Primary Gastric Melanoma: A Rare Cause of Upper Gastrointestinal Bleeding

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Primary gastrointestinal malignant melanoma is an unusual clinical entity. Rarer still is primary gastric melanoma. Most melanomas found in the stomach are metastases from cutaneous sources.[1] Primary gastric melanoma is underdiagnosed, its symptoms and signs are nonspecific, and specific staining techniques must be used to confirm the diagnosis. The following case of primary gastric melanoma involves a middle-aged white man who initially presented with upper gastrointestinal bleeding.

Case Report

A 50-year-old white man presented after 3 episodes of hematemesis and 1 episode of melena. He had a 9-month history of worsening epigastric pain and a 20-pound weight loss over the previous month, and his past medical history was significant for hypertension, pancreatitis, and peptic ulcer disease. In addition, the patient was a 40-pack-per-year smoker and a former alcoholic, and his family history was deemed noncontributory. On examination, the patient was hypotensive but not tachycardic, and pallor of the conjunctiva and mild epigastric tenderness were seen. Laboratory results were significant for a hemoglobin of 7.5 g/dL and hematocrit of 23.1%. Upper endoscopy revealed a large necrotic ulcerated mass extending from the antrum to the body of the stomach (Figure 1). Computed tomography scan of the abdomen was remarkable for thickening of the posterior wall of the body of the stomach, with the mass extending into the gastric lumen and the adjacent fat with 2 enlarged lymph nodes (Figure 2). Surgery demonstrated a mass measuring 12 cm × 10.5 cm × 2.5 cm involving 50% of the stomach, including the gastrocolic ligaments, and extending into the pancreas. Palliative resection was performed. Histopathology showed neoplastic cells in a sheet-like growth pattern showing no glandular differentiation (Figure 3). S100 protein, HMB-45 antibodies, and Melan A staining were strongly positive, thus confirming a diagnosis of gastric melanoma (Figure 4). The patient denied any history of cancerous lesions of the skin. A complete examination of his skin, including oral and anal mucosa, showed no suspicious lesions, and fundoscopic examination of the eye was normal. A diagnosis of advanced primary gastric melanoma was made. The patient was discharged to a correctional facility and subsequently lost to follow-up.

Discussion

Malignant melanoma most commonly develops in the skin. The vast majority of gastrointestinal melanomas are metastases from a cutaneous primary tumor.[1] In rare instances, primary malignant melanoma can arise from mucosa of the gastrointestinal tract, particularly from the

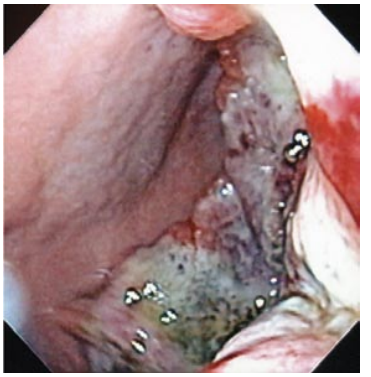

Figure 1. Upper endoscopy revealed a large necrotic ulcerated mass extending from the antrum to the body of the stomach.

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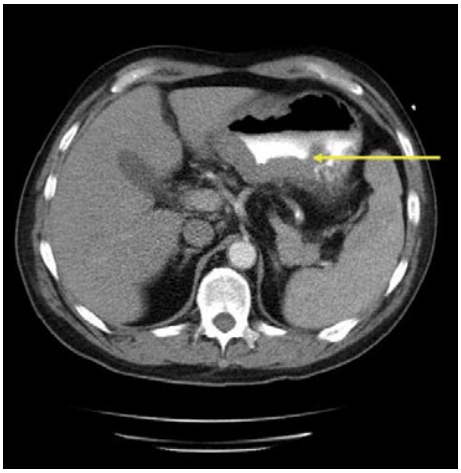

Figure 2. Contrast-enhanced computed tomography scan of the abdomen demonstrated thickening of the posterior wall of the body of the stomach with extension of the mass into the gastric lumen and into the adjacent fat (yellow arrow) with 2 enlarged lymph nodes.

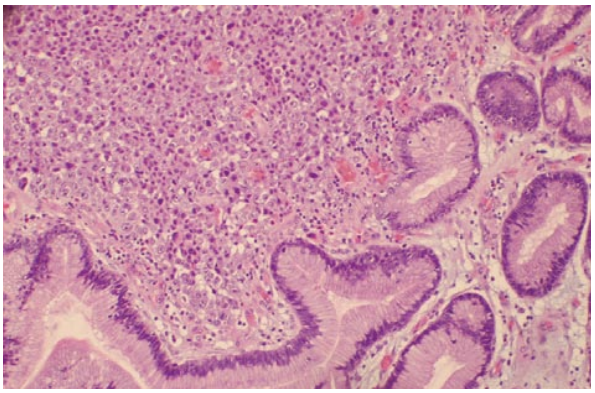

Figure 3. Biopsy of the mass showed neoplastic cells in a sheet-like growth pattern showing no glandular differentiation (hematoxylin & eosin stain, ×200).

