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Gastric Metastasis of Primary Neuroendocrine Tumor of Skin: Rare Tumor with Rare Presentation

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Abstract

Merkel cell carcinoma (MCC) is a rare primary neuroendocrine tumor of the skin. It has an aggressive biological behavior and shows early local and distant metastasis. Diagnosis of MCC is a challenge and requires confirmation by immunohistochemistry (IHC). However, metastasis of MCC to the stomach is extremely uncommon and is rarely reported in the literature. We hereby describe a patient with gastric metastasis of MCC, who presented with black tarry stool and was finally diagnosed on the basis of clinical history, histology, and IHC.

Keywords

- cutaneous
- Merkel cell carcinoma
- metastasis
- neuroendocrine
- stomach

Introduction

Merkel cell carcinoma (MCC), is a highly aggressive cutaneous neuroendocrine tumor. It is commonly seen in elderly Caucasian males in 6th to 7th decades and is related to sun exposure, UV light irradiation, and immunosuppression.[1] It mostly occurs in areas exposed to the sunlight, particularly the head, neck, and extremities of fair skinned people. On microscopic examination, MCC can simulate a variety of other small round blue cell tumors which include appendageal tumors of the skin, malignant melanoma, cutaneous primitive neuroectodermal tumor (PNET), cutaneous metastasis of small cell carcinoma of the lungs, and non-Hodgkin's lymphomas; hence, immunohistochemical (IHC) studies play an important role in confirming its diagnosis.

Case History

A 51-year-old Indian male patient presented to the emergency department with complaints of fatigue, weakness, palpitations, and passage of black tarry stool for the past few days. The patient was a known case of diabetes mellitus, hypertension, and coronary heart disease. Significantly, about a year ago, he had a history of a protuberant skin growth measuring 4×3 cm on the right side of the back (►**Fig. 1A**). That lesion was painless, firm, lilac in color with a cribriform appearance. A wide local excision was done and sent for histopathological examination, which was subsequently diagnosed as MCC on the basis of morphology and a battery of IHC tests. Three months later, the patient again presented with a 4×4 cm, painless, firm, and a mobile lymph node in the right posterior axillary area. Axillary dissection

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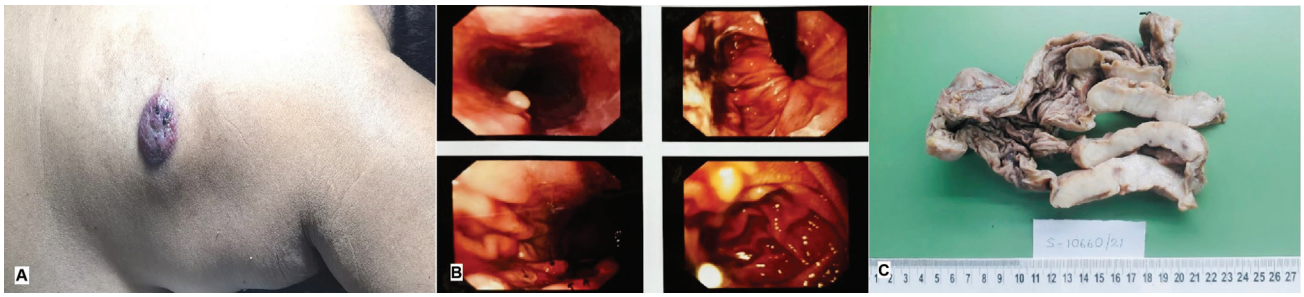

Fig. 1 (**A**) Clinical image of the protuberant skin growth on the right side of back. (**B**) Upper gastrointestinal endoscopy images showing an ulcerated mass in the greater curvature of the stomach. (**C**) Gross image of sleeve gastrectomy specimen showing a tumor in the wall of the stomach.

of lymph nodes was performed; however, no chemotherapy or radiotherapy was given.

