Anorectal Melanoma - Brownish Black Mass Not Always a Hemorrhoid

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Research Article

Keywords: Anus, Rectum, Melanoma, Haemorrhoid

Posted Date: July 1st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-651855/v1

Version of Record: A version of this preprint was published at Journal of Gastrointestinal Cancer on August 4th, 2021. See the published version at https://doi.org/10.1007/s12029-021-00678-y.

Abstract

The non-specific clinical symptoms of anorectal brownish-black mass do not help to differentiate colorectal cancer, hemorrhoids, rectal ulcers which result in a delayed diagnosis or lead to inadequate management of lethal anorectal melanoma. Primary malignant melanoma of the anorectal region is an uncommon tumor, constituting approximately 1% of anal canal tumors which may be misdiagnosed clinically as hemorrhoids. Because of aggressive behavior and poor prognosis, efficient and prompt diagnosis is required in these cases. We report the 2 cases of this rare tumor.

Introduction

Primary malignant melanoma of the anorectal region is an uncommon tumor, constitute about approximately 1% of anal canal tumors and 0.4–1.6% of all melanomas.[1, 2] Mucosal malignant melanomas are more common in dark-skinned inhabitant than white.[2] After the head & neck and vulvovaginal regions, the anorectal area is the most common site for primary mucosal malignant melanoma.[1] The median age at the time of diagnosis is 65 years with an age range from 3rd to 9th decade of life.[2, 3] The common clinical symptoms of anorectal malignant melanoma (ARMM) are rectal bleeding, palpable anal mass, anal pain, anal pruritus, tenesmus, and change in bowel habits.[1–3] The other symptoms which may be associated with a metastatic ARMM include anemia, generalized fatigue, pelvic and groin masses, weight loss, and bowel obstruction.[1–3] Because of its dark color, location as well as its clinical presentation, the diagnosis of ARMM is often delayed and initially misdiagnosed as hemorrhoids.[1, 3] The delayed diagnosis may contribute to the poor prognosis of ARMM and tumor invasion with or without the absence of metastasis at the time of diagnosis may correlate with patient survival.[1, 2, 4] We report the 2 cases of rare ARMM initially clinically misdiagnosed as a haemorrhoid.

Case Reports

Case 1

A 30-year-old male presented with abdominal and rectal pain, accompanied by bleeding per rectum for the last 6 months. On a digital rectal examination, a brownish-black, firm, friable rectal mass was discovered.

Case 2

A 65-year-old female presented with bleeding per rectum for the last 6 months accompanied by weight loss for the last 3 months. On a digital rectal examination, a brownish-black, firm mass was discovered.

In both cases, the initial clinical diagnosis of hemorrhoids was considered. However, on biopsy, the diagnosis of melanoma was rendered in both cases. The routine blood and serum investigations were within normal limits. Based on the size and extent of the lesion radiologically, wide local excision was not

possible and therefore, abdominoperineal resection (APR) was done in both the cases and specimens were sent for histopathological examination. Grossly, both the specimens show a solid, blackish, soft to firm mass measuring 9x7x…cm and 8x6.5x5 cm noted at the distal end of the rectum. (Fig. 1). Sections from the growth of both the cases show tumor cells arranged in diffuse sheets, nests, and cords, were round, polygonal, epithelioid to spindle shaped, large cells showing nuclear pleomorphism, prominent eosinophilic nucleoli, and abundant cytoplasm. Binucleation & multinucleation were also identified. At places, cells with clear cytoplasm and cell with small round cell morphology were also noted. Intracellular and extracellular melanin pigment present (Fig. 2). The tumor cells are immunopositive for S-100, and human melanoma black (HMB-45). Both the cases were immunopositive for CD117 and case 2 was immunopositive for BRAF (Fig. 3). The final diagnosis of ARMM was given. Postoperatively, patients had an uneventful recovery. The patient was orally allowed on post-operation day (POD) 4 and discharged on POD 8. The follow-up of case 1 for 2 months and case 2 for 15 days was uneventful. The written and informed consent was obtained from the patients for the presentation and publication.

