Case Report

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Primary melanoma of the rectum: a case report of a rare tumor

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Introduction and importance: Malignant melanoma has a generally poor prognosis and occurs primarily on the skin but may rarely be found in internal organs such as the small intestine, colon, or rectum.
Case presentation: This report presents a case of a 78-year-old male patient with stage IV gastrointestinal melanoma, which is a rare form of melanoma. The patient received first-line pembrolizumab with a complete response.
Clinical discussion: Surgery plays a crucial role in local and regional control for patients with localized stages. Immune checkpoint inhibitor therapy, including nivolumab or pembrolizumab, is a well-studied and proven effective treatment option for patients with advanced skin melanoma. In this case report, the patient with gastrointestinal melanoma also had a very good response to immunotherapy.
Conclusions: Understanding gastrointestinal melanoma is still limited due to the rarity of this clinical entity. Currently, there are no standard treatment guidelines for this rare group of patients. Immune checkpoint inhibitors could be the preferred first-line therapy for patients with distant metastases.

Keywords: case report, pembrolizumab, rectal melanoma

Introduction

Melanoma is a life-threatening malignancy that originates from melanocytes and occurs primarily on the skin but may sometimes occur in sites other than the skin, such as the eyes or, rarely, internal organs (e.g. small intestine, colon, rectum, etc.). The risk factors for gastrointestinal melanoma are still unknown. However, epidemiological data suggest an increased risk associated with HIV/AIDS infection that causes immunodeficiency in humans[1].

Malignant melanoma can metastasize to many organs in the body, including the gastrointestinal tract. In an analysis of 652 patients with metastatic melanoma performed by Gupta and Brasfield[2], the incidence of gastrointestinal metastases was shown to be: liver 68%, jejunoileal 58%, stomach 26%, colon 22%, duodenum 12%, rectum 5%, and anus 1%. Gastrointestinal melanoma is a rare disease entity with only a few case reports published. There is evidence suggesting this group of patients had primary melanoma of the gastrointestinal tract. However, their true origin remains controversial. Surgery is the essential treatment modality for localized disease. However, in the later stages of the disease, immunotherapy plays a key role, extending overall survival (OS) and progression-free survival in clinical trials such as KEYNOTE-001[3]. In this report, we would like to present a case of a 78-year-old male patient who was found to have stage IV primary gastrointestinal melanoma and was successfully treated with first-line immunotherapy. This study has been reported in line with the (Surgical CAse REport) SCARE 2020 criteria[4].

HIGHLIGHTS

- Malignant melanoma of the gastrointestinal tract is a rare form of melanoma.
- Immunohistochemistry is essential to differentiate melanoma from gastrointestinal adenocarcinoma.
- As in metastatic skin melanoma, pembrolizumab can play a key role in stage IV melanoma originating from other sites.

Case presentation

Our case is a 78-year-old male patient with a history of hypertension and diabetes for many years with regular treatment, hepatitis B being on antiretroviral therapy. He was admitted to our hospital with bloody stool for about 3 months and a weight loss of 3 kg per month. At the time of admission, rectal examination revealed a rectal tumor located 2 cm from the anal margin at the 6 o'clock position, which is firm and mildly bloody with poor mobility. A good anal sphincter was recorded. No skin lesions were detected on full-body examination. No

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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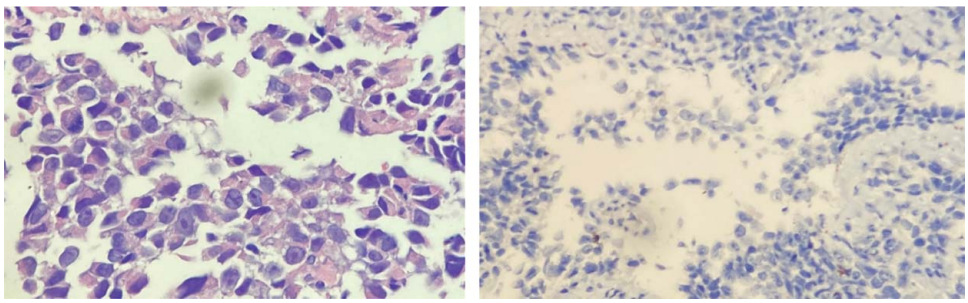

Figure 1. Histopathological features of the tumor.

