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Case Report
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A Rare Case of Symptomatic Gastric and Colonic Metastases of Cutaneous Malignant Melanoma

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Abstract

We present a case of a 72-year-old man who sought medical attention for fatigue, lightheadedness, and exertional chest pain and who had been surgically treated for cutaneous malignant melanoma of the lower back about 6 years prior. The patient was found to have severe iron deficiency anemia, and his endoscopic Gastrointestinal (GI) studies revealed synchronous metastatic lesions of the stomach and colon with discrete macroscopic features. A complete workup demonstrated widely metastatic disease including brain, lung, and bone. He underwent stereotactic radiosurgery of his brain lesions and initiated immunotherapy with nivolumab. This case illustrates a rare presentation of symptomatic GI metastases leading to prompt diagnosis and initiation of treatments for metastatic malignant melanoma.

Introduction

Cutaneous melanoma, one of the most diagnosed malignancies, has a propensity to metastasize. Even though the GI Tract (GIT) is the second least common location for melanoma metastasis [1], melanoma is one of the most common carcinomas to metastasize to the GIT [2]. Most GIT melanomas are metastases from cutaneous primaries, which sometimes occur after spontaneous regression of the primary cutaneous melanoma [3]. Extremities are the most common primary tumor location for melanoma with GIT metastasis (15% to 57%) followed by the trunk (13% to 54%) and least commonly head/neck (5% to 33%) [4]. However, GIT melanomas can rarely be a primary mucosal neoplasm, most of which develop in the anus or rectum [3]. Small bowel has been reported the most common site for GIT metastasis [3] and the upper GIT one of the least common [5], but a more recent retrospective study showed melanoma significantly more frequent in the upper GIT [2].

Case Presentation

A 72-year-old man with paroxysmal atrial fibrillation on apixaban presented with fatigue, postural lightheadedness, and exertional chest pressure for several weeks. Transthoracic echocardiogram and myocardial perfusion scan were unremarkable one month following symptom onset. Cardiac catheterization revealed mild, non-obstructive coronary artery disease. Serology showed severe Iron Deficiency Anemia (IDA), although there were no signs of Gastrointestinal (GI) hemorrhage. Apixaban was discontinued and an urgent upper and lower endoscopy ordered.

A cutaneous melanoma of the lower back (trunk) was diagnosed 6 years prior by punch biopsy (Breslow depth 2.25 mm invading the reticular dermis, Clark level IV) (Figure 1). He underwent a wide local excision, and the sentinel lymph node biopsy was negative. BRAF analysis was not performed based on the early stage of this "typical superficial spreader." Adjuvant therapies were experimental at the time and not prescribed. Subsequent bi-annual skin exams and periodic ophthalmologic exams remained clear. He was up to date on colorectal cancer screening, and his most recent colonoscopy removed a 25 mm tubular adenoma from the cecum 4 years ago.

Upper endoscopy revealed a polyp in the stomach body (Figure 2). Colonoscopy revealed a 12 mm ileocecal valve polyp, a partially obstructing ascending colon tumor (Figure 3), and a 12 mm hepatic flexure polyp (Figure 4). Biopsies revealed metastatic melanoma. Positron emission tomography identified metastatic disease in the lungs and right humeral head. Abdomen/pelvis

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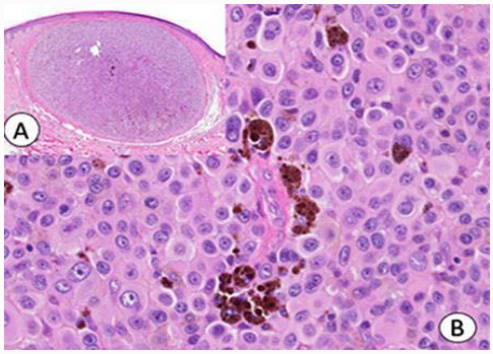

Figure 1: A) Skin, mid-right back, punch biopsy: non-encapsulated well circumscribed tumoral nodule (H&E, original magnification 40X). B) Malignant melanoma composed of a monomorphic population of epithelioid cells with melanin pigment (H&E, original magnification 400X).

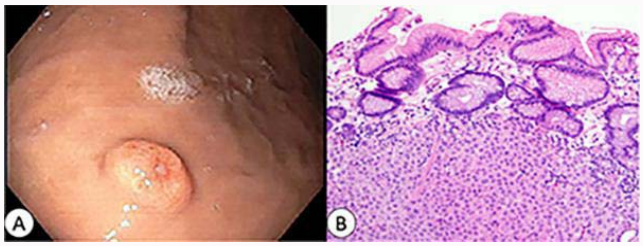

Figure 2: A) Stomach: Single 20 mm umbilicated/ulcerated nodule found on the posterior wall of gastric body. B) Stomach: Melanoma cells undermining gastric epithelium (hematoxylin-eosin (H&E), original magnification 200X).

