Complicated Metastatic Melanoma to the Gastrointestinal Tract

by Joseph P. Kingsbery, David M. Poppers

INTRODUCTION

etastatic melanoma to the gastrointestinal (GI) tract poses a unique clinical challenge. Previously believed to be rare, many patients have metastatic disease on autopsy yet rarely demonstrate GI symptoms. In the era of targeted immunotherapy capable of rapidly reducing the size of space-occupying lesions in the GI tract, case reports of bowel perforation have emerged as previously unforeseen complications of treatment. The following case of a patient treated with immunotherapy for malignant melanoma with known GI metastases highlights the importance of clinical

Joseph P. Kingsbery, M.D. New York University, Department of Gastroenterology David M. Poppers, M.D., Ph.D., NYU Preston Robert Tisch Center for Men's Health, Consultant/Educator for Olympus evaluation prior to initiating potent immunotherapy and risk-stratifying patients due to potential treatment complications.

Case

A 57-year-old man presented with complaints of post-prandial epigastric abdominal pain for the past month as well as an unintentional 5-pound weight loss. His past medical history was unremarkable. His physical exam revealed a normal abdominal exam without tenderness to palpation or palpable masses. Initial laboratory studies were remarkable for an aspartate transaminase (AST) of 56 (units/L), alanine transaminase (ALT) of 65 (units/L), and alkaline phosphatase of 192 (IU/L), with a normal bilirubin, international normalized ratio (INR) and platelet count. He was seen by a gastroenterologist, and an upper endoscopy and colonoscopy were planned

to evaluate his abdominal pain. In the interim, an abdominal ultrasound demonstrated multiple large, hypovascular peritoneal masses. Subsequent contrasted computed tomography scan of the abdomen and pelvis revealed innumerable tumor implants in the peritoneal cavity, mesentery, retroperitoneum and peritoneum with nodal metastases, a serosal implant in the pancreas as well as peri-and intra-gastric lesions (Figure 1). The primary site was unidentifiable.

The upper endoscopy revealed medium-sized, infiltrative mass lesions in the body of the stomach (Figure 2), as well as suspected external compression of stomach lumen; biopsies were taken of each lesion. Colonoscopy showed an infiltrating, non-obstructing 1 cm mass in the transverse colon (Figure 3) as well as a non-eroding lesion at the ileocecal valve and likely external compression of the cecum. Pathology from the lesions was consistent with malignant melanoma, BRAF wild-type. Staging was therefore reported as TxNxM1c with metastases to the lung, peritoneal cavity, peritoneal and mesenteric lymph nodes, pancreas, colon and stomach.

The patient was begun on combination PD-1 inhibitor (nivolumab) and CTLA-4 inhibitor (ipilimumab). His disease and treatment course were complicated by subsegmental pulmonary emboli, medication-induced pneumonitis, partial colonic obstruction by tumor burden, ongoing GI bleeding and septic shock secondary to a presumed intra-abdominal source. He ultimately died roughly two months after initial presentation; an autopsy was not performed.

Discussion

It is now recognized that malignant melanoma commonly metastasizes to the gastrointestinal tract, infrequently causing symptoms.^{1,4,5} Upon autopsy of 100 patients with cutaneous melanoma without GI symptoms, over half had metastatic lesions in the small intestine, and roughly a quarter had lesions in the stomach and colon.¹ Gastrointestinal metastases portend a poor prognosis, with survival averaging 4-6 months.⁴ For symptomatic disease, including intussusception and obstructive symptoms, consensus is that surgical intervention is indicated for palliation.^{5,6,7,8} However, there is no current recommendation to investigate for GI tract disease in asymptomatic patients as this typically does not alter clinical management.⁵

However, with the development of more targeted therapies for melanoma, specifically with biologic

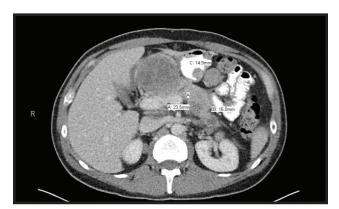


Figure 1. CT scan showing serosal implant along the posterior wall of the gastric antrum and a 1.5 cm nodule on the posterior aspect of the proximal gastric antrum.

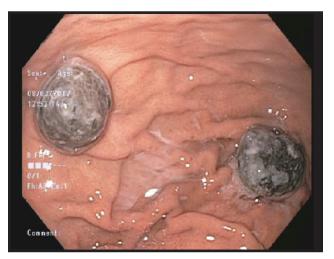


Figure 2. Upper endoscopy image: medium-sized infiltrative mass lesions in the body of the stomach.

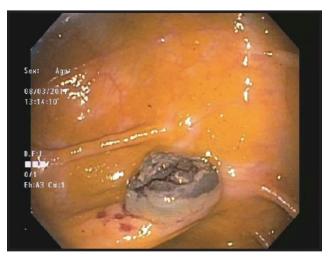


Figure 3. Colonoscopy image: an infiltrating non-obstructing 1cm mass in the transverse colon.

A CASE REPORT

therapy including PD-1 or CTLA4 inhibitors, case reports have emerged identifying bowel perforation as a complication of a robust response to these potent therapies. ^{2,3} In the age of targeted immunotherapy, it is possible that asymptomatic lesions may cause unforeseen treatment complications. Whether or not GI disease should be investigated or ruled out prior to treatment with these new agents remains to be elucidated. It does seem clinically prudent that such patients should be screened carefully for any symptoms of GI involvement prior to initiating immunotherapy to risk stratify for these events, which may be devastating if not entirely preventable.

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