Discussion

ARMM is an aggressive tumor with poor prognosis having a mean survival of only 2 years and overall 5-year survival rates around 20–30%.[2, 5] ARMM constitute approximately 25% of all mucosal melanoma.[6] The clinical symptoms closely mimic for colorectal cancer, hemorrhoids, rectal ulcer, and other primary lesions, hence, results in delay or inadequate management.[1, 3] In the last few years, the incidence of ARMM is raised in young adults, which is attributed either due to the refinement in the diagnostic facility.[4] Previously, ARMM is considered to be metastatic disease, however recent studies confirmed that primary malignant melanoma can arise from melanocytes residing in the gastrointestinal epithelium of the proximal anus or distal rectum or the melanocytes located in the basal layer of non-keratinized stratified squamous epithelium below the pectinate line.[4–8] Rectal malignant melanoma arises either primarily from melanocytes located in the laterobasilar part of the colorectal mucosa or due to proximal extension of anal melanoma arising near the anorectal junction.[5, 8] The pathogenesis of mucosal melanoma development is still not clear and also there is no relationship between ultraviolet radiation and mucosal melanoma.[2, 3] Few authors observe higher c-kit mutations in mucosal melanomas than in cutaneous melanomas and suggest that c-kit mutations may play a role in the pathogenesis of ARMM.[9] However, CD117 overexpression does not have an association between protein overexpression and mutation status.[9] The other somatic mutation which may involve in the development of ARMM is SF3B1, ATRX, TP53, ARID2, SETD2, NRAS, and BRAF.[1, 2, 4, 5] The role of HIV and smoking habit has also been proposed as mechanisms for the development of mucosal melanoma.[4] The present both cases were in the 4th & 7th decade of life, seronegative for HIV infection presented with bleeding per rectum and tumor was located in the anorectal region. The rectal examination delineates the size, ulceration, color especially if the lesion is pigmented and adherence to surrounding structures.[8] The radiological interventions such as endorectal ultrasonography, CT, and MRI may also help to determine the tumor size and presence of regional lymph node metastases.[8] Grossly, the tumor is usually present as a large,

expensive nodular mass with variable involvement of anal squamous epithelium and rectal mucosa.[2] The presence of melanin pigment may help in the diagnosis histologically and both pigmented & amelanotic melanoma are reported in the literature.[4,6–8]. Variable histomorphology like epithelioid, spindle-cell, pleomorphic, and small round cells either alone or in combination are reported. [5, 6, 8] The present cases show epithelioid, spindle-shaped, and small round cell morphology along with abundant intracellular and extracellular blackish-brown pigment which get bleached by hydrogen peroxide. The various mimickers of ARMM can be epithelioid sarcoma, spindle cell sarcoma, gastrointestinal stromal tumor, lymphoma, small round cell sarcoma, and undifferentiated adenocarcinoma.[4–6, 8] Hence, routine haematoxylin & eosin (H&E) stain may not be determiner enough to reaffirm the diagnosis of ARMM.[6] Immunohistochemistry (IHC) is obligatory and IHC markers such as S-100, HMB-45, Melan A, and SOX-10 are used to confirm the diagnosis of melanoma.[3–8] S-100 is a sensitive marker but have low specificity while Melan-A and HMB-45 are the most sensitive and specific marker for melanocytic lesions.[5, 8] The SOX-10, a recent marker, has demonstrated as a highly sensitive and specific, helps in detecting for both benign and malignant melanocytic lesions.[10, 11] It has strong nuclear staining helps to avoid the nonspecific cytoplasmic staining and melanin pigment interference as seen in melan-A and HMB-45 immunohistochemical stains.[10, 11] Charifa et al stated that SOX-10 can be used as the first-line screening IHC marker instead of S100 protein for the suspicion of ARM.[5] These markers also help to differentiate from its mimickers.[5] Our cases were immunopositive for S-100 and HMB 45. Both cases show overexpression of CD117 and case 2 showed expression of BRAF. Surgery such as APR and the wide local excision (WLE) are the two standard primary treatment modality of ARM.[1,3–8] APR can achieve better local control, negative margins and decrease the chance of local recurrence but due to removal of a large area with anal sphincter APR will affect the quality of patients' life due to permanent colostomy and also associated with higher morbidity and mortality.[7, 8] To improve the quality of life, some surgeons prefer WLE which requires a cutting edge ≥ 10 mm.[7, 8] However, the difference in the prognosis of these two surgical procedures is not observed.[7, 8, 12] The lymph node dissection is often recommended in nodal involvement cases but no difference in prognosis between the patients with and without a complete lymph node dissection is observed.[8] Adjuvant therapy for ARMM includes chemotherapy, immunotherapy, and radiation therapy.[1, 3, 4, 8, 9] There is no accepted standard adjuvant chemotherapy regimen for ARMM.[8, 9] Some authors stated that acceptable results can be achieved with therapeutic APR and adjuvant chemotherapy but the use of only chemotherapy without surgery has no satisfaction in the management.[8, 12, 13] The adjuvant radiotherapy after the surgical procedure is another tool that can be used in the treatment of ARMM.[8] Kelly et al observed that the use of hypofractionated radiotherapy after surgical excision helps to attain local control in 82% patients along with a decrease in local recurrence from 50–17% compared to WLE alone.[1, 8, 14] Few studies advocate the immunotherapy for the treatment of ARMM.[1, 8, 9] Postow et al use anti-CTL4–based immunotherapy and observed immune-related complete response, immune-related partial response, immune-related stable disease, and immune-related progressive disease in 1,1,5 and 23 patients respectively.[1, 15] Some authors also demonstrate the role of anti-Programmed cell death-1 (PD-1) therapy in mucosal melanoma.[1, 16] In

