Metastatic Malignant Melanoma to Colon from Cutaneous Melanoma: A Case Report

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Abstract

Metastatic melanoma to the Gastrointestinal (GI) tract is rare and the colon is a less common site of GI tract metastasis for this cancer. We report a case of a 76-year-old male with history of cutaneous malignant melanoma since 2018 and two years later he developed metastasizing to the brain, axillary lymph node and descending colon. He was treated with stereotactic radiosurgery (SRS) for single brain metastasis, he subsequently underwent a combined left axillary node dissection and left colectomy.

Importance of long-term surveillance and role of 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) and colonoscopy are discussed along with the role of surgical resection in improving survival. Nevertheless, metastatic malignant melanoma to the colon is difficult to identify diagnosis and treatment, multidisciplinary team discussion is necessary to determine the most appropriate treatment strategy.

Keywords: malignant melanoma, colon metastasis, gastrointestinal tract

Malignant melanoma, known as malignancy of melanocytes, is the most serious type of skin cancer. Worldwide, there have been more than 60,000 melanoma patient deaths per year. The World health organization reports that the number of deaths resulting from melanoma will rise from 20% in 2025 to 74% in 2040.[1] Cutaneous melanoma has an aggressive tendency for metastasis and the most common sites of metastases are the lymph node, lung, central nervous system and bone.[2] Gastrointestinal metastasis of malignant melanoma is found during autopsy in up to 60% of cases but they are diagnosed in 2-5% of patient while living.[2-4] Colon is an uncommon site of melanoma metastasis with an incidence of 0.3-2.1%.[5-8] We report a case of cutaneous melanoma metastasizing to brain, lymph node and colon followed by a review of literature.

Case Report

A 76-year-old man presented with complaints of mass at left forearm in December 2018. He had no history of any systemic illness. He denied prior history of skin cancer, other skin or ocular lesions and family history of melanoma. General physical examination was insignificant and his vital signs were within normal limits. Physical examination revealed solitary well-defined brightened red nodule with contact bleeding at left forearm.

An excisional biopsy was performed in January 2019 from a rural hospital and the result demonstrated malignant melanoma 4.5 mm thick, Clark level IV (invasion into the reticular dermis) and the lesion showed mainly vertical growth pattern. The patient was referred to oncologic surgeon for wide excision. Pathology from this procedure showed residual melanoma and the tumor was close to caudal deep margin. Afterwards re-wide excision was done in February 2019 and the specimen revealed no residual melanoma.

The follow ups 18F-FDG PET/CT were done in August 2019 and February 2020 showed no hypermetabolic activity that suggested local tumor recurrence or distant metastasis. He had been followed up regularly and remained free of obvious disease recurrence.

Unfortunately, in April 2021 he presented with right visual deterioration. The Magnetic Resonance Imaging (MRI) of the brain demonstrated 2.0x1.6-cm lobulated subcortical nodule at right occipital lobe and moderate surrounding brain edema compatible with history of malignant melanoma with brain metastasis. The 18F-FDG PET/CT was done for re-staging and suggested newly developed cerebral metastasis at right parieto-occipital region and left axillary node metastasis. Moreover, there was a new hypermetabolic polyp in the proximal descending colon near the splenic flexure (Figure1).

