

Partial Gastric Resection for Symptomatic Anemia following Diagnosis of Merkel Cell Carcinoma (MCC) of the Skin with Gastric Metastasis

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ABSTRACT: Merkel Cell Carcinoma (MCC) is a rare dermatologic malignancy with significant morbidity and mortality associated with metastatic disease. In this case, we discuss an extremely rare presentation of MCC with metastasis to the stomach in a patient that presented with profound anemia. Unfortunately, mortality following diagnosis of MCC with gastric metastasis approaches 67% at 4 months based on available published reports. Due to its rarity and high rate of mortality, there is a lack of available research and literature to help guide treatment of this rare presentation of MCC. This case report presents a positive outcome associated with a partial gastrectomy for the treatment of symptomatic MCC with gastric metastasis and continued survival with persistently stable hemoglobin at 12 months.

KEY CLINICAL MESSAGE:

Anemia may be a significant cause of the morbidity and mortality associated with MCC with gastric metastasis. Our case demonstrates a positive outcome associated with partial gastric resection and presents a possible treatment option for this rare disease process.

KEYWORDS: Carcinoma, Merkel cell, immunotherapy, anemia, refractory

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Introduction

Merkel Cell Carcinoma (MCC) is a rare, highly aggressive cutaneous dermatologic malignancy with an incidence of 0.7 per 100 000 persons that is typically seen in older, fair skinned adults.¹ Development of MCC is attributed to multiple risk factors such as Merkel Cell Polyomavirus, ultraviolet (UV) radiation, and immunosuppression.¹ MCC has a high propensity for metastasis with the most common sites being lymph nodes, skin, lung, liver, bone, and brain.^{1,2} Though the malignancy is uncommon, recorded metastasis to the stomach is exceedingly rare with only 13 identified cases reported in the literature.^{1,3–14} In this case report, we discuss the outcomes of a partial gastrectomy for the treatment of symptomatic MCC with gastric metastasis.

Case Description

An 84-year-old African American male with recently diagnosed metastatic MCC presented to the emergency room with progressively worsening shortness of breath, fatigue, and melena. A positron emission tomographic (PET) scan at the time of diagnosis showed bulky hyper-metabolic inguinal adenopathy and left hilar lymph node. He had been initiated on immunotherapy treatment with pembrolizumab. Patient denied any

recent history of peptic ulcer disease, anticoagulation therapy, or recent non-steroidal anti-inflammatory drug (NSAID) use. On physical exam, the abdomen was non-tender without guarding or rigidity, however rectal exam showed maroon colored stools. Laboratory analysis was notable for a hemoglobin of 4.8 g/dL. Aggressive intravenous fluid resuscitation, red blood cell transfusions, and proton pump inhibitor therapy was immediately initiated. Gastroenterology was consulted and performed an upper endoscopy which revealed a malignant appearing 3-cm ulcerated gastric nodule with stigmata of recent bleeding (Figure 1). Gastric biopsy results showed focally ulcerated MCC. A partial gastrectomy was performed during hospitalization with resolution of the patient's bleeding. Both biopsy and resection of the stomach mass showed gastric mucosa with a submucosal cellular proliferation arranged in sheets and expansile nests. Tumor cells showed increased nuclear size, scant cytoplasm, fine chromatin, and indistinct nucleoli. Mitoses were frequent (up to 4 mm²) and single cell necrosis was conspicuous in a background of crush artifact. No evidence of divergent differentiation or other elements was identified. Immunohistochemical staining was performed with appropriately staining controls. Tumor cells were positive for pancytokeratin, NSE, chromogranin, synaptophysin, and



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Figure 1. Endoscopic appearance of MCC with gastric metastasis.

