Amelanotic Metastatic Gastric Malignant Melanoma: A Case Report

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Case Report

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Abstract

Background

Melanoma is a cutaneous form of disease with an increasing incidence since 1970s, especially in western countries, accounting for nearly 75% of the death related to skin cancer. Clinical outcome varies a lot among different subtypes, and highest recurrence and mortality were observed within the type with distal metastasis. Furthermore, high incidence of gastrointestinal (GI) metastasis of malignant melanoma is frequently misdiagnosed due to lack of specific clinical manifestations. Amelanotic melanoma metastasis, especially the gastrointestinal metastasis, was rarely observed in clinical practice, accounting for only about 2% of all metastatic cases.

Case presentation

In the present study, we report a 36-year-old male patient with gastric cancer, who was diagnosed as amelanotic melanoma by Immunohistochemical (IHC) staining, demonstrating positive staining for melanoma markers including Melan A, S-100, Hmb45 and CD79a.

Conclusions

In conclusion, for the colorless tumor metastases found during gastroscopy in melanoma patients, detailed pathological examination should be carried out in combination with previous medical history to determine the nature of the tumor and treatment regime.

Background

Incidence of melanoma has kept rising since 1970s, with more than 232100 cases newly diagnosed in 2017, which account for about 1.7% of all new cancer cases worldwide, and causing about 55500 deaths (1). However, both the incidence and mortality differ widely among species, ranging from 0.2/100000 in Asian population to 7.7/100000 in Americans. (1) Risking factors for melanoma have been established as ultraviolet radiation, presence of dysplastic naevi, family or personal history of cutaneous melanoma. (2) Typical genetic alterations such like BRAF, the telomerase reverse transcriptase (TERT), the cyclin-dependent kinase inhibitor (CDKN2A), tumor protein 53 (TP53), phosphatase and tensin homology (PTEN) have been well documented. (2, 3) Of note, BRAF^{V600E} has been observed in nearly 50% of all the melanoma cases, and inhibitors targeting this mutation demonstrated promising benefits in clinical practice. Compared with localized disease, mortality for patient with distal metastasis remains disappointing, which due to insufficient understanding of the underlying molecular mechanism. Moreover, clinical diagnosis of the distal metastasis sites is easy to be ignored in clinical practice, especially for the amelanotic melanoma. Take together, thoroughly inspection should be warranted for patients with history of melanoma.

Case Presentation

A 36-year-old male presented with progressive anorexia, intermittent nausea and vomiting without obvious causes. On January 2, 2020, He underwent gastroscopy (Fig. 1) that showed a hemispherical protuberance of about 0.4 cm in size in the lower part of the body and the fundus of the stomach, respectively. The stomach lesions, which were soft and elastic were removed and sent for pathology biopsy. We highly suspected the body and bottom of the gastric as neoplastic lesions based on hematoxylin-eosin (HE) staining results (Fig. 2). Immunohistochemical (IHC) staining showed that the neoplastic cells of gastric body (Fig. 3) were positive for Melan A, S-100, Hmb45 and CD79a, focally positive for c-kit, and negative for AE1, CK, CD56 and Syn. IHC of the neoplastic cells of gastric fundus were positive for CD68 and negative for AE1 and CK. Combined with a history of right plantar melanoma resection in June 2019, the patient was diagnosed as metastatic stomach melanoma.

In 2014, the patient found a brown tough bulge on the right plantar with local pain, which was not diagnosed or treated. In April 2019, he found that the right plantar lesions (Fig. 4) had local ulceration and were darkened, accompanied by local pain. In May 27, 2019, skin biopsy was performed in the First Hospital of Peking University, which showed that most of the black cells in the middle and lower layers of the epidermis were hyperplastic, scattered and non-nested with obvious Atypia. The biopsy results confirmed the diagnosis of malignant melanoma. The lesions were removed by Mohs microsurgery in the First Hospital of Peking University on June 28, 2019. Postoperative pathology revealed that the lesions were invasive nodular malignant melanoma, whose Clark grade was 4 and Breslow depth was beyond 2.175 mm, with vertical growth. They were without ulcer formation, vascular involvement, nerve invasion, regression phenomenon, microsatellite lesions or active infiltrating lymphocytes. The mitotic ratio of melanoma was less than 1 mm². The melanoma from the right plantar was resected thoroughly and the surgical field (Fig. 4) had good restoration. After gastroscopy revealed metastatic gastric melanoma, the patient visited Beijing Cancer Hospital and underwent head, abdomen, and pelvic CT and enhanced CT, and whole-body bone imaging. According to his radiology results, he was diagnosed with multiple visceral and bone metastasis of melanoma.