In the present episode, his abdominal examination was unremarkable with no tenderness, guarding or rigidity. No other palpable lump was noted. The rest of the physical examination was within normal limits. Laboratory studies showed hemoglobin of 9 g/dL and red blood cell count of 3.31×10^{12}/L. Upper gastrointestinal endoscopy showed a large ulcerated mass in the greater curvature of the stomach (►**Fig. 1B**). Sleeve gastrectomy was done and the specimen was sent for histopathological examination. An already opened up sleeve gastrectomy specimen measuring 20 cm in length was received. On serial slicing, the wall of the stomach was thickened and showed a tumor measuring 9×5 cm, which was infiltrating full thickness of the gastric wall and reaching till the serosa (►**Fig. 1C**). The overlying mucosa was ulcerated. Microscopic examination revealed a cellular high-grade malignant tumor composed of small monomorphic cells. The tumor was chiefly involving submucosa, muscularis propria, and was focally infiltrating into the mucosa and subserosa (►**Fig. 2A–2D**). The cells were present in diffuse sheets and focal nested pattern (►**Fig. 3A**). The cells had high nuclear cytoplasmic ratio, scant cytoplasm, irregular nuclear membrane with the presence of notching and lobulation. High mitotic activity (>30/10 hpf) and occasional focus of tumor necrosis were observed (►**Fig. 3B**). Tumor cells were positive for EMA, synaptophysin, CK20, PAX-5, and p63; and were negative for CK, LCA, CK7, TTF-1, CEA, and vimentin (►**Fig. 3C–3F**). The biopsy results were consistent with the diagnosis of metastatic MCC to the stomach. The patient died on the second postoperative day due massive internal bleeding and cardiac arrest.

Discussion

Metastases to the stomach are rare and represent a late and progressed stage of malignant disease. Among the primary tumors spreading to the stomach, a high prevalence of breast

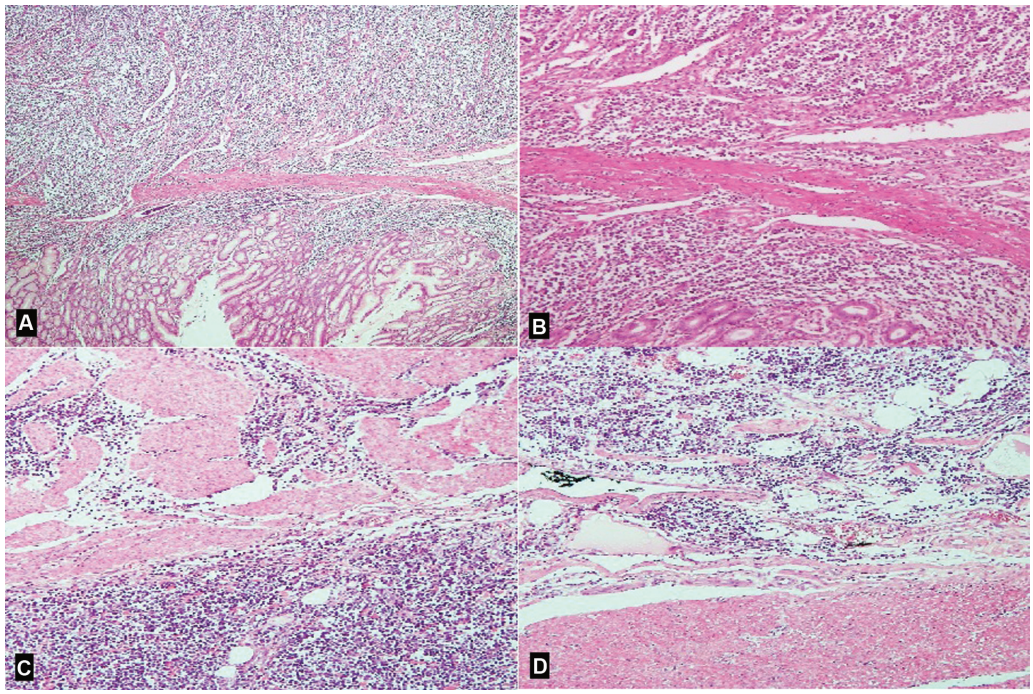

Fig. 2 (**A, B**) Cellular high-grade malignant tumor composed of small monomorphic cells and was diffusely involving submucosa and focally infiltrating the mucosa (H&E 10x). (**C**) Tumor cells involving the muscularis propria (H&E 10x). (**D**) Tumor cells focally infiltrating the subserosa (H&E 10x).