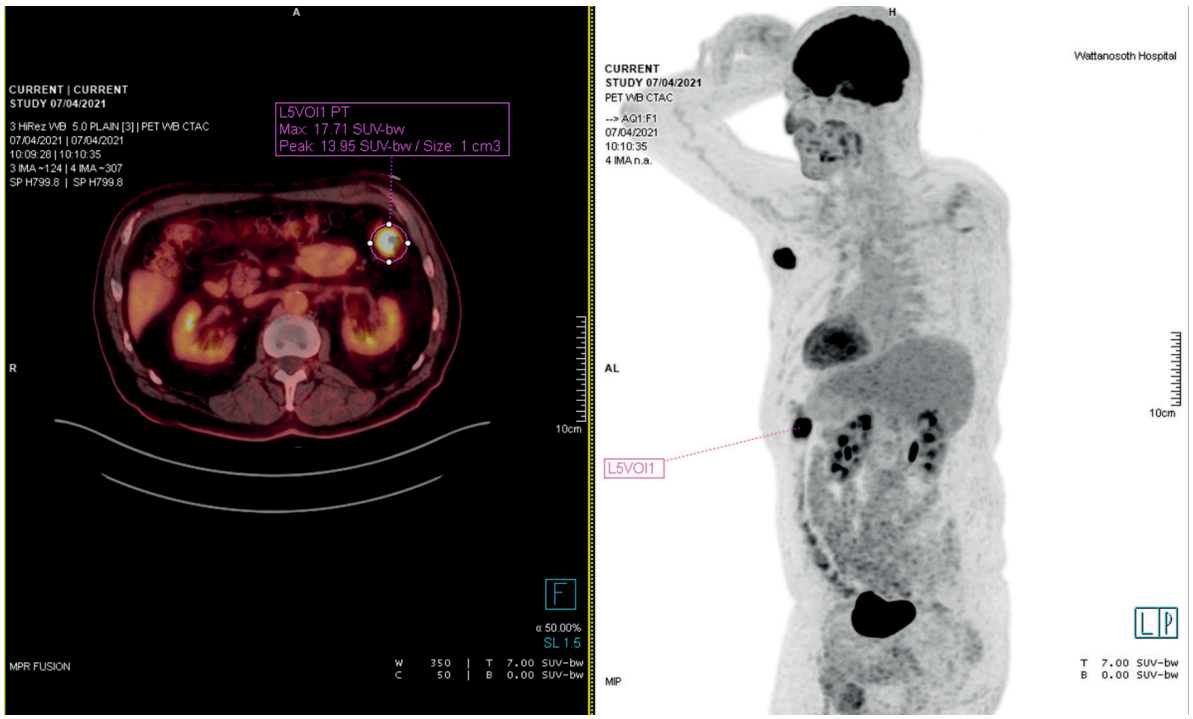

Figure 1: 18F-FDG PET/CT showed hypermetabolic polyp in the proximal descending colon near the splenic flexure

At the time of diagnosis, his general condition was fine and physical examinations showed enlargement of left axillary lymph nodes and otherwise was normal. The biochemistry studies including liver function tests, carcinoembryonic antigen (CEA) and lactate dehydrogenase(LDH) were within normal limits. The colonoscopy revealed a bleeding polypoid mass size 3x4 cm at 45-48 cm from anal verge (Figure2).

The colonic mass biopsy specimen consists of colonic mucosa occupied by malignant epithelioid cells. The differential diagnosis includes malignant melanoma, carcinoma or others.

The patient was treated with stereotactic radiosurgery (SRS) 20 gray for single brain metastasis at right occipital lobe on April 12, 2021 and he subsequently underwent a combined left axillary node dissection and left colectomy on April 17, 2021. Pathology from left axillary lymph nodes disclosed malignant melanoma involving 2 from 6 lymph nodes with extranodal extension. The tumor was positive for S-100 and HMB45.

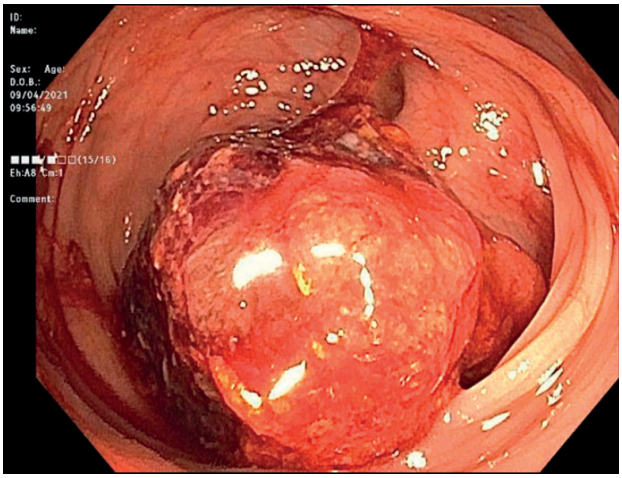

Figure 2: A bleeding polypoid and non-obstructing mass size 3x4 cm at 45-48 cm from anal verge.