Discussion And Conclusions

Malignant melanoma is highly prone to regional lymph node and distant metastasis, and gastrointestinal tract (GIT) metastasis is common but rarely diagnosed. In fact, only 1–4% of patients with malignant melanoma are diagnosed with GI metastases before death, while in the autopsy series of patients with malignant melanoma the incidence of GIT metastasis exceeds 60%. At the same time, malignant melanoma is the most common metastatic tumor of the GIT. According to autopsy, 23% of GI metastases came from malignant melanoma. (4) Comparison between melanoma gene expression score and fluorescence in situ hybridization for the classification of melanocytic lesions Distinguishing between a primary GIT melanoma and a melanoma metastatic to the GIT may be difficult, especially considering the possibility of regression and disappearance of primary skin lesions. The most common site of the GI metastasis of malignant melanoma is the small intestine, followed by the stomach. (5)

The main reason for the low rate of diagnosis of GI metastasis of malignant melanoma is that patients usually have no symptoms or lack of specific symptoms. The clinical manifestations of patients with metastatic gastric malignant melanoma are similar to those of gastritis, peptic ulcer and gastric cancer and the common symptoms are epigastric discomfort, poor receptivity, nausea and vomiting. In addition, the endoscopic results of melanoma are also atypical, so pathology and IHC are often required to confirm the diagnosis. The common endoscopic findings of melanoma are as follows (6): (1) single protuberance with smooth local surface, with the top being pitted or ulcerated, similar to submucosal tumors; (2) multiple protuberances, whose endoscopic features are the same as those of single protuberance; (3) diffuse protuberances, similar to Bormann IV gastric cancer. The surface of most GI melanomas often has varying degrees of pigmentation, which may be black, brown, gray, or dark brown. In this case, the clinical manifestations were loss of appetite with nausea and vomiting, which were not specific, and there was no pigmentation on the skin of the whole body on physical examination. The gastroscopy showed the lesions were very small atypical multiple protuberances, with smooth, soft and elastic surface, no pigmentation and no obvious characteristics of malignant tumors. The biopsy specimen was devoid of melanin granules and the nuclei of the tumor cells were very similar to that of lymphoma, malignant melanoma and poorly differentiated adenocarcinoma. Therefore, the initial HE staining could not confirm the diagnosis of melanoma. After further IHC examination, the final diagnosis of gastric metastasis of malignant melanoma was confirmed.

At present, the common IHC markers are S-100, MelanA, HMB45, SOX-10 for the diagnosis of malignant melanoma. New molecular techniques can also assist in the diagnosis of melanoma (7), including comparative genomic hybridization, fluorescence in situ hybridization (FISH), tumor gene expression profiling (8), and adhesive patch genomic analysis (9). FISH facilitates the assessment of melanoma-associated specific chromosomal abnormalities and is a direct diagnostic tool for ambiguous melanocytic lesions (10–12). This patient was diagnosed with gastric melanoma by a combination of the above-mentioned IHC parameters.

The median survival time of malignant melanoma patients with GI metastases is less than one year, and the high mortality rate observed in these patients is associated with multiple metastases to other organs, such as the lung, liver, pancreas and brain (13). Sun GY et al (14) showed that radical surgery can effectively relieve symptoms in patients with malignant melanoma that initially metastasizes to the stomach, and may be helpful in extending survival.

