Anorectal Melanoma—Brownish Black Mass Not Always a Hemorrhoid

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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 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 and 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, and 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 2 cases of ARMM initially clinically misdiagnosed as a hemorrhoid.

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 the 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 showed a solid, blackish, soft to firm mass measuring 9 × 7 × 4.5 cm and 8 × 6.5 × 5 cm noted at the distal end of the rectum (Fig. 1). Sections from the growths...
showed tumor cells arranged in diffuse sheets, nests, and cords. The cells were round, polygonal, epithelioid to spindle-shaped, large cells showing nuclear pleomorphism, prominent eosinophilic nucleoli, and abundant cytoplasm. Binucleation and multinucleation were also identified. At places, cells with clear cytoplasm and cell with small round cell morphology were also noted. Intracellular and extracellular melanin pigments were present (Fig. 2). The tumor cells were 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, both the patients had an uneventful recovery. The patients were 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 to 30% [2, 5]. ARMM constitutes 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 has increased in young adults, which is attributed to the refinement in the diagnostic facility [4]. Previously, ARMM is considered to

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Fig. 1 A and B—Gross: blackish brown growth in the anorectal region

Fig. 2 A—Rectal mucosa and tumor with focal intracellular and extracellular brownish-black pigment (H&E × 20). B—Anal mucosa and tumor with intracellular and extracellular brownish-black pigment (H&E × 40). 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 × 400)
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 mutations which may be involved in the development of ARMM are 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]. Both the present cases were in the 4th and 7th decade of life, seronegative for HIV infection with bleeding per rectum and tumor were located in the anorectal region. The rectal examination delineates the size, ulceration, color especially if the lesion is pigmented and adherent 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, expansive 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 and 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 showed epithelioid, spindle-shaped, and small round cell morphology along with abundant intracellular and extracellular blackish-brown pigment which got 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 hematoxylin and eosin (H&E) stain may not be 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 and helps to avoid the nonspecific cytoplasmic staining and melanin pigment interference as seen in melan-A and HMB-45 immunohistochemical stains [10, 11].
edge life, some surgeons prefer WLE which requires a cutting morbidity and mortality [7, 8]. To improve the quality of 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 to 17% compared to WLE alone [1, 8, 14]. Few studies advocate the immunotherapy for the treatment of ARMM [1, 8, 9]. Postow et al. used anti-CTLA4-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 demonstrated 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 does not incorporate the staging 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

ARRM may be misdiagnosed with non-neoplastic hemorrhoids as observed in both the indexed cases. Therefore, knowledge of this rare neoplasm and a prompt diagnosis are crucial for better management of this aggressive tumor.

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Data Availability Data are available in the institute.

Declarations

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

Conflict of Interest The authors declare no conflict of interest.

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