contrast to the cutaneous melanoma staging, the 8th edition of The American Joint Committee on Cancer staging system doesn't incorporate the for Mucosal melanoma of the urethra, vagina, rectum, and anus.[17] Falch et al proposed the staging system ARMM in 4 stages.[18] Stage I - Local tumor spread without infiltration of the muscular layer; Stage II - Local tumor spread with infiltration of the muscular layer; Stage III - Regional tumor spread and/or positive lymph-node metastasis and stage IV - Disseminated tumor spread.[18] Sarac et al observed that genital mucosal melanomas had the most favorable and ARMM had the worst outcome.[19] The age and stage at first the medical examination may act as independent prognostic factors while gender and mutational status did not affect survival in mucosal melanoma.[19] Both the present cases were in stage III.

Conclusion

On account of its likely for misdiagnosis with non-neoplastic hemorrhoids as observed in both the indexed cases, the efficient, prompt, and effectual diagnosis is necessitating in these aggressive tumors for better management.

Declarations

Funding / Financial Support: Nil

Conflict of Interest: The authors declare no potential conflict of interest.

Availability of data and material: Data available in the institute.

Authors' contributions: - Drafting of manuscript: Jitendra Singh Nigam, Avinash Singh, Nishit, Prerna Tewari. **Literature search:** Tarun Kumar, Jitendra Singh Nigam, Avinash Singh, Nishit, Prerna Tewari. **Case acquisition:** Jitendra Singh Nigam, Nishit, Avinash Singh, Tarun Kumar, Jagjit Kumar Pandey. **Case analysis & interpretation:** Avinash Singh, Prerna Tewari, Jitendra Singh Nigam, Nishit. **Manuscript preparation:** Jitendra Singh Nigam, Avinash Singh, Nishit, Prerna Tewari. **Manuscript editing:** Tarun Kumar, Jitendra Singh Nigam, Jagjit Kumar Pandey. **Manuscript review and approval:** Tarun Kumar, Jitendra Singh Nigam, Jagjit Kumar Pandey, Avinash Singh, Nishit, Prerna Tewari

Consent for publication: The written and informed consent was obtained from the patients.