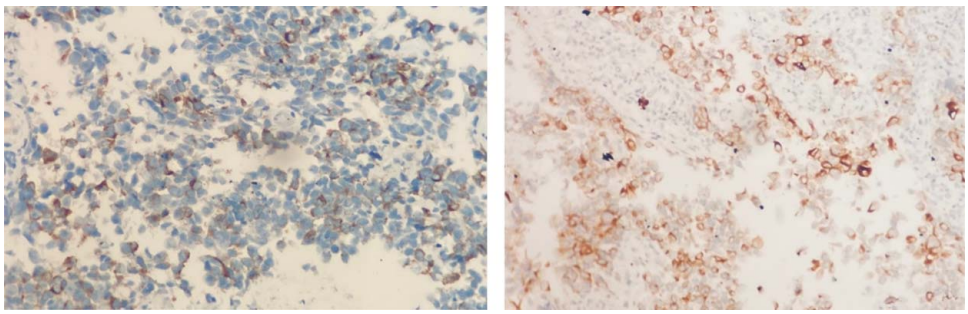

Figure 2. Immunohistochemical imaging with S100 and HMB45.

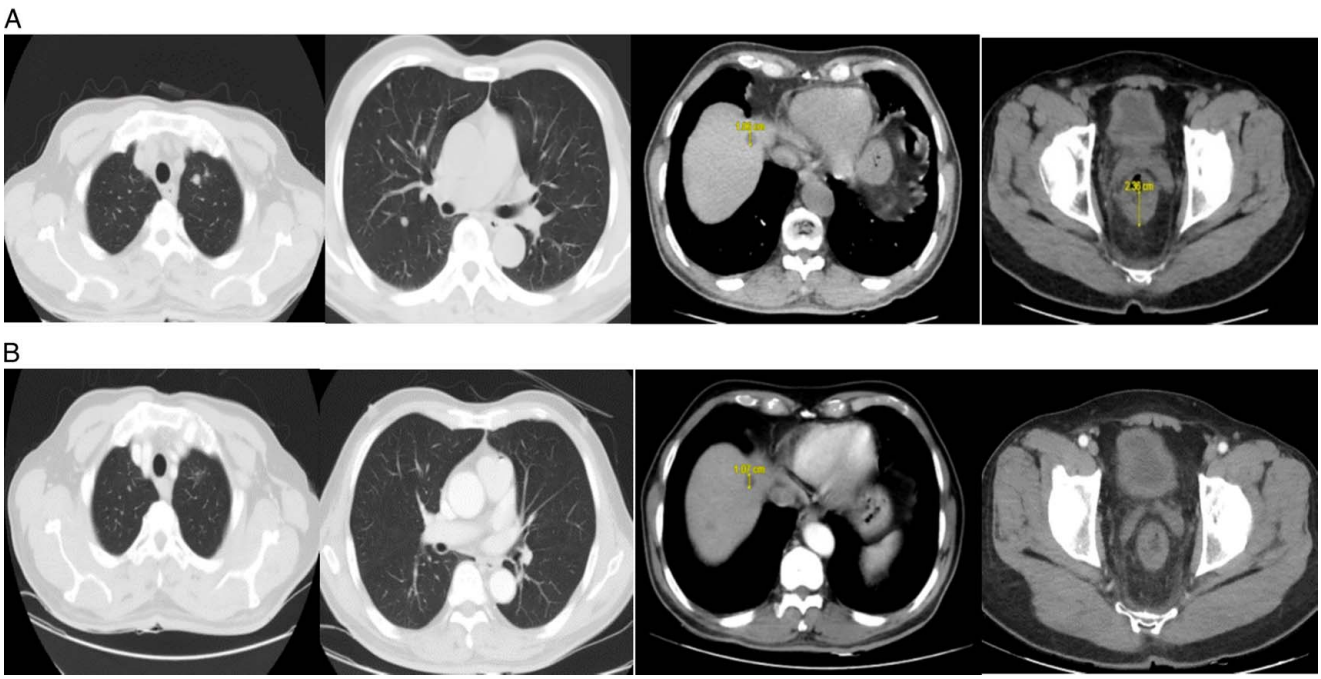

Figure 3. (A) Computed tomography image of the chest–abdomen before treatment. (B) Computed tomography image of the chest–abdomen after four cycles of treatment.

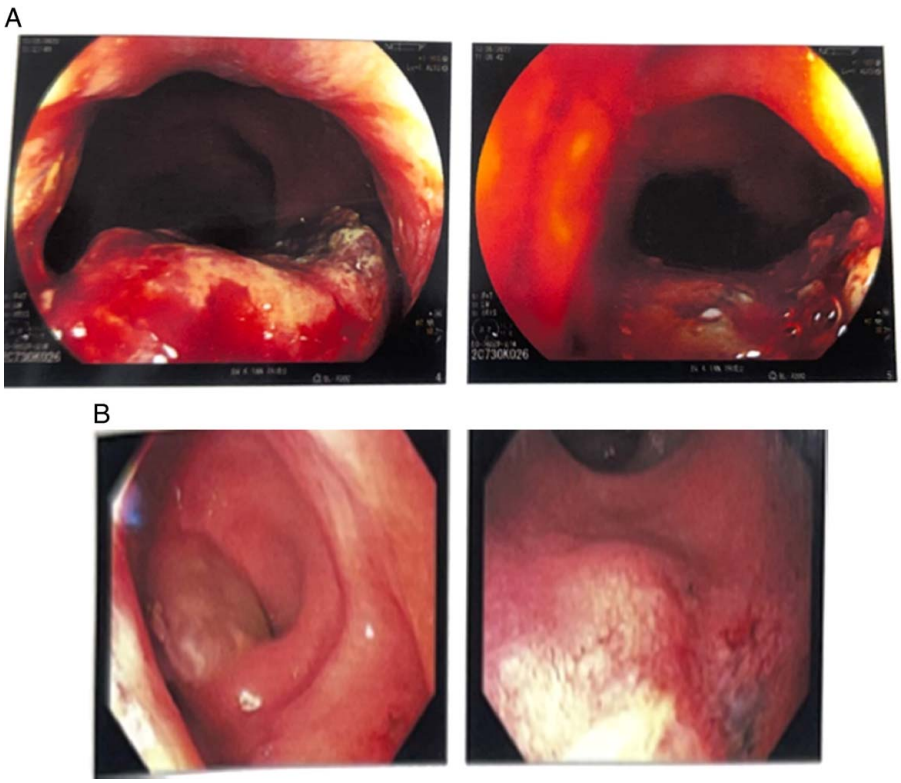

Figure 4. (A) Image of the rectal tumor before treatment. (B) Rectal image after four cycles.

abnormalities were detected in other organs. Pelvic MRI showed a low rectal tumor, 9 mm from the anal margin with the invasion of the mesentery but without sphincter invasion, along with six perirectal lymph nodes 8×12 mm in size. Chest computed tomography (CT) scan showed multiple bilateral solid lung nodules 6 mm in size, indicating lung metastases. Abdominal CT scan showed low rectal wall thickening of 11 mm and several low-density liver nodules 11 mm in size, suggesting liver cysts. A colonoscopy revealed a low rectal tumor close to the anal canal, spreading for 1/3 of the circumference. The patient underwent endoscopic biopsies, of which the result was highly suggestive of carcinoma. Immunohistochemical staining confirmed the diagnosis of melanoma with S100 (+), CDX-2 (–), CD56 (–), CK AE1/AE3 (–), HMB45 (+), melan-A (+), and synaptophysin (–) (Figs 1, 2).