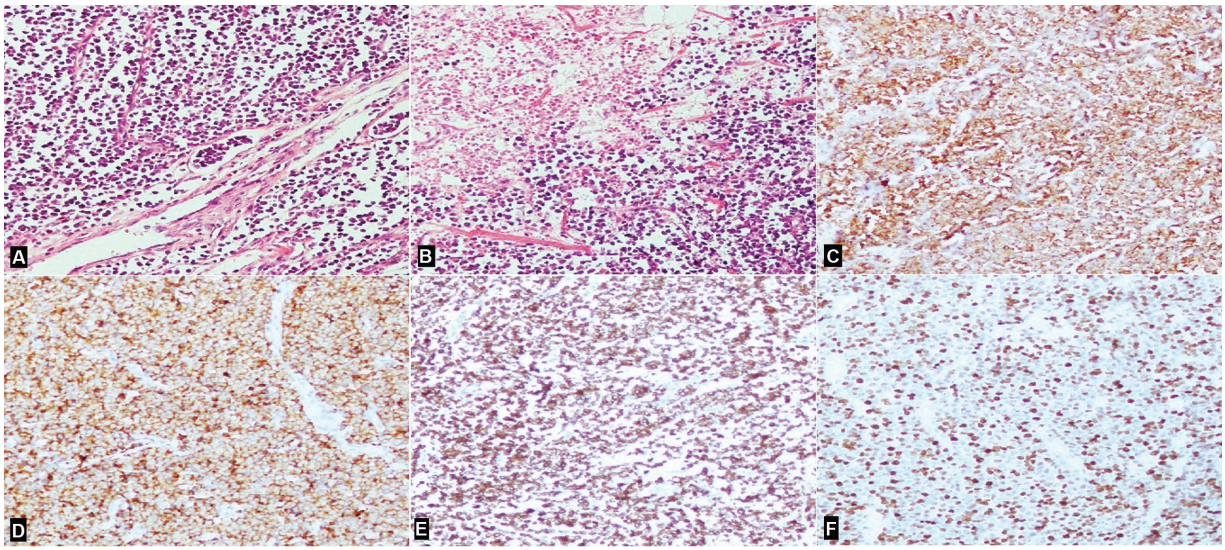

Fig. 3 (**A**) Tumor cells present in focal nested pattern. (**B**) Tumor cells with occasional focus of the tumor necrosis (H&E 20x). (**C**) IHC staining: EMA positive (20x). (**D**) IHC staining: synaptophysin positive (20x). (**E**) IHC staining: CK20 positive (20x). (**F**) IHC staining: Ki67 proliferative index 35–40% (20x).

cancer, lung cancer, renal cell cancer, and malignant melanoma has been reported.[2] Merkel cell carcinoma is a rare neuroendocrine malignancy of the skin with an annual incidence of 0.2 to 0.45 per 100,000 population.[3] As emerged from our thorough literature search, metastasis of MCC to the stomach is a very rare clinical presentation with only eight cases reported so far, including the present case (►**Table 1**). Within these limited number of cases, the age of presentation ranged from 51 to 91 years with our case being the youngest one. Most of the cases were male patient (7) and only one case was female patient. The present case is the second case ever reported from the Indian subcontinent. Gastrointestinal

Table 1 Comparison of published cases of Merkel cell carcinoma metastasis to stomach with our case