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Figures

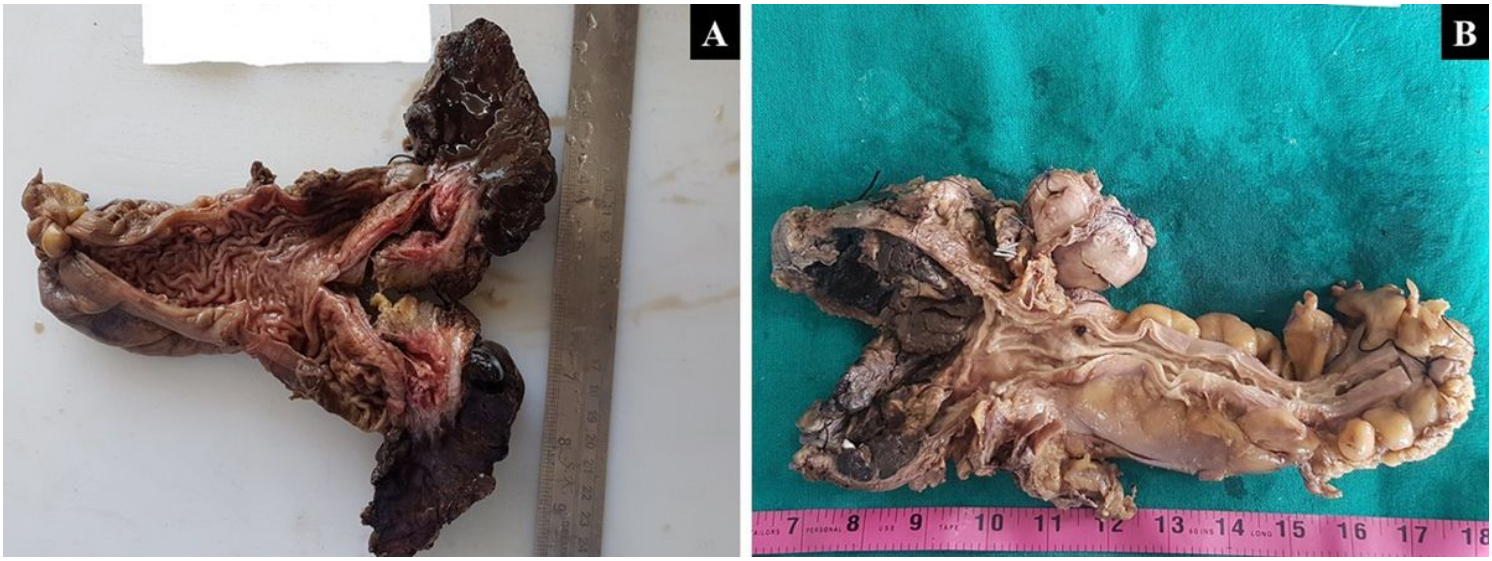

Figure 1

A. & B. Gross: Blackish brown growth in the anorectal region

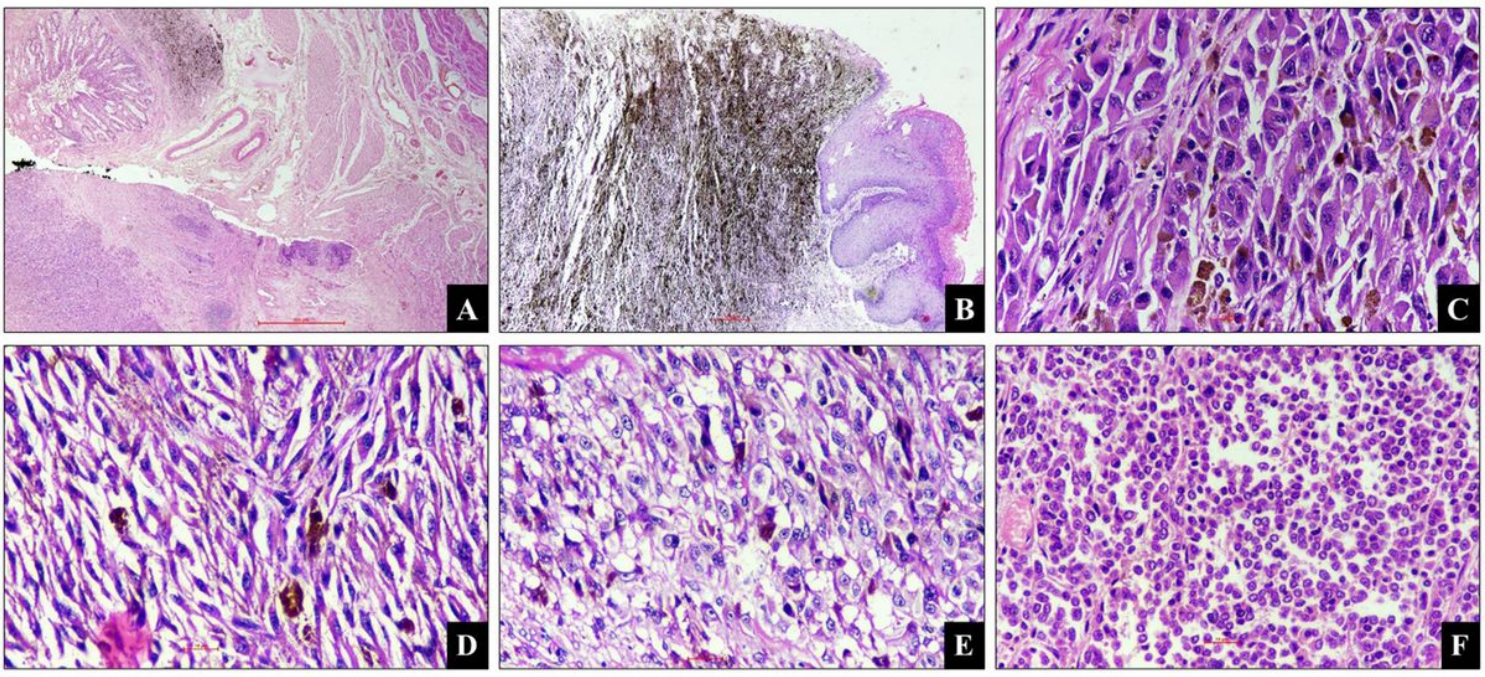

Figure 2

A. Rectal mucosa and tumor with focal intracellular and extracellular brownish-black pigment. (H&E x20) B. Anal mucosa and tumor with intracellular and extracellular brownish-black pigment. (H&E x40) C. to F.: Tumor arranged in diffuse sheet and intersecting fascicles. Tumor cells display epithelioid (Fig C), spindle-shaped (Fig D), clear cells (Fig E), and round cell (Fig F) morphology. (H&E x400)

