

The Potential of Hypofractionated Radiotherapy: A Revolutionary Treatment for Anorectal Malignant Melanomas

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Abstract

Mucosal melanomas generally arise from mucosal epithelium lining the respiratory, alimentary, and genitourinary tracts and usually carry worse prognosis than cutaneous melanomas. Anorectal melanomas account for 50% of gastrointestinal tract melanomas and 0.3 to 1% of all malignant melanomas. There are no specific treatment guidelines due to the scarcity of the disease, its unique biology, and challenges in management owing to the anatomic location. We report a case of anorectal malignant melanoma treated successfully with abdominoperineal resection followed by hypofractionated radiotherapy in a setting where financial toxicity limits treatment options. The patient presents complete response 2 years postdiagnosis, emphasizing that radiation therapy can be utilized for more than just palliation.

Keywords

- ▶ malignant melanoma
- ▶ hypofractionated radiotherapy
- ▶ anorectal melanoma

Introduction

Mucosal melanomas generally arise from mucosal epithelium lining the respiratory, alimentary and genitourinary tracts and usually carry worse prognosis than cutaneous melanomas. In the US, mucosal melanomas make up just 1.3% of all melanomas.¹ Anorectal melanomas account for 50% of gastrointestinal tract melanomas and 0.3 to 1% of all malignant melanomas.^{2,3} With a mean presentation age of 52.8 years, it occurs more commonly in females than in males.^{4,5} There are no specific treatment guidelines due to the scarcity of the disease, its unique biology, and challenges in management owing to the anatomic location.

Case Presentation

A 50-year-old woman from Chamba, Himachal Pradesh, a farmer by occupation, presented to the hospital complaining of rectal bleeding for two months, sometimes associated with mildly-painful defecation. She had undergone abdomino-perineal resection with colostomy on March 20, 2023. The postoperative histopathological report was suggestive of a 4 × 2 × 1-cm growth, 1 cm from the anal canal. There was another growth 5 cm from the anal canal measuring 2 × 2 × 1 cm. Microscopy was suggestive of malignant melanoma with transmural infiltration reaching up to the serosa (▶ **Fig. 1**). Resection margins were free of tumor, and no

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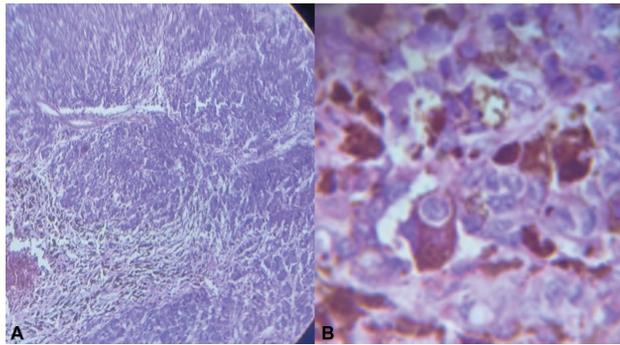


Fig. 1 Histopathological picture: (A) sheets and nests of tumor cells; (B) malignant melanoma cells with pigment.

lymph nodes were identified. Postoperative contrast-enhanced computed tomography (CECT) of the abdomen and pelvis was done, and it was suggestive of focally-enhanced presacral soft tissue density measuring 45×40 mm, along with thickening in the mesorectal fascia, extending up to the bilateral sacral ala (**Fig. 2**). Re-surgery was denied; patient underwent positron-emission tomography CT (PET-CT) to decide further course of adjuvant therapy. The PET-CT was suggestive of a hypodense area with peripheral rim of ^{18}F -fluorodeoxyglucose (FDG) uptake in the presacral region, with the maximum standardized uptake value (SUV-max) of 9.70. Intense area of increased FDG uptake was seen in continuity of this lesion in the region of the anal canal/postsurgical site, with an SUVmax of 10.70 (**Fig. 3**). In view of non-affordability to immunotherapy, the patient was started on adjuvant chemotherapy on October 23, 2023, with cisplatin 20 mg/m^2 D1-D4; vinblastine 1.6 mg/m^2 D1-D5, and dacarbazine 800 mg/m^2 D1 every 3 weeks. The patient did not tolerate chemotherapy well, and after 3 cycles of chemotherapy she was referred for local radiotherapy in view of the disease not being metastatic. A dose of 45 Gy in 15 fractions by 6 MV photons by intensity-modulated radiation therapy (IMRT) was delivered was 18-12-23 to 20-1-24. Three months following hypofractionated radiotherapy (HFRT), the melanoma had completely regressed, and there

