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CASE REPORT | COLON

An Extraordinary Cause of Colonic Obstruction: Merkel Cell Carcinoma of Unknown Primary

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ABSTRACT

Merkel cell carcinoma is an aggressive and rare neuroendocrine skin cancer with documented metastases to the liver, lungs, and, seldom, the gastrointestinal tract. Metastases to the colon are rare but are seen with primary skin lesions or recurrent disease. Presented is a patient with large bowel obstruction secondary to a large hepatic flexure mass. Pathologic workup revealed Merkel cell carcinoma, and a dermatologic evaluation did not identify a primary cutaneous lesion. This is the first reported case of Merkel cell carcinoma of unknown primary presenting as large bowel obstruction.

KEYWORDS: Merkel cell carcinoma; Merkel cell carcinoma of unkown primary; colon cancer

INTRODUCTION

Merkel cell carcinoma (MCC) is a rare small cell neuroendocrine skin carcinoma which clinically mimics other primary cutaneous cancers.[1] It presents at a late stage, and approximately one-third of cases develop distant metastasis to the lymph nodes, liver, and

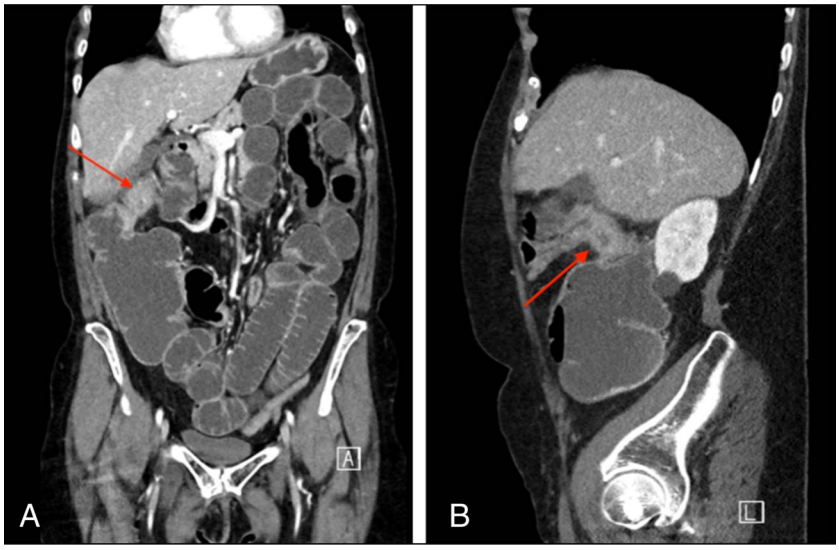

Figure 1. (A and B) Abdominal CT demonstrating dilated loops of the small intestine suggestive of large bowel obstruction with a right colon mass. CT, computed tomography. Red arrows denote the colonic mass.

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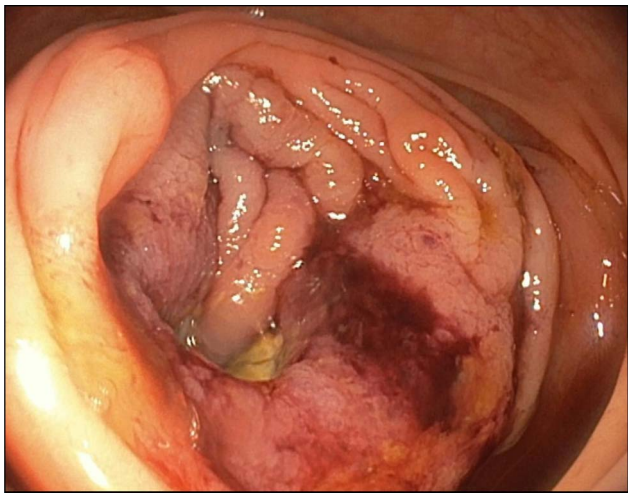

Figure 2. Colonoscopy showing a partially obstructing hepatic flexure mass with a stricture.

lungs, but gastrointestinal (GI) involvement has rarely been documented.[2,3] If MCC is determined in the absence of a known diagnosis or a primary cutaneous lesion, which is estimated to occur in one-third to half of all cases of MCC, pathologic techniques are used to characterize these tumors as MCC of unknown primary (MCCUP).[3–5] While MCC is commonly linked with sun exposure, both MCC and its rarer counterpart MCCUP have been attributed to Merkel cell polyomavirus (MCPyV) infection.[3,6] Prior reports of MCC with GI involvement have presented with symptoms ranging from fatigue and unintentional weight loss to GI bleeding.[7] Because MCCUP is uncommon, symptoms of MCCUP metastatic to the GI tract have not been well-documented and are nonspecific.