While waiting for test results, the patient received 30 Gy palliative radiotherapy, and his symptoms initially improved. Afterward, the multidisciplinary tumor board decided to give the patient first-line immunotherapy with pembrolizumab 2 mg/kg every 3 weeks.

After the first two cycles, the patient tolerated the drug well and had no side effects. He was free of constipation and no longer had supportive drugs such as laxatives or probiotics. After completing four cycles, the patient was re-evaluated with a partial response, in which the rectal tumor had a complete response on clinical examination. CT of the chest only shows ground glass lesions in the apex and at the base of the lungs, with no more nodular lesions. Abdominal CT only shows mild rectal thickening, probably due to inflammation (Fig. 3). Colonoscopy showed smooth mucosa and a lower rectal soft fibrous scar lesion (Fig. 4).

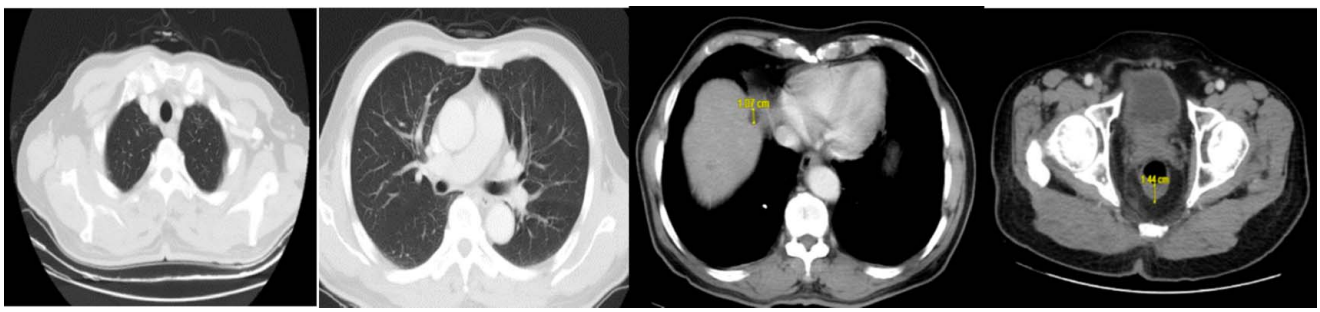

Figure 5. Computed tomography image of the thorax–abdomen after eight cycles.

Table 1

The previous reports of primary anorectal melanoma

Author	The number of patients	Treatment	Overall survival
Belbaraka *et al.* (2012)[11]	17	- 7 patients: surgery - 8 patients: palliative chemotherapy	8 months
Miguel *et al.* (2014)[12]	10	- 7 patients: surgery - 1 patient: palliative chemotherapy - 2 patients: best supportive care	- 1-year OS: 30% - 2-year OS: 20%
Adileh *et al.* (2022)[13]	47	- 29 patients: ICI - 18 patients: NI	Median OS: 52 months in those with ICI and 20 months in those with NI
Ogata *et al.* (2023)[14]	47	ICI	2-year OS: 61.4%

ICI, immune checkpoint inhibitor therapy; NI, non-immunotherapy; OS, overall survival.

After eight cycles with pembrolizumab, no side effects were recorded during the treatment. Chest CT showed no lung metastases, and the abdominal CT rectal wall was only mildly thickened (Fig. 5).

