A Rare Case of Metastatic Malignant Melanoma to a Single Site in the Gastrointestinal Tract

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Abstract

Introduction: Melanoma is the most malignant skin cancer and has the potential to metastasize to various parts of the body, usually with multi-organ involvement and poor prognosis. Single site metastasis, especially to an intra-abdominal site is rare.

Case Report: Here, we present a patient who had vaginal melanoma which metastasized only to the stomach, with a review of the available literature on diagnostic and treatment options.

Conclusion: Complete resection of gastrointestinal metastasis of malignant melanoma can palliate and may also prolong survival of these patients.

Keywords: Melanoma; metastatic; gastrointestinal tract; surgery

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Introduction

Melanoma is the most malignant of skin cancers, with the ability to metastasize to various parts of the body – lymph nodes, skin, lung, liver, brain, bone, adrenal glands, and the gastrointestinal tract. It has been shown that 60% of patients who die of melanoma have metastases to the gastrointestinal tract at autopsy[1, 3]. However, only 1-4% of patients with malignant melanoma will manifest gastrointestinal symptoms in their lifetime [2]. In addition, patients with gastrointestinal metastases will often also have other sites of metastatic disease, and hence, our case represents a very rare phenomenon of melanoma, metastasizing to a single focus in the gastrointestinal tract, and presenting with symptoms of gastrointestinal bleeding.

Presentation of the Case

Our patient is a 60 year old Chinese female who presented with post-menopausal bleeding. On examination, she was found to have a necrotic vaginal polyp, for which a polypectomy was done. Histology revealed malignant melanoma with extensive surface ulceration and positive resection margins, 54 mitoses per 10 high power field (hpf) that was negative for BRAF mutation but positive for KIT mutation, with exon 11 substitution (Figure 1 & 2). A staging computed tomography (CT) scan of the brain, neck, thorax, abdomen and pelvis did not show evidence of distant metastasis. In addition, a positron emission tomography (PET) - CT scan was performed which showed a hypermetabolic focus in the left lower vagina suggestive of residual disease. There were no other FDG avid lesions elsewhere in the body. She was advised for a wide excision of the residual focus of melanoma and a sentinel node biopsy. A sentinel node scan was done just prior to surgery, which showed positive lymph nodes along her external and internal iliac vessels (Figure 3). She refused a biopsy of the sentinel pelvic lymph nodes and possibly pelvic lymph node clearance if positive, but agreed to the wider excision of the vaginal lesion. The wider excision vaginal specimen revealed residual foci of melanoma in situ with no invasive component, and negative margins on final histology. In view of her positive uptake of pelvic lymph nodes noted on the PET scan, she was treated as a Stage III disease (regional lymph node involvement with no evidence of distant metastasis) and further adjuvant therapy with interferon and temozolomide with cisplatin was discussed, but the patient declined further treatment. She remained on close follow-up with her gynaec-oncologist and medical oncologist, with clinical and radiologic evaluation on a six-monthly basis, during which time she was asymptomatic and disease-free. One year after her initial surgery, she was referred to the surgical oncologist for melena and a sudden drop in her hemoglobin levels by 5g/dL to 6.3g/dL. Physical examination did not reveal any abdominal masses but revealed the presence of a pigmented spot in the vaginal canal. Repeat surveillance CT scan did not reveal any abnormalities. She was investigated by means of an esophagogastroduodenoscopy, which showed a malignant looking ulcer at the incisura and lesser curve, to be the likely source of bleeding (Figure 4). A biopsy of the ulcer revealed the presence of metastatic melanoma. The specimen was strongly positive for Melan-A and HMB45 and patchily positive for S100. Despite a course of iron supplements, her haemoglobin level continued to drop and she remained symptomatic as a result of the melena and anaemia. Her case was discussed at our multi-disciplinary tumour board meeting. She was offered palliative resection or radiotherapy, as means to control the bleeding and after deliberation, she decided for surgical intervention. She was optimized for surgery and underwent a laparotomy. Intra-operatively, a large ulcerative lesion...
was identified at the gastric incisura. No other intra-abdominal lesions were seen. A pigmented spot was also noted in the mid-vaginal canal, closely associated with the previous excision site. She underwent a palliative subtotal gastrectomy (Figures 5 & 6) and excision of the vaginal lesion. The surgery was uneventful and she was discharged well on post-operative day seven. The melena resolved, along with her symptoms of anaemia and her haemoglobin levels remained stable at 11g/dL. The histology of the resected specimen confirmed metastatic melanoma, 70mm in diameter, involving the gastric wall but not breaching serosa, clear margins, with 1/15 lymph nodes positive (Figure 7) and presence of melanoma within the vaginal specimen.