Authors	Age (in years)	Ethinicity	Primary site	Clinical presentation of gastric metastasis	Treatment	Follow-up period (in months)	Metastasis/ recurrence/ death
Wolov et al[8] (2008)	80/M	NA	Right upper extremity	Fatigue and melena	Chemotherapy	NA	Abdominal wall metastasis, Death
Syal et al[4] (2012)	68/M	NA	Left lower extremity	Fatigue and melena	Chemotherapy	NA	Alive
SantosJuanes et al[9] (2016)	52/M	NA	Right thigh	Anemia	Chemotherapy	6	Death
Hu et al[10] (2016)	91/M	Caucasian	Left elbow	Syncope, fatigue, melena, early satiety, weight loss	Patient denied chemotherapy and radiotherapy	Few weeks	Death
Trivedi et al[11] (2017)	53/M	Vietnamese	Left buttock	Perforation of the gastric lesion	Surgery, Chemotherapy, Radiotherapy	18	Metastasis to larynx, Death
Kini et al[12] (2018)	75/F	Indian	Left buttock	Recurrent vomiting and jaundice	Surgery, Chemotherapy	9	Death
Eagle et al[13] (2021)	84/M	African American	NA	Fatigue and melena	Surgery, Immunotherapy	12	Alive
Present case (2021)	51/M	Indian	Right side of back	Fatigue, melena and palpitations	Surgery	Patient died on 2nd post-operative day	Death

bleeding was the most common manifestation in these cases.[4] Six out of 8 patients, including the present case came with complaints of fatigue and melena. Distinguishing GI metastasis of MCC from the primary neuroendocrine tumors is said to be difficult. Diagnosis can be made based on the combination of clinical clues, endoscopic findings of GI tract, biopsy morphology, and IHC analysis of the suspicious lesion. Cytoplasmic dot-like staining pattern for CK20 is said to be most important in distinguishing MCC from other differentials such as metastasis from small cell carcinoma of lung, tumors of skin appendages, and malignant melanoma.[5] To rule out other possible primary or metastatic lesions, a panel of IHC markers such as TTF-1 (for metastatic small cell carcinoma of lung), LCA (for non-Hodgkin's lymphoma) and HMB-45 and S-100 (for malignant melanoma) can be applied. In addition, the GI neuroendocrine tumors display CK 20 negativity.

This tumor has an aggressive biological behavior and carries a dismal prognosis as it shows a high rate of local recurrence, regional lymph nodes metastasis, and distant metastasis.[6] Distant lymph nodes, skin, lungs, central nervous system and bones are the most common sites of metastasis.[6,7] Metastasis of MCC to the stomach is extremely uncommon and a rare presentation of disease progression; only a few case reports are available in the published literature.[4,8–13] Due to its rarity, there may be a delay in correctly diagnosing this metastatic disease and subsequent delay in further systemic treatment. The life expectancy ranges from 1 week to 1 year with an average mortality rate of 67% at 4 months following the diagnosis of gastric metastasis.[8–13] There is no unanimous treatment protocol for patients with GI metastasis. Primary treatment of MCC is wide resection. The use of radiotherapy to reduce chances of local recurrence, dissection of regional lymph nodes to minimize the chances of lymph nodal metastasis and chemotherapy is debatable. Because the number of the cases are few for gastric metastasis of MCC, clear guidelines on treatment are not available. The use of partial gastrectomy (wide resection preferred over radical surgery) along with radiotherapy/chemotherapy including various platinum-based drugs is controversial and very few case reports have illustrated their use.[8–13]

Conclusion

The rarity of this unusual metastatic disease limits its clear characterization. To solve the classical diagnostic issue of small round cell tumors, being primary or metastatic, the clinical information, histopathological, and IHC features are crucial for diagnosing them. Gastrointestinal tract is a rare site of Merkel cell carcinoma progression; however, in general metastatic MCC disease is associated with dismal prognosis.

Declaration of Patient Consent

The authors certify that they have obtained the appropriate consent from the parent. The parent has given his consent for the images and other clinical information to be reported in the journal. The parent understands that the name and initials will not be published, and due efforts have been made to conceal the same.

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Conflict of Interest

None declared.

Guarantor of Submission

The corresponding author is the guarantor of submission.

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