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CASE REPORT | STOMACH

An Unusual Case of Primary Gastric Balloon Cell Melanoma

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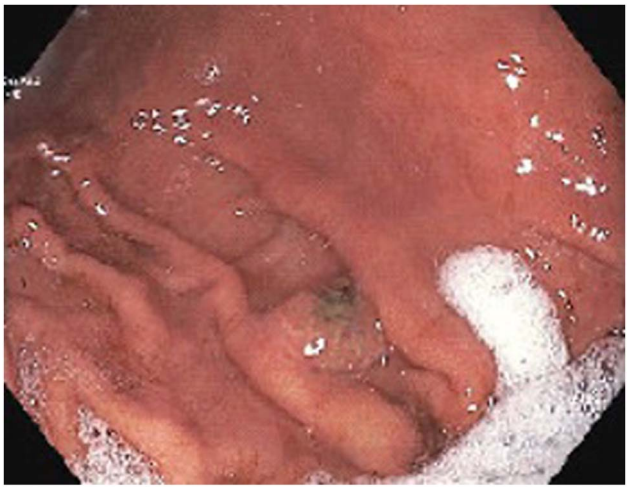
ABSTRACT

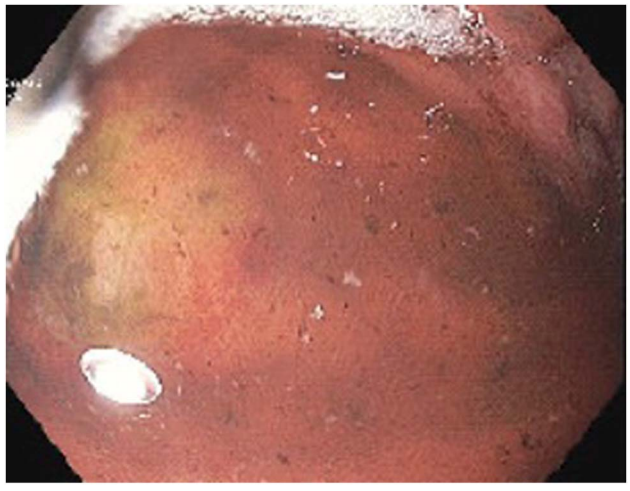
Most cases of melanoma found in the gastrointestinal tract are the result of metastasis. Although uncommon and only described in isolated case reports, primary gastric melanoma should be considered when patients present with vague gastrointestinal symptoms and a mass is identified on esophagogastroduodenoscopy or imaging. We describe a case of primary gastric balloon cell melanoma in a 73-year-old man who presented with melena. Given the high morbidity and mortality of gastric mucosal melanoma, early diagnosis and initiation of treatment can lead to improved outcomes and survival.

KEYWORDS: gastric melanoma; malignancy; balloon cell

INTRODUCTION

Melanoma is an aggressive malignancy that occurs in melanocytes. It represents about 1% to 3% of all malignant cancers and has a predilection for metastasis to the gastrointestinal (GI) tract, bones, brain, and lungs and carries high morbidity and mortality.[1] Although melanoma is predominantly a cutaneous cancer, mucosal melanoma comprises 1.3% of all melanocytic malignancies.[2] However, primary gastric melanoma (GM) is a rare entity and only described in isolated case reports. We report a case of a primary gastric balloon cell melanoma presenting as a GI bleed.





Figures 1 and 2. Initial esophagogastroduodenoscopy showing ulcers in the stomach.

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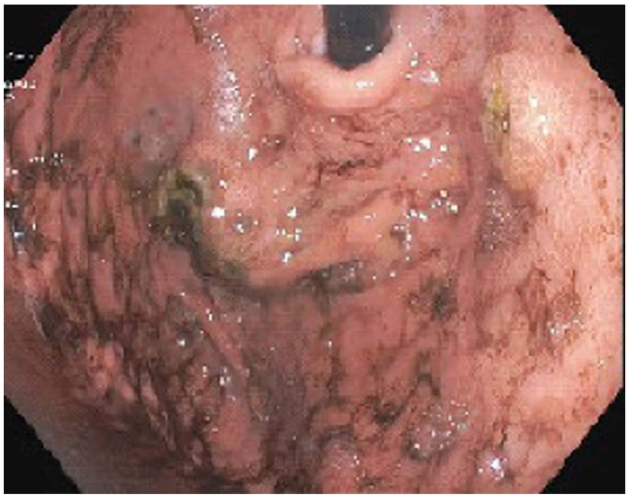