was no evidence of residual cutaneous pigmentation or anal canal extension. At 12 months after presentation, in view of the patient's financial situation, PET-CT could not be afforded, so the follow-up was done with CECT of the chest, abdomen, and pelvis, which was not suggestive of any abnormal thickening or enhancement. At 24 months after the diagnosis, a PET-CT was performed, which was with no evidence of any clinically-significant hypermetabolism anywhere in the body (**Fig. 4**). The patient is currently free of long-term radiation side effects, and there is no clinical indication of recurrence. The patient has no complaints at present and is doing well with her routine activities.

Discussion

Anorectal melanoma is an uncommon, aggressive cancer with vague signs. Its incidence is reported to be higher in females than in males and it increases with age. It usually has poor prognosis, and there is still uncertainty regarding its treatment. Surgery, radiotherapy, chemo-immunotherapy, and targeted therapy provide inconsistent results.

The cornerstone of treatment is still surgical resection; however, the best surgical approach for primary tumors is debatable and can range from an abdominoperineal resection (APR) to extensive local excision or endoscopic mucosal resection (EMR). Sometimes EMR can eliminate melanoma while maintaining long-term survival.⁶ Wide local excision (WLE) preserves the anal sphincter and has very little morbidity or damage to local function.⁷ Abdominoperineal resection is frequently linked to high risk of morbidity and functional impairment. There are no appreciable changes in patient survival between APR and WLE, according to the limited number of studies.

There is not much research on the benefits of radiation therapy in anorectal malignant melanoma, either with or without surgery, and radiation is not the norm currently. Studies have shown benefit in local recurrence rate with the addition of radiotherapy after WLE without any overall survival benefit.⁸ Because anorectal melanomas are thought to be

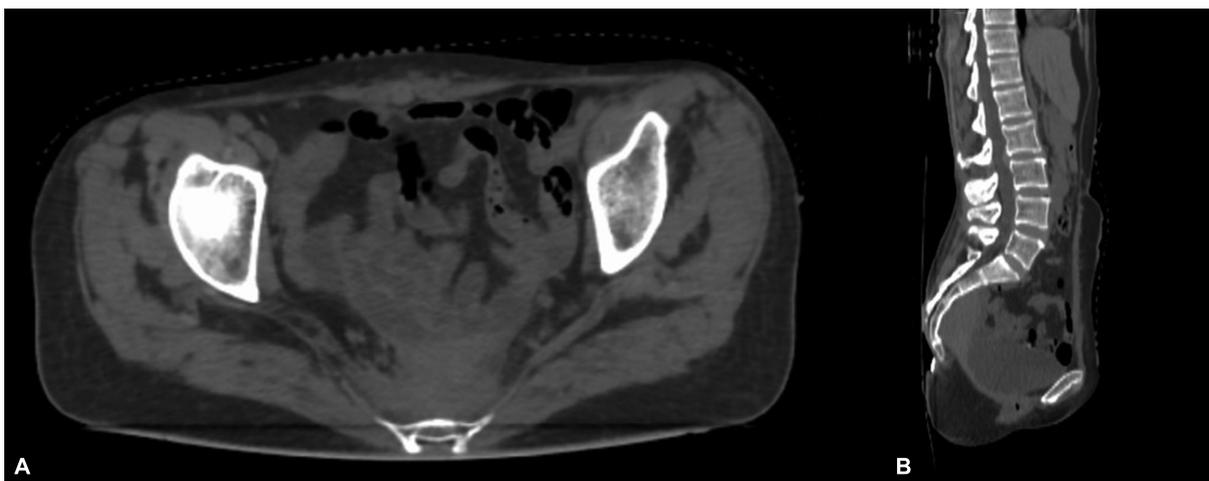


Fig. 2 Contrast-enhanced computed tomography (CECT) scan of the abdomen and pelvis showing enhanced presacral soft tissue: (A) axial view; (B) sagittal view.



