomography for staging, which only demonstrated non-specific mild focal uptake in the midline upper lip. After evaluation by head and neck surgery, medical oncology, and radiation oncology, given stage 1 disease, the initial plan was for WLE of the primary tumor with SLN biopsy. However, given that the patient's preference was to maximize preservation of lip function and the primary tumor was poorly defined on clinical examination, a shared decision was made to perform MMS for the primary tumor after first undergoing a SLN biopsy with head and neck surgery.

SLN biopsy was performed on 3 lymph nodes, all of which were negative for malignancy. Following the SLN biopsy, patient underwent MMS. The first stage of MMS (Fig 3, *A*) revealed keratinocyte atypia involving the full thickness of the epidermis, consistent with SCC *in situ* without a residual invasive component or evidence of MCC. The second stage was negative for residual malignancy. The central

clinically apparent tumor that was debulked prior to MMS was sent to dermatopathology for confirmatory evaluation, confirming residual MCC, without neurovascular invasion. The lip defect was then repaired by full thickness wedge closure (Fig 3, *B*). The patient healed well without impairment of lip function or loss of the oral aperture (Fig 3, *C*). Given the high-risk anatomic site and propensity for MCC to invade subjacent structures, the patient underwent adjuvant radiation 2 months after MMS.

DISCUSSION

MCC is an aggressive, rare skin cancer with high mortality, requiring prompt diagnosis and treatment. In 2013, the estimated incidence rate in the United States was approximately 0.7 cases per 100,000 person-years and increases with age.[1,5] Other risk factors include the Merkel cell polyomavirus, sun exposure, immunosuppression, lighter skin color, history of other malignancies, and cancer predisposition genes in early-onset MCC.[1,5] Notably, approximately 20% of MCC are Merkel cell polyomavirus negative and cytokeratin-20, an immunohistochemical marker for MCC, is absent in 10% to 15% of cases.[1,6] A combined MCC with SCC is rarer, seen commonly in the elderly with chronic sun-damaged skin and portends a worse prognosis.[4] Furthermore, a higher proportion of MCC with associated SCC are negative for Merkel cell polyomavirus.[7] There are various theories regarding the pathogenesis of combined MCC/SCCs, including that the tumors are derived from one another because of coinciding mutations on whole-exome sequencing or, in contrast, that they are unrelated collision tumors.[7]

Treatment of MCC with MMS offers several advantages including complete circumferential peripheral and deep margin assessment and a tissue-sparing approach. Several studies have evaluated the efficacy of MMS for MCC, with overall mixed data when compared with WLEs. For example, one recent study analyzed patients with stage 1 and 2 MCC from the National Cancer Database and found that those with localized MCC had improved overall survival when treated with MMS compared with WLE.[2] However, there are limitations to this study including its retrospective nature and selective bias for MMS in patients with MCC who have more favorable survival factors. In another retrospective study based on the Surveillance, Epidemiology, and End Results database comparing MMS versus WLE, the authors found no difference between MCC-specific and overall survival in patients with localized MCC treated with MMS versus WLE.[8] Similarly, no significant differences were seen between MMS and WLE groups in cancer recurrence after primary tumor resection.[9]

Although more data is needed to better elucidate the efficacy of MMS for treatment of MCC in comparison to WLE, MMS should be considered for patients with localized MCC involving the face to preserve function and avoid permanent disfiguration. For our case, MMS was favorable because of challenges with reconstruction involving the vermilion border and oral commissure. SLN biopsy should be performed before MMS per the National Comprehensive Cancer Network guidelines given the potential for alterations in SLN mapping after tumor resection and reconstruction.[3] Adjuvant radiation therapy is also indicated for those with high-risk tumors.[3,10]

Our case highlights the benefits of MMS in the treatment of localized MCC of the left lower vermilion lip without nodal disease, including achieving clear margins while maximizing tissue preservation for lip function. Furthermore, our case demonstrates a pathologically unique tumor, with a combined MCC and SCC that is positive for immunohistochemical tumor markers such as insulinoma-associated protein 1 but negative for cytokeratin-20. This may be a collision tumor in the setting of risk factors such as heavy UV exposure. Future investigations are needed to better understand the efficacy of MMS in skin cancers including MCC and combined tumors.

Conflicts of interest

None disclosed.

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