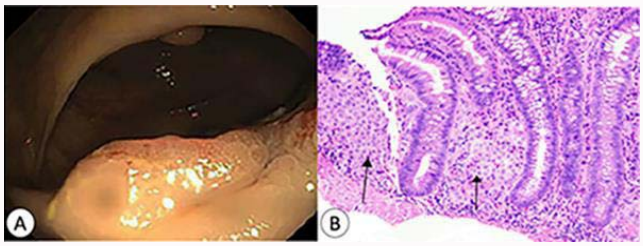

Figure 3: A) Ascending colon: Infiltrative and ulcerated partially obstructing 4-cm mass involving one-half of the lumen circumference. B) Ascending colon: Tumoral cells (arrows) flanked by colonic crypts (H&E, original magnification 200X).

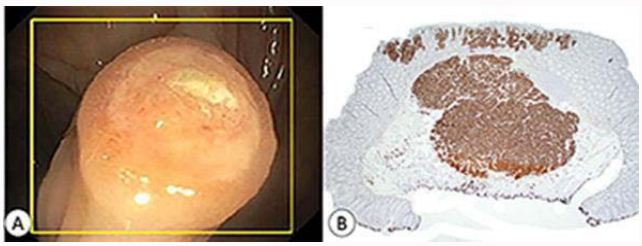

Figure 4: A) Hepatic flexure: endoscopic appearance of the 12-mm sessile polyp. B) Melanoma cells stain strongly for melanocytic marker SOX-10 (SOX-10 immunohistochemical stain, original magnification 20X).

CT scan with intravenous contrast was unrevealing, but a chest CT scan demonstrated bilateral solid pulmonary nodules up to 2.5 cm consistent with metastases. Brain MRI showed left caudate and left cerebellar metastases. Serum Lactate Dehydrogenase (LDH) was normal, but GI metastases harbored the BRAF V600E mutation.

The patient's treatments included two IV iron infusions for symptomatic iron deficiency anemia. He noticed gradual symptomatic improvement after these infusions, and his hemoglobin and hematocrit subsequently returned to normal. He was evaluated by a radiation oncologist who recommended stereotactic radiosurgery to treatment the brain metastasis, which was performed in one session. He tolerated the stereotactic radiosurgery without difficulty or signs of neurological complications. Additionally, his oncologist recommended immunotherapy with nivolumab every four weeks with repeat imaging to assess his response. Thus far he has had no noticeable side effects following nivolumab.

Discussion

Given our patient had upper GIT metastases, we searched for melanoma cases of the upper GIT at the University of Florida from 2006-2021 and only found six total cases, two of which were gastric and four duodenal. Given the proposed criteria for diagnosing primary small bowel melanoma [3], multiple GIT lesions in our patient make it unlikely to be primary GI-mucosal melanoma, despite the absence of a cutaneous primary. A 2004 literature review of GI metastases from melanoma identified 16 studies and calculated 43.8 months as the average time from primary tumor treatment to finding a GI metastasis [6]. Interestingly, a more recent 2017 single-institutional case series of 5 melanomas reported a much longer period, 120 months, as the median time between primary melanoma treatment and detecting upper GI metastasis [7].

In most cases, GI metastases are asymptomatic and difficult to diagnose. Only 1% to 5% of patients with melanoma have clinically apparent GI involvement [4]; however, up to 43.5% of melanoma patients have GI metastasis at autopsy [5]. Endoscopy is superior to radiography for diagnosing GIT metastases and evaluating complications [8]. Metastases to the GIT appear as either pigmented or amelanotic ulcerated polypoid lesions [2,5,8]. The most common signs and symptoms of GI metastasis are abdominal pain, dysphagia, GI bleeding (including anemia and fatigue), small bowel obstruction, and perforation [2,5,8]. Our case illustrates the importance of prompt diagnosis of GI metastasis for timely treatment prior to life-threatening complications including GI hemorrhage or perforation. Clinicians should be alert to the possibility of GI metastases in patients with prior melanoma presenting with IDA.

Any GIT metastasis is a poor prognostic marker (5-year survival 14%, median survival 12.5 months) [4], but these patients often have multifocal secondary tumors (55%) [2] or metastases in multiple organs at autopsy (95%) [1]. GI metastases are not usually the cause of death which is most often due to respiratory failure from lung metastasis [1]. Although LDH elevation is not melanoma-specific, it is a negative predictor of survival in The American Joint Committee on Cancer (AJCC) staging system [9]. Half of cutaneous melanomas have BRAF mutations [10], and the most common V600E mutation is associated with decreased overall survival in advanced melanoma, a population treated since 2011 with BRAF inhibitors to improve survival [10].

Conclusion

Melanoma often progresses to metastatic disease including multifocal GIT metastases. Although GIT metastasis is usually asymptomatic, it has a poor prognosis because of late diagnosis and treatment. Consider GIT metastases when patients with IDA have a melanoma history.

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