Prior reports of GI involvement have highlighted metastasis most commonly to the stomach, but metastases to the colon are exceedingly rare.[8–14] To our knowledge, MCC metastatic to the colon has not been documented in the absence of a corresponding primary cutaneous lesion. Described is a patient who presented with bowel obstruction secondary to a large, circumferential hepatic flexure colon mass. Biopsy showed a small cell neuroendocrine carcinoma. Subsequent resection specimen immunohistochemical evaluation for MCPyV was positive, confirming the diagnosis of metastatic MCCUP.

CASE REPORT

A 69-year-old woman with a history of bilateral ductal carcinoma of the breast, pulmonary adenocarcinoma, and anal squamous cell carcinoma presented with progressive abdominal pain, distention, and reduced bowel movements. Her abdominal computed tomography demonstrated dilated loops of the small bowel with a prominence of the right colon to the hepatic flexure concerning for partial obstruction (Figure 1).

Colonoscopy showed an edematous and necrotic-appearing mass of at least 4 cm in size at the hepatic flexure and a stricture through which the scope could not pass (Figure 2). Biopsy revealed small round blue cells with greater than 3 mitoses per high-power field in the lamina propria. Immunohistochemistry displayed positivity for keratin AE1/AE3, in a paranuclear dot-like pattern, and for synaptophysin, supporting a diagnosis of high-grade small cell neuroendocrine carcinoma (Figure 3). She subsequently underwent a right hemicolectomy. The surgical specimen confirmed small cell neuroendocrine carcinoma, involving the entire wall of the colon extending into the pericolic adipose tissue to the radial margin, with serosal and subserosal deposits.

On resection, the small round blue cells were positive for keratin Cam5.2 in a paranuclear dot-like pattern, synaptophysin, and MCPyV, confirming MCC (Figure 4). Ki-67 showed a greater than 98% proliferative index (Figure 5) with foci of tumor necrosis and easily identified mitotic figures, features expected in high-grade small cell neuroendocrine carcinomas, including MCC. Fourteen of 17 tested lymph nodes stained positive for metastases, many with extracapsular spread. Dermatologic evaluation revealed no primary lesion of MCC. Genetic testing was negative for pathologic mutations.

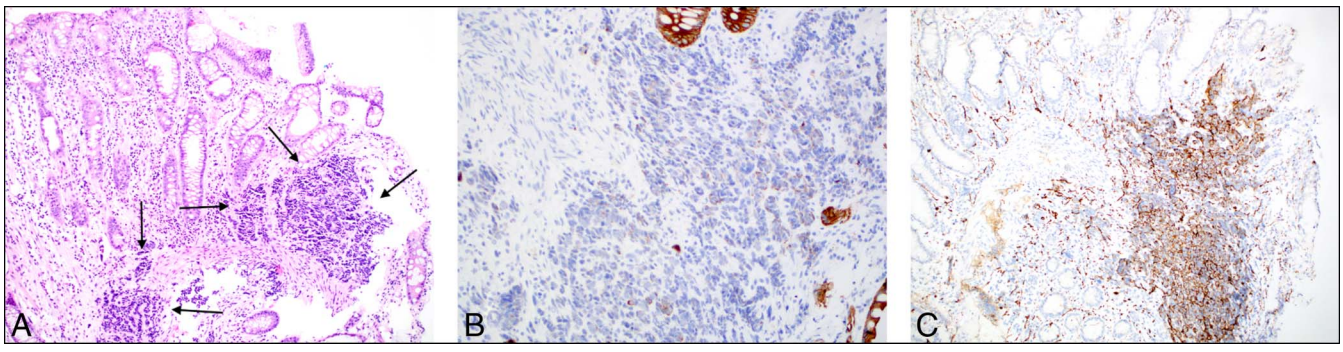

Figure 3. (A) H&E of a hepatic flexure colon mass showing infiltrate of small, round blue cells in lamina propria (black arrows) (100 magnification; 10×). (B) Keratin AE1/AE3 marking the small round tumor cells as a carcinoma in a paranuclear dot-like pattern (200 magnification; 20×). (C) Synaptophysin marking the small cell carcinoma as neuroendocrine (100 magnification; 10×).

