CASE REPORT

Case Report: Primary Duodenal Melanoma with Brain Metastasis

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ABSTRACT

Malignant duodenal tumors can be primary or secondary. Although the most common primary tumor involving the duodenum is an adenocarcinoma, primary malignant melanomas arising in the small intestine are exceedingly rare and remain a controversial clinical entity. In this report, we present a unique case of primary duodenal melanoma with brain metastasis managed successfully by surgical excision, stereotactic radiation, and adjuvant immunotherapy.

CASE PRESENTATION

A 61-year-old white man was sent to the emergency department at Kaiser Permanente Riverside by his primary care doctor because of decreased hemoglobin levels and fatigue for 1 month. His medical history was significant for restless leg syndrome, a history of peptic ulcer disease more than 20 years earlier, and remote tobacco use disorder (0.8 pack-years, quit 30 years previously). Medication use included ibuprofen 800 mg twice daily for the past 3 months for chronic low back pain. On admission, his vital signs and physical examination were unremarkable. Laboratory studies confirmed microcytic anemia with a hemoglobin level of 6.3 g/dL (baseline hemoglobin, 14.5 g/dL 3 years prior). Anemia workup revealed ferritin < 8 ng/mL, consistent with iron-deficiency anemia. A stool screening for Helicobacter pylori antigen was negative. He received 3 U of red blood cell transfusions.

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the abdomen showed high-grade partial obstruction at the fourth portion of the duodenum (Figure 1C), which was then confirmed by esophagogastroduodenoscopy (Figure 1D). The patient underwent successful surgical management with exploratory laparotomy and intestinal resection of the duodenal mass. Two weeks postoperatively, nivolumab was resumed.

The patient tolerated treatment well except for hypothyroidism, which was treated with levothyroxine.

The patient is currently doing well 38 months after surgery without any further evidence of recurrence or distant metastasis despite the initial aggressive presentation of the tumor. His most recent CT scan of the chest–abdomen–pelvis and MRI of the brain (Figure 3C) revealed no new masses or lymphadenopathy. He continues to be on treatment with nivolumab. Figure 4 summarizes the course of events since his initial diagnosis to the present.

**DISCUSSION**

Melanoma is a malignant tumor that develops from melanocytes, a pigmented, dendritic-like cell, present mainly in the skin and less commonly in the eyes, meninges, and gastrointestinal (GI) mucosa. Melanomas account for 1% to 3% of all malignancies. The incidence has been increasing globally and an estimated 48,000 patients die each year from this malignancy. Although the GI tract is the most common site of metastatic involvement, given its rich blood and lymphatic supply, primary malignant melanomas arising in the small intestine, particularly the duodenum, are exceedingly rare and remain controversial. Current literature is limited to only a few case reports.

There are several theories regarding the origin of primary malignant melanoma in the small intestine. One theory argues that GI melanoma without a primary visible skin lesion may represent either an undiagnosed or spontaneous regression of a cutaneous malignancy caused by infection or changes in the immune system. However, there is growing literature on primary melanoma in the small intestine without evidence of a cutaneous source. Some experts have postulated that GI melanomas arise from the migration of multipotent neural crest cells into the bowel and differentiate into specialized cells. As such, melanoblasts in the small bowel may serve as precursors to malignant melanoma. Histological and immunohistochemical studies have been shown to support this hypothesis by showing the presence of normal melanocytes in the mucosa of the GI tract.

Often, primary duodenal melanoma may be asymptomatic or may manifest with nonspecific clinical symptoms. In the advanced stage, it may present with upper GI tract bleeding.
or intestinal obstruction. Therefore, the diagnosis of primary intestinal melanoma has been a challenge, in combination with its rarity. Several criteria have been proposed. Among them, Sachs et al defined primary malignant melanoma in the small bowel with the following criteria: 1) biopsy-proved melanoma from the intestine at a single focus; 2) no evidence of disease in any other organs, including the skin, eye, and lymph nodes outside the region of drainage at the time of diagnosis; and 3) disease-free survival of at least 12 months after diagnosis. Our patient fits the 3 criteria of diagnosis. He was diagnosed with solitary biopsy-proved duodenal melanoma with absence of a cutaneous or choroidal lesion from thorough dermatological and ophthalmological examination performed by the experts. Moreover, the patient has been doing well 38 months after initial diagnosis.

Upper GI endoscopy and CT scanning remain the crucial modalities for the detection of lesions and diagnosis. Ultimately, immunohistochemical staining is needed to confirm the diagnosis.
confirm the diagnosis. It is important to note that the sensitivity of S100 ranges between 33% and 100% whereas HMB-45 antibodies have a sensitivity of 80% to 97% and a specificity of 100%, respectively. To date, the incidence of metastasis in primary duodenal melanoma is not clear. Positron emission tomography is helpful for staging and identifying the sites of metastasis.3,9,18,19 Our patient had asymptomatic brain metastasis on MRI, with a positron emission tomographic scan confirming no other avid disease after initial diagnosis of duodenal melanoma.

Surgical excision is the treatment of choice for duodenal melanoma. There is no standardized surgical strategy because of the overall low incidence and the complex anatomy of the duodenum, given its rich supply of blood vessels. Therefore, the surgical approach is tailored individually based on the expertise of the surgeons.20 Pancreatoduodenectomy is applicable in all cases. For nonampullary lesions, partial duodenal resection and subtotal gastrectomy are deemed appropriate. Meanwhile, other methods, such as adjuvant radiotherapy and chemotherapy have not been shown to have concrete evidence of survival benefit. In addition, the presence of BRAF, NRAS, PTEN, and KIT mutations warrant the emergence of newer anticancer drugs for the treatment of melanoma. This option did not apply in this case because our patient had a BRAF-negative tumor.

Since 2011, immune checkpoint inhibitors have been approved for advanced melanoma treatment. Ipilimumab is a monoclonal antibody against cytotoxic T-lymphocyte-associated protein 4. The newer immune checkpoint inhibitor is nivolumab, which is an antiprogram cell death 1 monoclonal antibody. In phase 3 of the CheckMate 067 trial, the median overall survival was 19.9 months with ipilimumab monotherapy and 36.9 months with nivolumab monotherapy, although the median overall survival of nivolumab plus ipilimumab was not reached at a minimum follow-up of 48 months.21-23 In our case, the patient developed grade 4 colitis after the first cycle of combined nivolumab and ipilimumab. Therefore, ipilimumab was discontinued. He continued to do well on nivolumab only, with an adverse effect of hypothyroidism that was subsequently controlled with levothyroxine.

Overall, the prognosis of duodenal melanoma is poor, mainly because of the delay in diagnosis. The 5-year survival of untreated primary GI melanoma is reported to be 14%, with a typical duration of survival of only 12.5 months.24,25 Among published case reports, Li et al26 reported a case of primary duodenal melanoma treated successfully by surgical
excision, with the longest survival duration of more than 46 months with no reported relapse. Similarly, our patient has been doing well with no signs of relapse 22 months after curative resection.

CONCLUSION

Primary duodenal tumors are exceedingly rare; thus, they remain a controversial clinical entity. To our knowledge, our report is the first of its kind to report a case of primary duodenal melanoma with brain metastasis treated successfully by surgical excision, stereotactic radiosurgery, and immunotherapy with nivolumab.

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Author Contributions

Sonha Nguyen, MD and Naila Khan, MD performed a literature search and drafted the manuscript. Mary Le, MD assisted with histological images and revised the manuscript. Christine Duong, MD and Vishal Ranpura, MD supervised with patient care and revised the manuscript.

References