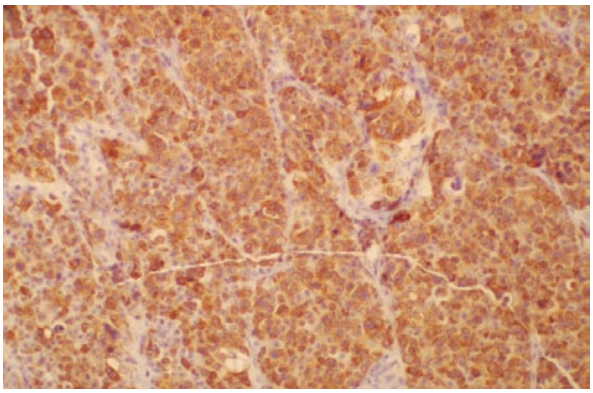

Figure 4. Tumor cells were strongly positive for immunoperoxidase staining for Melan A (× 200).

esophagus, anorectum, and small bowel.[2] Fewer than 15 cases of primary gastric melanoma have been documented in the literature.[3-6]

There has been speculation in the past as to whether primary melanoma can occur in the stomach, as benign melanocytes are absent in the normal gastric wall. However, melanosis of the stomach has been well documented in the case of anal and esophageal melanoma.[6,7] Thus, it is possible that primary gastric melanoma can occur in unusual circumstances.

Criteria for the diagnosis of primary gastric melanoma include the absence of concurrent lesions and the lack of a history of melanoma or atypical melanocytic lesion removal from the skin or other organs.[8] Disease-free survival of at least 12 months after curative surgical excision of the involved organ has been proposed as a criterion for the distinction of a primary lesion from a metastatic lesion, as 50% of patients with stage IV melanoma of the skin or visceral disease from an unknown primary lesion die 12 months after diagnosis.[9]

The clinical manifestations of primary gastric melanoma are similar to those of other gastric tumors, with weight loss, upper gastrointestinal bleeding, and anemia as the most common symptoms. Most patients are asymptomatic until the tumor becomes advanced. Computed tomography scan of the abdomen, upper endoscopy, and subsequent biopsy are the main diagnostic modalities. On upper endoscopy, a mass-like lesion with black pigmentation may be seen. Immunohistochemical stains with S100 protein, Melan-A, and HMB-45 antibodies have increased the diagnostic sensitivity of biopsy and cytology and play a key role in the diagnosis of these lesions.[10] Chemotherapy options include interferon, interleukin-12, and other agents.[8,11] Prognosis is extremely poor due to the frequent delay in diagnosis, the inherently more aggressive nature of the tumor, and earlier dissemination due to the rich lymphatic and vascular supply of the gastrointestinal mucosa.[12]

Primary gastric melanoma is an extremely uncommon clinical entity. Amelanotic melanoma such as the one in this case can be missed in poorly differentiated tumors unless appropriate staining tests are performed. Primary malignant melanoma of the stomach may be an underdiagnosed phenomenon. Early detection and surgical intervention is critical for long-term cure,[4] though overall prognosis is very poor.

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Review

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The dearth of information regarding mucosal melanoma corresponds with the rarity of the disease. In a review of 84,836 melanoma cases from the National Cancer Data Base that were entered between 1985 and 1994, 91.2% were cutaneous, 5.2% were ocular, 1.3% were mucosal, and 2.2% were unknown primaries.[1] Mucosal melanoma was first described by Weber in 1856 and later classified as a distinct entity in 1869.[2,3] In the United States, the incidence of cutaneous melanoma continues to rise at a rate higher than that of any other form of cancer. The incidence of noncutaneous melanoma, however, remains stable. Exposure to ultraviolet radiation is a major predisposing factor to cutaneous melanoma. The occurrence of melanoma in areas of the body that have never been exposed to sunlight, such as the gastrointestinal tract, may provide important insights into the pathogenesis of melanoma in general.

Ravi reported a case of upper gastrointestinal bleeding due to a primary gastric melanoma[4] and noted that the tumor is extremely rare and has a very poor prognosis. A high index of clinical suspicion is essential to reach this diagnosis. Unusual appearance or nonhealing gastric ulcers should prompt the endoscopist to obtain multiple biopsies and consult with the pathologist to reach a diagnosis.

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The distribution of mucosal melanomas tends to center near mucocutaneous junctions, where the melanomas are thought to arise from melanocytes that have migrated from the neuroectoderm and undergone malignant transformation. Their function in these locations is believed to differ from that of cutaneous melanocytes and likely has been the reason for the lack of understanding of this malignancy. Malignant melanoma can arise in gastrointestinal mucosal sites such as the esophagus,[5] anorectum,[6] and small bowel.[7,8] Cases of primary melanoma of the stomach have rarely been reported.[9-11] The debate over the nature of such lesions early in development still persists. Thus, specific criteria have been proposed for the diagnosis of primary melanoma, including the absence of concurrent lesions and the lack of a history of melanoma or atypical melanocytic lesion removal from the skin or other organs.[6] Partial or complete regression of melanocytic nevi and melanomas is well recognized.[12] However, there are no data as to how many melanomas regress completely without metastasis. The exact mechanism of regression remains unknown and is difficult to study.[13] Such knowledge would provide an insight into cancer immunology, in general, and melanomas, in particular.

It is known that melanocytes come from neural crest cells and migrate to the skin, hair follicles, and retina; however, their function in the mucosa is not certain. Melanin may be seen in the submucosa of the