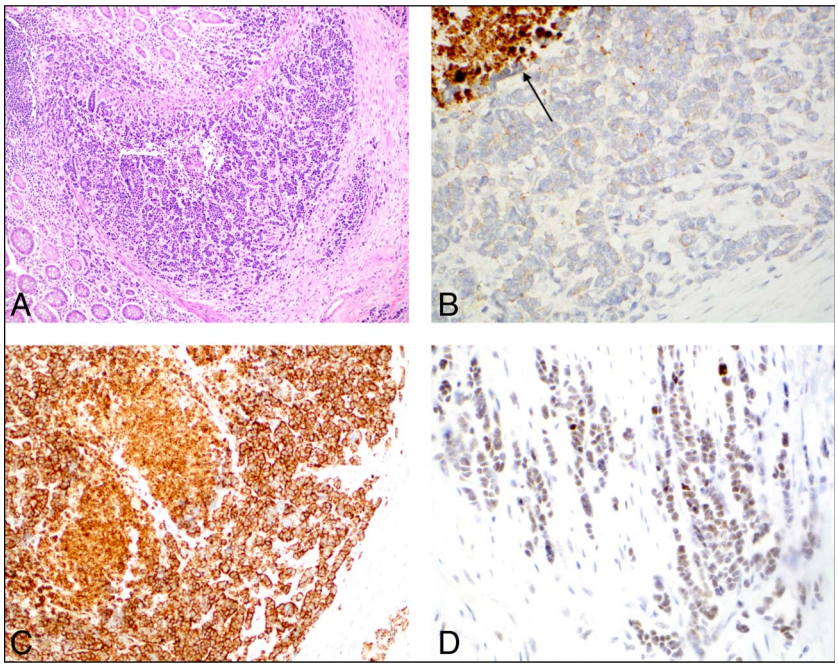

Figure 4. (A) Resection specimen with high-grade small cell carcinoma filling the mucosa and submucosa (100 magnification; 10×). (B) Keratin Cam5.2 marking the small cell carcinoma in the resection specimen with a paranuclear dot-like pattern; the arrow marks necrotic carcinoma cells (400 magnification; 40×). (C) Synaptophysin marking the carcinoma in the resection specimen as neuroendocrine (400 magnification; 40×). (D) Merkel cell polyomavirus positivity in the small cell carcinoma, confirming Merkel cell carcinoma (400 magnification; 40×).

DISCUSSION

To our knowledge, this is the first case of MCCUP presenting with a colonic mass described in the literature. Previously described cases of MCC metastatic to the colon were not tested for MCPyV and were linked to a known cutaneous lesion.[8–14] Confirmation of metastatic MCCUP to rare sites of the colon is difficult because of low incidence, lack of primary lesion, and range of symptomatic presentations. Diagnosis of cutaneous MCC is confirmed by biopsy of a suspicious lesion with appropriate ancillary immunohistochemical studies correlated with imaging studies and possible lymph node biopsy. However, in the absence of dermatologic findings, incisional and nodal biopsies can be used to discern MCCUP from other types of small, round blue cell tumors that are more commonly found in the GI tract by panels of ancillary immunohistochemical stains, including lymphoma, metastasis from other primary site small cell neuroendocrine carcinomas such as pulmonary or small bowel, small cell-appearing melanomas, basaloid squamous cell carcinomas, or small cell anaplastic carcinomas.[15]

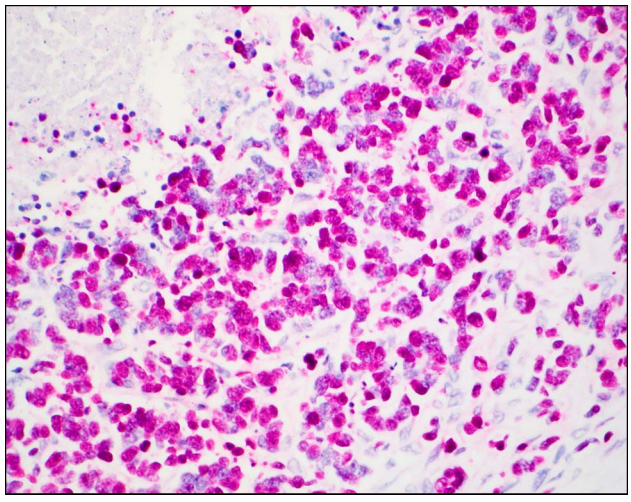

Figure 5. Ki-67 by immunohistochemistry marking nearly every carcinoma cell, for a proliferative index greater than 98% (400 magnification; 40×).