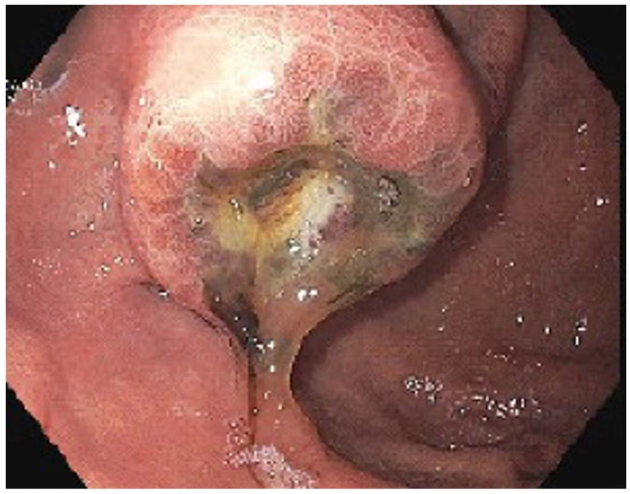

Figures 3 and 4. Repeat esophagogastroduodenoscopy, at the time of diagnosis, showing multiple submucosal ulcerated and necrotic masses in the stomach.

CASE REPORT

A 73-year-old man with medical history of hypertension, obesity, diabetes, and chronic obstructive pulmonary disease presented to the emergency department with 2 days of melena and some hematochezia. He denied abdominal pain, unintentional weight loss, and an unknown amount of nonsteroidal anti-inflammatory drug use. He was hemodynamically stable, and his physical examination was unremarkable without suspicious skin lesions. Laboratory values revealed hemoglobin of 11.4 mg/dL (baseline hemoglobin 13.0 mg/dL) and mean corpuscular volume of 83 μm^3 but was otherwise unremarkable. He presented with similar symptoms 2 months earlier and was found to have ulcers on esophagogastroduodenoscopy, which was attributed to nonsteroidal anti-inflammatory drugs (Figures 1 and 2). Computed tomography of the chest, abdomen, and pelvis revealed distal gastric body wall thickening. It also revealed an inferior right upper lobe lung nodule measuring 1.6 cm and an enlarged right hilar lymph node suspicious for malignancy.

A repeat esophagogastroduodenoscopy revealed multiple submucosal ulcerated and necrotic masses with irregular borders. The largest lesion measured approximately 3 to 4 cm in the gastric body (Figures 3 and 4). Biopsy revealed balloon-like submucosal epithelioid neoplasm with necrosis and intracytoplasmic pigment concerning for melanoma with balloon cell differentiation (BCM) (Figure 5). Immunohistochemical testing resulted positive for melan-A, SOX10, and S100 and negative for pankeratin, PAX8, and CD68, confirming melanoma. Furthermore, BRAF V600E and program cell death ligand (PD-L1) were negative.

The patient was referred to oncology and underwent a positron emission tomography (PET) scan, which confirmed intense uptake in the stomach and hypermetabolic pulmonary nodules, but no hypermetabolic skin lesions. A computed tomography–guided biopsy of the pulmonary nodules was negative for malignancy and believed to be a reactive process, further confirming primary gastric melanoma. The patient had lack of social support and was deemed a poor surgical candidate. He is currently undergoing palliative pembrolizumab therapy, and his most recent PET scan (after 6 cycles of therapy) shows resolution of the increased uptake in the stomach. He remains under close monitoring.

DISCUSSION

Melanoma is an aggressive malignancy that has a predilection for metastasis to the GI tract. GM is commonly the result of metastatic disease, given that up to 60% of patients with metastatic melanoma have GI involvement.[3] Primary GM is a rare entity and is reported sparingly in the literature. The pathogenesis remains unclear, but 2 possible mechanisms