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Histology of the colonic mass showed mixed epithelioid and spindle cell proliferation occupied in the mucosa, submucosa and muscularis propria. Tumor nuclei have moderate pleomorphism with irregular membrane and visible nucleoli (Figure3). Mitotic activities were present. Some tumor cells contained brown pigments. Immunohistochemistry was positive for Melan-A, Vimentin, HMB-45 (Figure4) and negative for AE1/3. All of these findings were consistent with metastasis malignant melanoma.

After patient did well postoperatively, the medical oncologist started Nivolumab which is a first line systemic treatment for metastatic malignant melanoma.

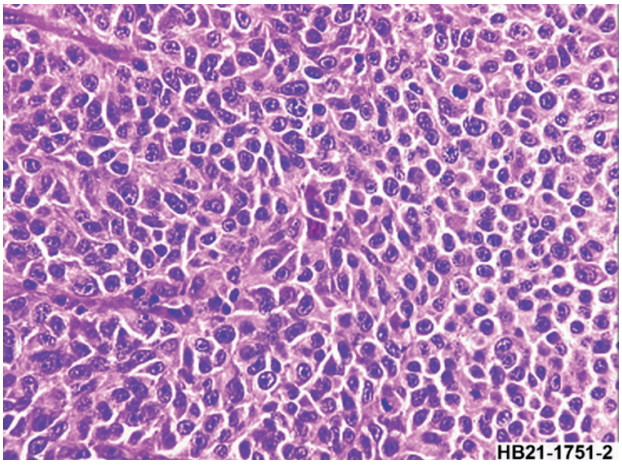

Figure 3: Colon mass showing mixed epithelioid and spindle cell proliferation.

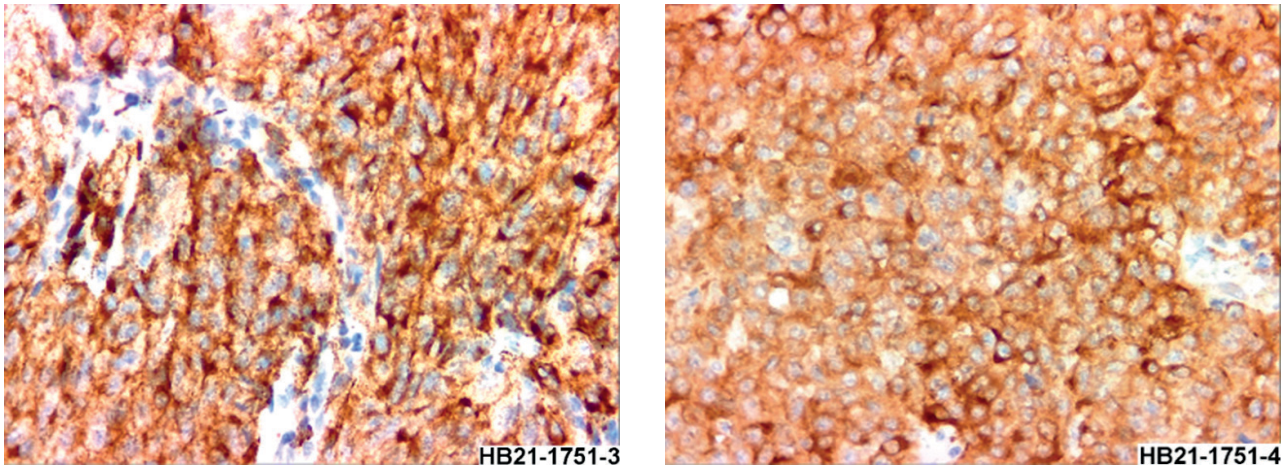

Figure 4: Immunohistochemistry of colon mass showing HMB-45 positivity(Left) and melan-A positivity(Right)

Discussion

Malignant melanoma of GI tract can be either primary or metastasis, however the incidence of metastatic melanoma is more common.[9] GI metastasis of malignant melanoma is found up to 60% during autopsy but fewer than 5% of patients are diagnosed before death.[2-4] Typically, metastatic melanomas in GI tract are regularly found in stomach and small bowel.[10] The colon is a less common site of GI tract metastasis for this cancer[5] and it is difficult to diagnosis pre-mortem with an incidence of 0.3-2.1%.[5-8] The interval time between primary melanoma diagnosis to colon metastasis is usually long and can vary between 24 months and 7 years,[8,11] so long term follow up and awareness of colon metastases is necessary.

