

Primary Anorectal Melanoma

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Key Words

Primary anorectal melanoma · Abdominoperineal resection · Chemotherapy

Abstract

Primary malignant melanoma of the anus and rectum is a rare and aggressive neoplasm that tends to invade locally and metastasize early in the course of the disease. It is often misdiagnosed as hemorrhoids or as one of the other benign anorectal conditions and is thus linked to an overall poor prognosis and a 5-year survival rate of less than 20%. Optimal treatment is still controversial, and current evidence does not show any preferential survival benefit from abdominoperineal resection over wide local excision. Chemotherapy or radiotherapy may be used for advanced disease. We report a 71-year-old female presenting with painful bowel movements and blood in stools. She was eventually found to have a mass arising from the anorectal junction with regional lymph node involvement. The patient underwent an abdominoperineal resection and is currently scheduled for chemotherapy.

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Introduction

Anorectal melanomas comprise approximately 1% of all melanomas and about 0.5–2% of all anorectal malignancies [1]. Common presentations for anorectal melanoma include rectal bleeding, anorectal pain, change in bowel habits or a rectal mass [1]. Therefore, given the lack of pathognomonic clinical complaints, early diagnosis is difficult to make [1]. This represents a significant clinical challenge since early diagnosis and treatment are crucial.

Conventionally, therapy for anorectal melanoma consists of a complete surgical resection of the tumor for local control of the disease. This can be done by means of sphincter-sparing wide local excision (WLE) or abdominoperineal resection (APR) in cases of large tumors or when WLE is not feasible [1]. Radiotherapy may be used to enhance regional control but has no impact on overall survival [2]. The majority of patients progress to

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metastatic disease, and the use of chemotherapy has been advocated in such cases to improve the overall survival [3].

Case Presentation

In April 2013, a 71-year-old female with no significant past medical history presented to our institution with painful bowel movements for the last 3 months. The patient also noticed blood-streaked stools and reported a 16-lb unintentional weight loss over a 1-year period. The review of her systems was negative otherwise. On examination: the woman was 5' 7.5" (1.715 m) tall, weight was 172 lb (78.019 kg), with a BMI of 26.54, and her vital signs were normal. Digital examination of the rectum revealed two small hemorrhoids at the 6 o'clock position and a firm, nonobstructing mass near the anal verge. The patient underwent a colonoscopy in September 2013 which revealed a nonobstructing, ulcerated anal mass, approximately 1 cm from the anal verge. A biopsy of the mass demonstrated an invasive, poorly differentiated carcinoma (fig. 1). Stains for CK5/6 and P63 were positive, likely suggesting a primary squamous cell carcinoma of the anus. Tumor markers including CEA, CA 15–3 and CA 27–29 were negative. A CT of the abdomen and pelvis demonstrated an abnormal mass at the anorectal junction, with no evidence of lymph nodes or liver metastases in September 2013 (fig. 2). PET combined with a CT scan demonstrated marked metabolic activity in the primary anal mass and a 1-cm perirectal lymph node near the coccyx, suggesting a node-positive disease in October 2013 (fig. 3). An MRI of the pelvis confirmed the PET/CT findings (fig. 4). The patient's tumor was sent to an outside institution for a second opinion, and the report was concluded as the tumor may in fact be a malignant melanoma. The patient subsequently underwent an exploratory laparotomy with an APR and left-end colostomy in October 2013. The patient tolerated the surgical procedure without any complications. The pathologic specimen confirmed a malignant melanoma arising in the anal skin and extending into the rectum, involving the anal and perirectal soft tissue and 6 regional lymph nodes (fig. 5). The tumor was classified as grade 3, poorly differentiated, stage IIIA, T2N1M0 according to the tumor-node-metastasis classification of colorectal cancer [4]. Immunohistochemical analysis results were positive for the expression of the S-100 protein, HMB-45 and vimentin, whereas negative for the expression of cytokeratin and SMA (fig. 6). The patient agreed to the plan of starting chemotherapy with mitomycin and 5-fluorouracil (for the anorectal melanoma).

Discussion

Primary malignant melanoma of the anus and rectum is a rare and highly lethal malignancy of the elderly, which often manifests at an advanced stage [5]. Mucosal melanomas represent approximately 1.2% of all melanomas and anorectal melanomas account for less than 25% of all mucosal melanomas [6]. It is the third most common location after cutaneous and ocular melanomas [1]. In addition, it is the most common primary melanoma of the gastrointestinal tract [7] and accounts for approximately 0.5% of all colorectal and anal cancers [8]. The tumor commonly affects females in their fifth or sixth decade [9, 10] with a 1.7-fold higher prevalence in Caucasians than in African Americans [10]. The incidence rate is reported as 0.4% per million [9] with a 1.8-fold increase in incidence in the last 2 decades, suggesting either a true increase in incidence or an improvement in diagnosis [10].