Discussion

Gastrointestinal melanoma is a rare tumor that accounts for about 1.3% of melanoma in the United States[5]. Overall, the incidence of skin cancer is increasing in the United States, but the incidence of gastrointestinal melanoma has remained stable[6]. Gastrointestinal melanoma can arise in any part of the gastrointestinal tract, such as the oral cavity, esophagus, small intestine, colon, rectum, and anus. In patients with no cutaneous lesions, confirmation of gastrointestinal melanoma is based on immunohistochemical markers such as HMB45 and S100 containing melanocytes[7]. Distinguishing between primary gastrointestinal or metastatic melanoma is still tricky since it is still mainly based on clinical evidence that no primary skin lesions were detected or in cases with isolated lesions in the gastrointestinal tract without any other metastatic lesions. The diagnosis of melanoma is primarily dependent on the pathologist.

Anorectal melanoma accounts for ~0.05% of all colorectal malignancies and 1% of all anal canal cancers[1]. Although the risk factors for anorectal mucosal malignancies are unknown, epidemiological data suggest an increased risk associated with HIV/AIDS infection with impaired immunity in humans[1].

Most cases arise from the skin-mucous junction; however, they can also occur from the perianal skin, the transitional epithelium of the anal canal, or the lining of the rectum. Patients often present with tumor bleeding, anorectal pain, or change in bowel habits. Occasionally, malignancy is an incidental finding during the pathological evaluation of hemorrhoid or anal polyp specimens. Anorectal malignancies are pigmented only in one-third of cases[5]. The disease is typical at a mean age of 70 years, more women than men[1].

Once the diagnosis is confirmed, staging for patients with rectal melanoma is similar to other rectal malignancies, including CT scans of the chest and abdomen to evaluate for metastases. Surgery plays a crucial role in local and regional control for patients with localized stages, prolonging the OS of the patient. In a series of 251 cases from the Swedish National Cancer Registry, the 5-year survival rate after radical surgery for those with an R0 resection was 19%, compared with 6% in those who did not have radical surgery[8]. In patients with distant metastases, in the past, cytotoxic chemotherapy such as paclitaxel – carboplatin, dacarbazine, and temozolomide, etc. was widely used, although this method has never been proven to improve survival. Response rates are typically less than 20%, and the median disease control time is 4–6 months. Therefore, the role of chemotherapy should only be considered in patients who have progressed after optimal treatment with other systemic therapy options.

Immune checkpoint inhibitor therapy, including nivolumab or pembrolizumab, is well-studied and has been proven to be an effective treatment option for patients with advanced skin melanoma. Still, limited data are available on those with gastrointestinal melanoma. Clinical trials, including KEYNOTE-001 and KEYNOTE-252, showed that pembrolizumab prolonged OS up to 38.6 months and progression-free survival (PFS) reached 16.9 months[9,10]. Melanomas of gastrointestinal origin generally have a worse prognosis than those from cutaneous sites. The previous reports of primary anorectal melanoma have been summarized in Table 1. It can be seen that immunotherapy improves survival outcomes; 2-year overall survival can reach 61.4% compared to 20% of chemotherapy. In our case, the patient with primary rectal melanoma was treated with pembrolizumab and had a complete response, which contributes to strengthening the evidence for the effectiveness of immunotherapy in the treatment of this disease entity.

Conclusion

Understanding gastrointestinal melanoma is still limited due to the rarity of this clinical entity. Surgery remains the priority for localized tumors. Immune checkpoint inhibitor therapy is an essential systemic treatment modality for metastatic melanoma. Currently, there are no recommendations or standard treatment guidelines for this rare group of patients. Immune checkpoint inhibitors could be the preferred first-line therapy for patients with late-stage, distant metastases.

Ethical approval

This study was approved by the ethics committee of the Vietnam National Cancer Hospital.

Consent

The patient has given written consent to publish their case (including the publication of photographs).

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Author contribution

T.T.: lead physician, responsible for manuscript reporting; P.T.P.: patient follow-up, manuscript writing, and editing the final version; H.T.N. and C.T.H.: editing the manuscript.

Conflicts of interest statement

The authors declare that they have no conflicts of interest.

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Guarantor

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Data availability statement

Datasets generated during and/or analyzed during the current study are publicly available upon reasonable request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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