Figure 1 & 2 Initial vaginal melanoma showing pleomorphic epithelioid tumour cells with brown cytoplasmic pigments, staining positive for HMB45.
Figure 3: FDG avid lymph node localized to the region of the bifurcation of the left internal/external iliac vessels.

Figure 4: Endoscopic view of the bleeding metastatic melanoma showing the characteristic polypoidal mass.
Figure 5 & 6 Photo of the resected specimen, showing the polypoidal mass with a bull’s eye lesion suggestive of metastatic malignant melanoma at the incisura/lesser curve of the stomach.
Discussion

Malignant melanoma is an extensively studied skin malignancy. It has been established that the presence of metastasis equates a poor prognosis – The American Joint Committee on Cancer (AJCC) indicates a Stage IV 5-year survival of 10% [4, 5]. Metastatic melanoma can present in a synchronous fashion or is occasionally detected many years after the initial treatment. The mean time to diagnosis of a gastrointestinal metastasis is quoted to be less than 4 years, even in the presence of clear excision margins of the primary lesion [2]. 95% of these patients will have multiple organ involvement of metastases, with the majority (80-90%) involving the lymph nodes and lung [3]. Our patient only had one confirmed site of metastatic disease, the stomach. For gastrointestinal metastasis, the distribution of organ involvement based on large review of autopsies from Memorial Sloan Kettering Cancer Center is as follows: liver 68%, small bowel 58%, colon 22%, stomach 20%, duodenum 12%, rectum 5%, esophagus 4% and anus 1% [5]. Median survival of these patients is usually less than a year, or less than 10% at 5 years [5]. Of all the sites of metastasis, autopsy data of patients who died from melanoma showed that the brain is still the preferred site for single metastasis [3].

Diagnosis of gastrointestinal metastasis can be obtained from biopsy of lesions seen on endoscopy and also with radiological tools. On endoscopy, there are several characteristics of metastatic melanoma – multiple nodules, bull’s eye appearance, extrinsic mass lesions, ulceration and polypoidal tumour mass [1]. It may be difficult to differentiate from high-grade mucosa- associated lymphoid tissue but pigmentation and correlation with the patients past medical and surgical history often guide the diagnosis [1].

Several radiological modalities have been used for detection of melanoma metastasis. CT alone has a sensitivity of 69.7%, and PET alone, 88.8% whereas PET-CT has a sensitivity of 98.7% [6, 7]. Melanoma cells usually present with a high FDG uptake and therefore PET-CT should be done whenever possible [7]. Our patient had a PET-CT performed at the time of diagnosis, which did not show any evidence of metastatic disease. She subsequently had a CT scan done during her diagnosis of gastric metastasis and there was no evidence of other sites of metastasis.
Surgical intervention for gastrointestinal metastasis is most commonly done for anemia (40.8%) or bowel obstruction (32.4%), with low surgical mortality rates [6]. Options for surgery can be palliative or therapeutic, depending on the presence or absence of other distant metastatic disease. Despite being of palliative intent, surgery for symptomatic or imminently symptomatic gastrointestinal metastasis of melanoma is done not only because it relieves symptoms, but it may also prolong survival [9]. The 5 year survival of patients with metastasis to the GI tract can be significantly improved to 28.3% at 5 years if complete resection of the metastatic lesions is achieved [10].

Genetic mutations in patients with melanoma, such as BRAF, KIT, NRAS have become another target of treatment for those with metastatic disease. BRAF mutation is found in 50%, KIT in 2%, and NRAS in 15-20% of patients with detected genetic mutations in the western population [11]. A study done on the Chinese population showed the KIT mutation to be 10.8% [12]. Of the patients with KIT gene mutations, 10-20% will have acral and mucosal melanomas, such as those derived from the genital regions [11, 13]. Presence of such mutations provides further options for adjuvant therapy such as Imatinib and Nilotinib. A phase II clinical trial in using Imatinib in metastatic unresectable melanoma with KIT mutations show improv overall survival overall response rate up to 23.3% [14]. Further studies can be done to study the overall response and survival in patients with complete resection of metastatic melanoma with KIT mutation and adjuvant imatinib therapy.

Summary

95% of Stage IV malignant melanoma have multi-organ involvement and are associated with an extremely poor prognosis [3]. A single focus of gastrointestinal metastasis is rare, albeit still confers a poor prognosis. However, in the face of solitary gastrointestinal metastasis, we can palliate symptoms and perhaps prolong survival by surgical resection of the affected organ. Advances in diagnostic modalities and adjuvant therapy based on detectable genetic mutations allows us to detect the spread of disease early, treat for cure and afford the patient a longer overall survival rate and progression free rate.

References


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