Because MCPyV is present in over half of MCC tumors, ancillary immunohistochemical testing for MCPyV is a useful diagnostic tool in the workup of a small cell neuroendocrine GI tumor, especially when CDX-2 and TTF-1 are negative and no primary skin MCC is known.[16,17]

This case describes an otherwise difficult to diagnose small cell neuroendocrine carcinoma. The tumor was keratin AE1/AE3 and Cam 5.2-positive in a paranuclear dot-like pattern and positive for synaptophysin, confirming a neuroendocrine neoplasm. Immunohistochemical ancillary studies showed a high proliferative index with easily identifiable mitoses, confirming high-grade neuroendocrine carcinoma. Immunohistochemical MCPyV positivity suggests MCPyV-induced small cell neuroendocrine carcinoma. Negative CDX-2, CK7, TTF-1, and CD45 by immunohistochemistry in conjunction with positive keratin and neuroendocrine stains excluded primary

Table 1. Reported cases of MCC metastatic to the colon and outcomes

Authors	Known primary?	Presentation	Symptoms	Treatment	Outcome
Shalhub et al (2004)	Yes	62M with remote MCC of the neck later found with enlarged axillary and inguinal lymph nodes	Lymphadenopathy	Carboplatin and etoposide	Deceased
Huang et al (2007)	Yes	76M with type 2 diabetes and MCC of the shoulder	Tenesmus, weight loss, and hematochezia	Proctectomy with coloanal anastomosis, palliative chemotherapy	Clinical remission
Cheung et al (2010)	Yes	74F with MCC of antecubital fossa and axillary nodal recurrence	Early satiety, bloating, colicky pain, and vomiting	Palliative chemotherapy	Deceased
Veness and Howle (2011)	Yes	74M with MCC of the neck and smoking history	Abdominal discomfort	Superficial parotidectomy and upper neck dissection, radiotherapy, 4 cycles of etoposide, and carboplatinum chemotherapy	Clinical remission
Tuktamyshov et al (2015)	Yes	70F with MCC of the groin and recurrence as an ascending colon polyp	Lower back pain, and weakness	Four cycles of cisplatin and etoposide, followed by 8 cycles of cyclophosphamide, doxorubicin, and vincristine	Clinical remission
Nahab and Kozman (2019)	Yes	86M with MCC of the leg previously resected	Abdominal distention and bowel obstruction	Palliative chemotherapy	Deceased
Liu et al (2019)	Yes	71F with MCC of skin with jejunal metastasis recurring in the transverse colon	Hematochezia and diarrhea	Hospice care without chemotherapy	Deceased
Ganjineh et al (2023)	No	69F with cancer and radiation history	Abdominal pain, distention, and constipation	Hospice care without chemotherapy	Deceased

MCC, Merkel cell carcinoma.

small cell neuroendocrine carcinomas of the small bowel, lung and thyroid, and lymphoma, respectively.[16–18] Unusual, but seen in a small subset of MCCs, CK20 was negative.[17] When most or all keratin stains are negative, a second neuroendocrine stain, such as INMS1 or CD56, may be helpful for confirmation.[6]

Adjuvant therapies for this patient's prior malignancies, including chemotherapy and radiation, raise concern for immunosuppression. Although radiation is associated with MCC and other dermatologic cancers, the relationship between MCCUP and radiation has not been elucidated.[19] Immunosuppression may increase the risk of MCC, and although rare, several cases of MCCUP in immunosuppressed patients have been outlined.[19,20] Thus, MCC should be considered in immunosuppressed or extensively radiated patients.

To date, there have been 8 cases documenting existing or recurrent MCC metastatic to the colon (Table 1).[8–14] Our case is the first describing MCCUP of the colon, highlighting the need for awareness of MCC and MCCUP as a root cause of neuroendocrine tumor of the GI tract. In patients with an extensive cancer history or who may be immunocompromised, a thorough GI workup inclusive of biopsy and pathologic staining is necessary to distinguish a potentially insidious malignancy.

DISCLOSURES

Author contributions: B. Ganjineh: writing, editing, and publication consent. W. Abel: writing and editing. S. Reddy: writing and editing. K. Fagan: writing and editing. D. Grider: writing, editing, pathology review, and article guarantor.