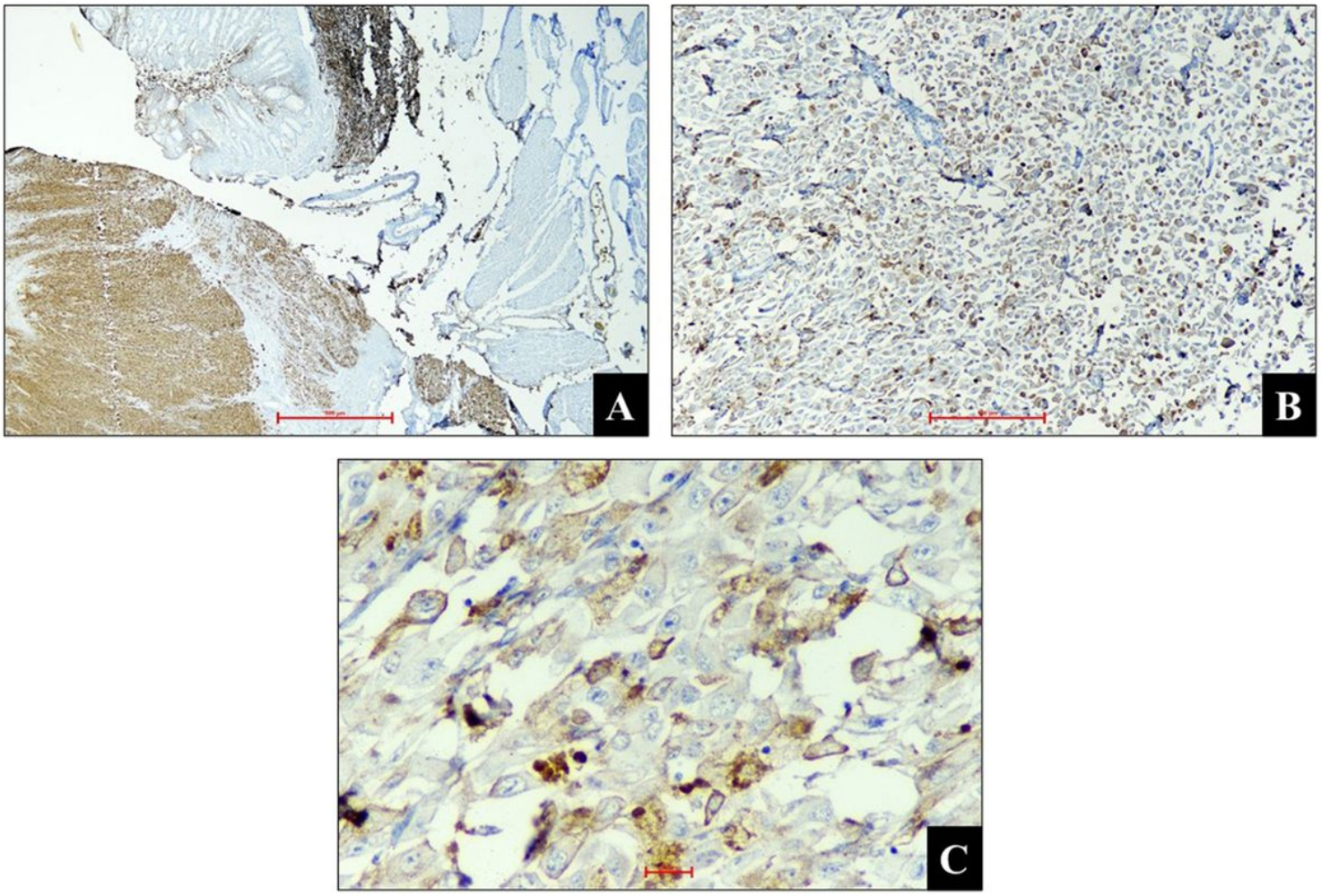

Figure 3

A. HMB-45: Strong and diffuse cytoplasmic Positivity in tumor cells. (x20) B. CD117: Weak and focal membranous positivity in tumor cells. (x100) C. BRAF: Weak and focal cytoplasmic positivity in tumor cells. (x400)