Fig. 3 Postoperative positron-emission tomography–computed tomography (PET-CT) scan suggestive of hypodense area with peripheral rim of 18F-fluorodeoxyglucose (FDG) uptake in the presacral region: (A) axial view; (B) sagittal view.

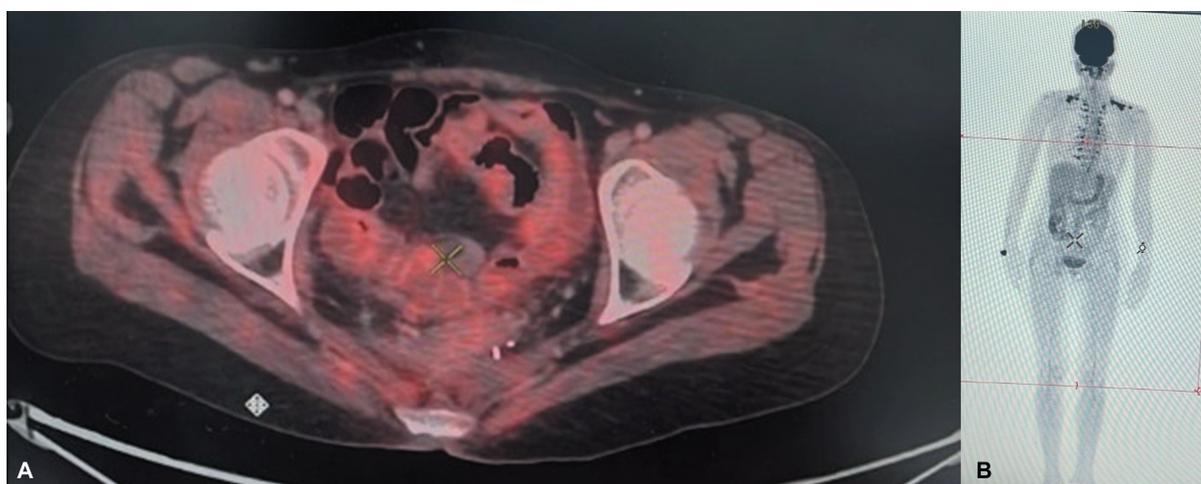


Fig. 4 Positron-emission tomography–computed tomography scan: No evidence of any clinically significant hypermetabolism anywhere in the body: (A) axial view; (B) maximum intensity projection image.

radioresistant, radiotherapy is rarely suggested for them, even for palliation.^{9,10} A high degree of uncertainty exists regarding the benefit of radiation therapy or chemotherapy. As our understanding of the biology and immunology of advanced melanoma advances, the therapy used to treat this illness is changing quickly. According to the findings of palliative irradiation for cutaneous melanoma, around half of the patients can achieve complete remission, whereas 72% of patients with head and neck mucosal melanomas treated with radiotherapy alone have achieved complete remission.^{11–14} There have been reports of people with head and neck cutaneous melanomas benefiting from radiation treatment as an adjunct to surgery. Seen the results of radiotherapy in other sites, it is also being used in the adjuvant setting in anorectal melanomas.

Radiotherapy in the dose of 45 (range: 36–52.5) Gy with a median of 15 fractions (range: 12–17) demonstrated that HFRT is a safe and efficient local therapeutic option that offers melanoma patients sustained local control with minimal toxicity.¹⁵ Whenever feasible, immunotherapy should be pursued as an alternative treatment modality; however, in situations

like ours, when non-resectability and financial toxicity tilt the tide, radiation plays an intrinsically advantageous function. Without suffering any severe side effects, the patient reacted quite well to radiation therapy, which might provide an additional option for managing this difficult condition. Specifically, radiation treatment can be utilized for more than only palliation; it can also be used for local disease control.

Authors' Contributions

VT: data collection, data curation, data analysis and interpretation, writing – original draft, accountability for all aspects of the work; PP: provision of study material and patient care; HS: writing – original draft, critical review and editing of the manuscript; AT: writing – review & editing; AJ: conception and design; PV: final approval of the manuscript.

Informed Consent

Informed consent was obtained from all patients included in the study.

Conflict of Interests

The authors have no conflict of interests to declare.

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