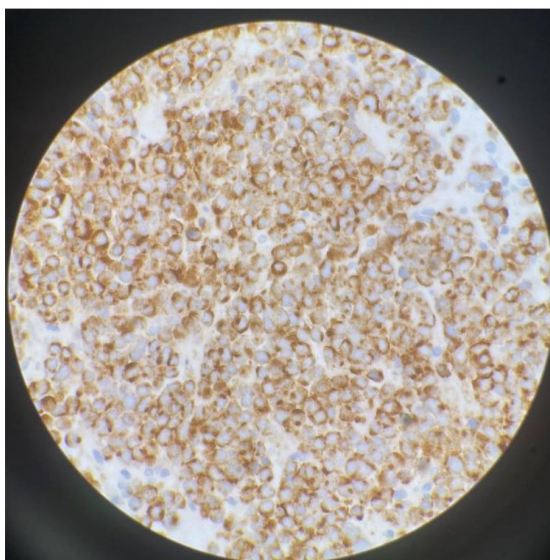


Figure 2. Chromogranin stain, 600× magnification of gastric mucosal biopsy.

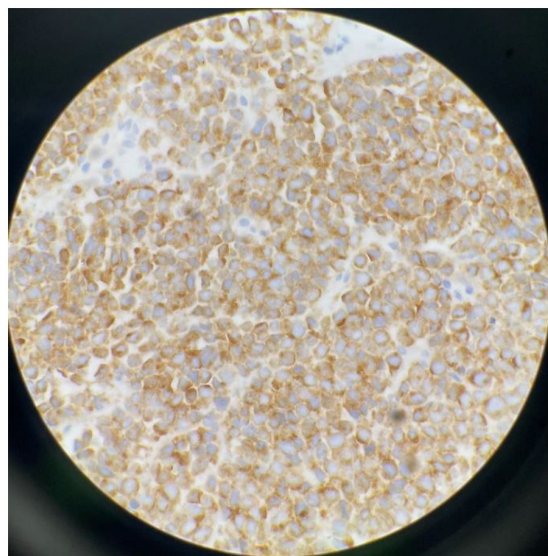


Figure 3. Synaptophysin stain, 600× magnification of gastric mucosal biopsy.

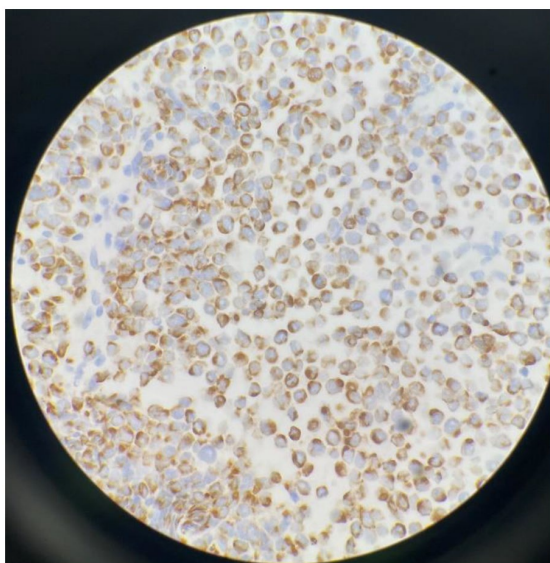


Figure 4. CK20 stain, 600× magnification, Gastric mucosal biopsy depicting tumor cell positivity in the characteristic paranuclear dot-like pattern.

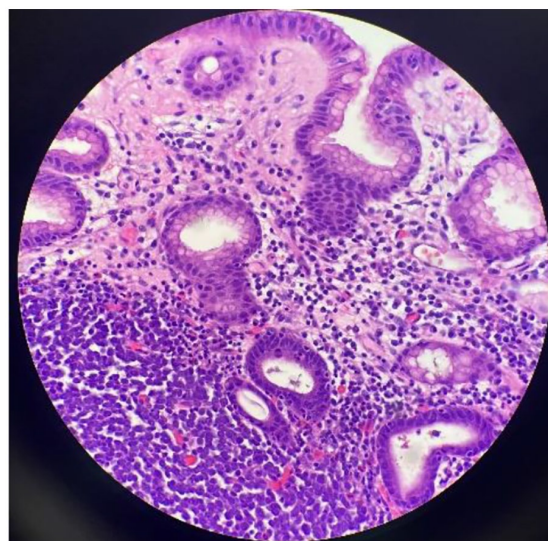


Figure 5. Hematoxylin and Eosin stain, 400× magnification of gastric wedge resection depicting gastric mucosa with tumor cells in the lamina propria.