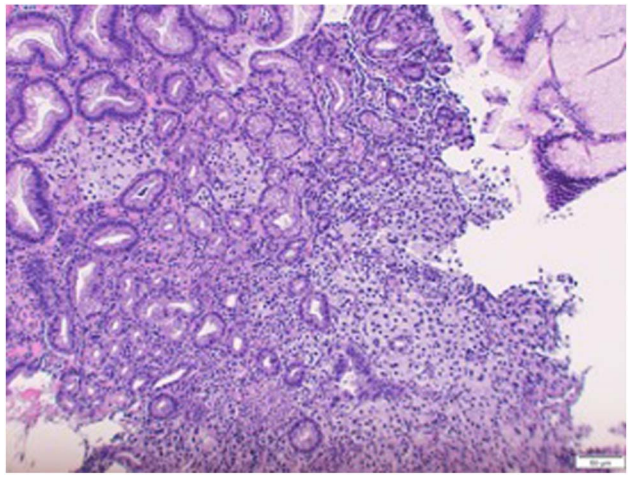

Figure 5. Hematoxylin and eosin image showing lamina propria replaced by infiltrating enlarged, voluminous balloon-like cells with oval nuclei, prominent cherry nucleoli, and intracytoplasmic pigment.

have been proposed. The first theory is that amine precursor uptake and decarboxylation cells, which are neural crest derivatives that function as the endocrine cells of the GI tract, may gain or retain the ability to dedifferentiate into melanocytes and subsequently undergo malignant transformation.[4] The other theory is that melanocytes undergo ectopic migration into the GI tract, making primary gastric melanoma a reasonable possibility.[5–7]

There are no risk factors associated with mucosal melanoma, such as ultraviolet exposure, that correlate with the incidence of primary GM. The incidence does seem to increase with age and peaks around 70 years.[8] Patients tend to present with vague systemic symptoms such as weight loss, fatigue, and generalized abdominal pain. The presentation of an upper GI bleed is common as well, with most cases appearing as stable, chronic bleeds as seen in our patient.[8]

The rarity of GM should always raise suspicion for metastatic melanoma and regressed primary cutaneous melanoma. Although not validated, diagnostic criteria have been proposed to preclude these possibilities.[9] It includes (i) histologically proven single lesion of melanoma in the stomach, (ii) no concurrent lesions elsewhere, (iii) no history of melanoma, and (iv) disease-free survival of at least 12 months after curative surgery. A thorough patient history with particular attention to sun exposure and previous cutaneous lesions is critical. Furthermore, PET imaging can define the extent of the disease, ensuring limitation to the stomach. Immunohistochemical staining with S100 protein, melan-A, and HMB-45 antibodies help increase diagnostic sensitivity. Histologic examination relies on the identification of melanin, and rarely, BCM can be observed, as was the case in our patient. BCM is a unique histopathological subtype seen in less than 1% of malignant melanoma.[10] The prognosis of BCM depends on the Breslow depth, not cytological characteristics, although BCM may infer an advanced phase of the malignant melanoma.

Because of the scarcity of cases and the poorly understood disease mechanism, there are limited treatment guidelines established for adjuvant therapy; therefore, multidisciplinary care is crucial. The existing literature recommends surgery as first-line treatment. A systematic review by Mellotte et al[8] reviewed the efficacy of surgical and medical management and found that surgical intervention is necessary for positive outcomes in primary GM. Surgical resection was unfortunately not a possibility for our patient, given his comorbidities, poor support system, and deconditioning. Instead, he was treated with palliative pembrolizumab with good response. Chemotherapy alone has failed to demonstrate therapeutic benefit because melanoma tends to be chemotherapy-resistant, but combining chemotherapy with immunotherapy has proved beneficial in certain cases of cutaneous melanoma.[11] Landmark trials such as KEYNOTE-811 and Checkmate-649 have proven several immune checkpoint inhibitors targeting PD-L1, its receptor PD-1, and cytotoxic T-lymphocyte–associated protein-4 to be beneficial in various malignancies, including cutaneous melanoma and advanced gastric cancers.[12,13] Given the therapeutic efficacy of these drugs, clinical trials are needed to extend their use in mucosal melanoma.

The prognosis of mucosal melanoma remains poor compared with other malignancies of the GI tract. The median survival time is 5 months, and the 5-year survival rate is only 3% for GI mucosal melanomas.[14] Further studies investigating the molecular basis of mucosal melanoma are needed for the development of targeted treatments and to standardize efficacious adjuvant therapy. Our case emphasizes that symptoms of a GI bleed should be evaluated diligently because malignancies can present in a subtle manner and early recognition can lead to a prompt diagnosis and initiation of life-saving treatment.

DISCLOSURES

Author contributions: H. Chaudhry, V. Green, J. Lin, and J. Lewis reviewed the literature, drafted the manuscript, revised it for important intellectual content, and were involved in the final approval of the version to be published. H. Wong revised the article for important intellectual content and was involved in the final approval of the version to be published. H. Chaudhry is the article guarantor.

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