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REFERENCES

1. Walsh NM, Cerroni L. Merkel cell carcinoma: A review. *J Cutan Pathol.* 2021;48(3):411–21.
2. Kouzmina M, Koljonen V, Leikola J, Böhling T, Lantto E. Frequency and locations of systemic metastases in Merkel cell carcinoma by imaging. *Acta Radiol Open.* 2017;6(3):205846011770044.
3. Lewis CW, Qazi J, Hippe DS, et al. Patterns of distant metastases in 215 Merkel cell carcinoma patients: Implications for prognosis and surveillance. *Cancer Med.* 2020;9(4):1374–82.
4. Deneve JL, Messina JL, Marzban SS, et al. Merkel cell carcinoma of unknown primary origin. *Ann Surg Oncol.* 2012;19(7):2360–6.
5. Girard R, Djelouah M, Barat M, et al. Abdominal metastases from Merkel cell carcinoma: Prevalence and presentation on CT examination in 111 patients. *Diagn Interv Imaging.* 2022;103(1):41–8.
6. Kassem A, Schöpflin A, Diaz C, et al. Frequent detection of Merkel cell polyomavirus in human Merkel cell carcinomas and identification of a unique deletion in the *VP1* gene. *Cancer Res.* 2008;68(13):5009–13.

7. Hu ZI, Schuster JA, Kudelka AP, Huston TL. Merkel cell carcinoma with gastric metastasis and review of literature. *J Cutan Med Surg.* 2016;20(3):255–8.
8. Shalhub S, Clarke L, Morgan MB. Metastatic Merkel cell carcinoma masquerading as colon cancer. *Gastrointest Endosc.* 2004;60(5):856–8.
9. Huang WS, Lin PY, Lee IL, Chin CC, Wang JY, Yang WG. Metastatic Merkel cell carcinoma in the rectum: Report of a case. *Dis Colon Rectum.* 2007;50(11):1992–5.
10. Liu MC, Ahmed S, Mehta S. Mercurial metastatic Merkel cell carcinoma: A case of colonic involvement. *ACG Case Rep J.* 2019;6(6):e00102.
11. Nahab F, Kozman MA. Rare intestinal metastasis of Merkel cell carcinoma causing bowel obstruction. *AZN J Surg.* 2019;90:1–2.
12. Tuktamyshov R, Jain D, Ginsburg PM. Recurrence of Merkel cell carcinoma in the gastrointestinal tract: A case report. *BMC Res Notes.* 2015;8(1):188.
13. Cheung M, Lee H, Purkayastha S, Goldin R, Ziprin P. Ileocaecal recurrence of Merkel cell carcinoma of the skin: A case report. *J Med Case Rep.* 2010;4(1):43.
14. Veness MJ, Howle JR. Merkel cell carcinoma metastatic to the transverse colon: Disease free after six years–cure or just prolonged remission? Metastatic Merkel cell carcinoma. *Australas J Dermatol.* 2011;52(4):295–7.
15. Reddy S. *Hepatic Metastasis Presenting as Merkel Cell Carcinoma of Unknown Primary*, 2018 (https://journals.lww.com/ajg/fulltext/2018/10001/hepatic_metastasis_presenting_as_merkel_cell.2348.aspx).
16. Leech SN, Kolar AJO, Barrett PD, Sinclair SA, Leonard N. Merkel cell carcinoma can be distinguished from metastatic small cell carcinoma using antibodies to cytokeratin 20 and thyroid transcription factor 1. *J Clin Pathol.* 2001;54(9):727–9.
17. Paik JY, Hall G, Clarkson A, et al. Immunohistochemistry for Merkel cell polyomavirus is highly specific but not sensitive for the diagnosis of Merkel cell carcinoma in the Australian population. *Hum Pathol.* 2011;42(10):1385–90.
18. Liu C, Lai F, Chang S, Chuang S. Diagnostic clues for differentiating Merkel cell carcinoma from lymphoma in fine-needle aspiration cytology. *Diagn Cytopathol.* 2022;50(1):E23–27.
19. Ma J, Brewer J. Merkel cell carcinoma in immunosuppressed patients. *Cancers.* 2014;6(3):1328–50.
20. Rizzo JM, Harms PW, Harms KL, Plaska A, Brenner C, Durham AB. Unknown primary Merkel cell carcinoma in the immunosuppressed patient: Case series. *JAAD Case Rep.* 2021;8:19–22.