CK20 (classic perinuclear dot-like pattern) (Figures 2, 3, and 4). The Ki67 proliferation index was increased (80%). TTF-1 and CD45 were negative, arguing against metastatic small cell carcinoma of the lung and lymphoma, respectively. These morphologic and immunohistochemical features along with the patient's history of MCC were consistent with a diagnosis of metastatic MCC (Figure 5). One year after resection, our patient remains asymptomatic with stable hemoglobin.

Discussion

Though rare, the incidence of MCC has tripled over the last decade and mortality from advanced MCC has risen by over 300%.^{15,16} The exact reason for the increasing incidence and mortality is not well understood at this time but may be due to improved understanding of the pathogenesis, aging populations, increased immunocompromised patients, and refined diagnostic tools.¹⁴

The diagnosis of MCC begins with high clinical suspicion. The AEIOU acronym was developed by Heath et al and summarizes the common clinical findings: asymptomatic, expanding rapidly, immunosuppressed, older age, and UV exposure.¹⁷ The gold standard for diagnosis is biopsy as MCC must be differentiated from other neuroendocrine tumors, melanoma, cutaneous lymphoma, and small cell lung carcinoma.¹⁸ Immunohistochemical staining is necessary to demonstrate positivity for broad spectrum keratins (AE1/3), neuroendocrine markers (chromogranin, synaptophysin, neuron specific enolase, CD56), and CK20 positivity in a classic dot-like paranuclear pattern.^{18,19} Available literature regarding MCC tumor cells immunoprofiles notes the use of maspin as a possible marker to assist the diagnosis of MCC, particularly in relation to sun exposure.¹⁹ Though this stain was not readily available at our institution, its positivity appears to be suggestive of MCC and could be used as an additional marker when available. Negative staining with cd57, pax5, tdt, CK7, ttf-1, s-100, and LCA help rule out metastasis from other sites (small cell lung carcinoma), lymphoma, and melanoma.¹⁸⁻²⁰

According to the National Comprehensive Cancer Network, immunotherapy with PD-1/PD-L1 blockade is typically used for metastatic MCC due to improved side effect profile when compared with chemotherapy or surgery.^{21,22} Given the rarity of metastasis of MCC to the gastric mucosa, no clear treatment guidelines have been established. Gastrointestinal bleeding appears to be the most common presentation of MCC with gastric metastasis.^{1,3-14} Mortality rates range from 1 week to 24 months with an average mortality rate of 67% at 4 months following diagnosis of gastric metastasis.^{1,3-14} Of the 13 case reports identified, 2 patients underwent aggressive surgical intervention in addition to traditional pharmacologic regimens. One prior study reports the use of a Billroth II resection with subsequent survival at 24 months follow-up.¹⁴ Another study describes a patient that underwent an emergent wedge resection following gastric perforation and continued survival at

18 months.³ Partial gastric resection was pursued in our patient as he was already on immunotherapy and was high risk for recurrent symptomatic anemia. Over 12 months after resection, the patient had no recurrent bleeding events with a stable hemoglobin of 13.9 g/dL.

Anemia may play an important role in the morbidity and mortality associated with MCC with gastric metastasis. Our patient demonstrated hematologic stability and symptomatic improvement following partial gastric resection. However, given the rarity and early mortality associated with this presentation, further research into the efficacy of partial gastric resection may prove difficult. Our case report demonstrates a positive outcome associated with partial gastric resection and presents a possible treatment option for this rare disease process.

Author Contributions

Zachary R Eagle, Francis Essien, Wassem Juakim: Study conception and design. Zachary R Eagle, Amia Jones, John McKee, Wassem Juakim: Data collection. Zachary R Eagle, Wassem Juakim: Analysis and interpretation of results. Zachary R Eagle, Francis Essien, George Shahin, Wassem Juakim: Draft manuscript preparation. All authors discussed the results and contributed to the final manuscript. Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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