Patients with gastric metastases from malignant melanoma have no typical clinical presentation and are often accompanied by a history of malignant melanoma of the skin and other sites. Therefore, clinicians need to ask for a detailed history to diagnose metastatic gastric melanoma. Recently there are few cases of GI metastasis of malignant melanoma in the literature at home and abroad, most of which are case reports and there is a lack of understanding of this disease and treatment experience. It is easy to miss the diagnosis of gastric melanoma by gastroscopy and pathological biopsy without IHC staining, which leads to delayed treatments. Therefore, it is necessary to improve endoscopists' understanding of GI malignant melanoma. During endoscopy, any suspicious lesions, especially protrusion lesions, whether

single or multiple, with or without pigmentation, need to be carefully observed, actively sent for pathological tissue biopsy combined with IHC to achieve an early diagnosis to improve the prognosis of patients with melanoma. At the same time, for patients with a previous record of melanoma, regular physical examination is required and when GI-related symptoms occur, abdominal-enhanced CT, GI endoscopy and other examinations should be completed in time to determine whether there is metastasis of melanoma. Besides, pathology is still the gold standard for melanoma diagnosis. In our case, the patient was diagnosed with metastatic gastric malignant melanoma, relying on the relevant medical history of plantar melanoma, gastroscopic biopsy with special IHC staining. At present, the imaging results of the patient in January 2020 suggested that the melanoma had multiple organ metastases. For this patient, from the diagnosis of plantar melanoma to the multiple organ metastases of melanoma, the duration was only six months. For advanced patients with distant metastasis of plantar melanoma, systemic therapy including a complete resection of metastatic lesions, chemotherapy, targeted therapy and immunotherapy remain the most important treatment options. But specific treatment methods vary from person to person. We ultimately recommend that the patient visit a specialized hospital for melanoma.

In summary, for patients with a history of malignant melanoma, if they present nonspecific GI symptoms, they should be alert to the possibility of GI metastasis, and GI endoscopy and gastroscopic biopsy with special IHC stains should be performed promptly. If necessary, novel molecular techniques can also be used for the diagnosis of melanoma. Patients with GI metastasis of malignant melanoma have a poor prognosis and their survival time is often no more than one year. Treatment includes surgical resection of solitary metastases, chemotherapy, immunosuppressive agents, biological chemotherapy and so on. Different patients need to be treated individually and precisely.

Abbreviations

GI: gastrointestinal; IHC: Immunohistochemical; HE: hematoxylin-eosin; GIT: gastrointestinal tract;

Declarations

Ethics approval and consent to participate

The study and manuscript have been approved by the PLA general hospital and agreement from the participate.

Consent for publication

The present study has got the consent from the patient.

Availability of data and materials

All the data and materials involved in the manuscript are available upon request.

Competing interests

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Figures

A **B** **C**

Figure 1

The endoscopic images of amelanotic metastatic gastric malignant melanoma. Hemispherical protuberance of about 0.4 cm gastric metastatic sites without pigmentation that found in the lower curvature of the body and the fundus of the stomach.

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The endoscopic images of amelanotic metastatic gastric malignant melanoma. Hemispherical protuberance of about 0.4 cm gastric metastatic sites without pigmentation that found in the lower curvature of the body and the fundus of the stomach.

Figure 2

Specimen from stomach biopsy. Metastatic melanoma stained with hematoxylin-eosin, original magnification 200 X.

Figure 2

Specimen from stomach biopsy. Metastatic melanoma stained with hematoxylin-eosin, original magnification 200 X.

Figure 3

immunohistochemistry of cancer biomarkers. CK (-), 200X; HMB45 (+), 200X; S-100 (+), 200X; MelanA (+), 200X.

Figure 3

immunohistochemistry of cancer biomarkers. CK (-), 200X; HMB45 (+), 200X; S-100 (+), 200X; MelanA (+), 200X.

A

B

Figure 4

Picture of primary lesion of melanoma in patient's heel. The lesion before (upper image) resection and post resection (lower image).

A

B

Figure 4

Picture of primary lesion of melanoma in patient's heel. The lesion before (upper image) resection and post resection (lower image).

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