Some malignant melanoma may be amelanotic or atypical histology. The use of special immunohistochemical stains is useful in confirming the diagnosis. S-100 is highly sensitive while HMB-45 and Melan-A are highly specific in diagnosing malignant melanoma.[9]

Moreover, distinguishing between a primary GI mucosal melanoma and a metastatic to the GI tract may be difficult. Many studies proposed that primary GI melanoma is suggested if the patient has no obvious primary cutaneous or ocular melanoma, has a precursor lesion or histological evidence of melanosis or has a solitary GI lesion without other extraintestinal metastases.[12-14] The colon mass in this case is likely to be metastatic malignant melanoma rather than a primary malignant melanoma. Although the patient had a single lesion in the colon, he had a history of cutaneous melanoma, with a morphology compatible with the colonic mass. Furthermore, he had extra gastrointestinal metastases and no precursor lesion in the colon.

Symptoms are often identical to those of other GI tumors, including GI bleeding, abdominal pain, chronic anemia, bowel obstruction, bowel peroration and weight loss.[15] Asymptomatic cases were reported at approximately 15%.[6] Bowel perforation and obstruction are significantly correlated with poor survival.[5] Our patient had no abdominal symptoms and we accidentally found metastatic melanoma to colon during a re-staging 18F-PET/CT scan.

Diagnosis of metastatic melanoma is generally made by computer tomography (CT), ultrasonography, barium studies and endoscopic evaluation. Around 60-70% of colon metastases were able to be visualized by CT,[14] however, recently PET-CT is the most accurate tool in detecting and staging melanoma metastases.6,16,17 Akcali et al.[18] reported that the sensitivity and specificity of a PET/CT scan for the detection of metastatic melanoma were 91% and 92%, respectively. Therefore, if clinical indicates melanoma but the CT scan shows a negative result, further studies should be undertaken. Colonoscopy has the greatest diagnostic value with high sensitivity and specificity and allows for tissue biopsy. Colon mass usually appears as multiple ulcerated polypoid lesions and may be either pigmented or amelanotic.[15]

Colon metastasis indicates poor survival outcome. Five-year survival from diagnosis metastasis are reported at less than10%.[14,19] Several studies have reported survival improvement associated with complete resection of all metastasis either in GI tract or other distant sites.[6,7,20-22] Ollila et al.[19] reported curative resection exhibited significant longer survival time than patients in the palliative group. Wysocki et al.[23] presented a case of a patient who achieved long-term disease-free survival of 101 months after surgical resection of metastatic malignant melanoma to ileum and colon.

Unfortunately, most patients with completely resected melanoma metastases will experience a disease relapse and response to classical chemotherapy lacks an overall benefit. Currently, immunotherapy such as Nivolumab and Pembrolizumab and targeted therapy that targets the mutated BRAF V600 proteins such as Dabrafenib, Trametinib and Vemurafenib have become standard treatment in resected metastatic malignant melanoma.[24] Despite surgery and new developments in systemic treatment, the disease still has high prevalence of recurrence. As recommended by National comprehensive cancer network (NCCN) guidelines, a multidisciplinary team discussion is often helpful to determine the most appropriate treatment strategy.[24]

Conclusion

In GI tract, differentiating primary malignant melanoma from metastatic can be very challenging. Diagnosis requires careful inspection of the mucosa for metastatic lesions and biopsy with special immunohistochemical stains. Malignant melanoma patients should be screened long term for gastrointestinal symptoms because the interval time between first diagnosis to colon metastasis is usually long. CT scan, PET/CT scan and colonoscopy were important diagnostic tools for detecting early metastatic disease. Both curative resection and complete resection of all metastatic sites improve prognosis and overall survival. However, metastatic malignant melanoma is difficult to determine diagnosis and treatment, and a multidisciplinary team discussion is often helpful to determine the order of therapies.

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