A melanoma of the anus and rectum was first reported by Moore [11] in 1857. Lesions can affect the anal canal, the rectum or both, with the majority occurring within 6 cm of the anal rim [12]. Common presenting symptoms include rectal bleeding, anorectal pain or discomfort, change in bowel habits, prolapsed tumor mass and hemorrhoids. This represents a significant clinical challenge since early diagnosis and treatment are crucial. Our patient had a similar presentation. Primary anorectal malignant melanomas are in almost 80% of the times mostly misdiagnosed as hemorrhoids, polyp, adenocarcinoma or rectal ulcer [12]. Grossly, the majority of lesions appears polypoid, with or without pigmentation, and can be ulcerated as well [5]. The tumor is amelanotic in about 30% of the cases [13], and with considerable morphologic variability, misdiagnosis as lymphoma, carcinoma or sarcoma is common [14, 15]. The use of immunohistochemistry panels, including S-100 proteins, MelanA, HMB-45 and tyrosinase, can help in the diagnosis [5]. In our case, immunohistochemistry analysis was positive for the S-100 protein. Chute et al. [5] reported 4 histologic cell types: epithelioid, spindle cell, lymphoma-like and pleomorphic. The mitotic rate averaged 2.8 mitotic figures per high-power field in 17 cases of a primary anorectal malignant melanoma.

It is presumed that primary anorectal malignant melanoma arises from normal melanocytes in the intestinal epithelium distal to the dentate line and extending proximally into the rectum [16]. KIT expression can be present in anorectal malignant melanomas and, when present in spindle cell subtypes, can lead to confusion with gastrointestinal stromal tumors [5]. As in cutaneous melanomas, loss of c-kit expression is associated with aggressive clinical behavior, it was postulated that a loss of KIT might play a role in the pathogenesis [5, 17], therefore suggesting a role of kinase inhibitors such as imatinib [17]. The 5-year survival rate has been reported to be less than 20% for anorectal melanomas, with a median survival of 24 months [6]. Prognostic factors include the stage of the disease at the time of diagnosis [18] and the tumor thickness [19]. Common sites of distant metastasis are the liver and lung [20].

As this is a relatively rare entity, we lack randomized control trials regarding appropriate management, and current evidence is mostly based on retrospective studies, reported as a limited number of cases or data collected over prolonged time periods, including patients with an age of up to 64 years [21, 22]. Optimal treatment is still controversial. Surgical approaches include WLE and APR. Our patient underwent APR. A meta-analysis of 426 patients did not demonstrate any survival advantage with either approach [23]. Preoperative tumor thickness may be a valuable tool to plan the surgical approach [24]. Studies reported that local disease seems to be more effectively controlled with APR [21, 25, 26]. Recent studies suggested the initial treatment of choice to be WLE because radical surgery failed to show any survival advantage and also to avoid the need for colostomy [25, 26].

Local recurrences are common with WLE and with no documented effect on survival [25]. Radiation therapy has reported to provide a better local control after WLE [5] and also seems beneficial for sphincter preservation [21]. Most patients die regardless of the chosen therapeutic strategy due to the aggressive nature and the rapid progression of the tumor. Kim et al. [27] conducted a retrospective review on 18 patients with metastatic anorectal melanoma treated with cisplatin-based chemotherapy in combination with interferon alpha-2b or interleukin-2. They reported that combination chemotherapy was effective against metastatic anorectal melanoma. The response was similar to that of cutaneous melanoma.

Disclosure Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

- 1 Singer M, Mutch MG: Anal melanoma. *Clin Colon Rectal Surg* 2006;19:78–87.
- 2 Kelly P, Zagars GK, Cormier JN, Ross MI, Guadagnolo BA: Sphincter-sparing local excision and hypofractionated radiation therapy for anorectal melanoma: a 20-year experience. *Cancer* 2011;117:4747–4755.
- 3 Kim KB, Sanguino AM, Hodges C, Papadopoulos NE, Eton O, Camacho LH, Broemeling LD, Johnson MM, Ballo MT, Ross MI, et al: Biochemotherapy in patients with metastatic anorectal mucosal melanoma. *Cancer* 2004;100:1478–1483.
- 4 Jessup J, Gunderson L, Compton C: Colon and rectum; in: Edge SB, Byrd DR, Compton CC, Fritz AG, Trotti A (eds): *AJCC Cancer Staging Manual*. New York, Springer, 2010, vol 7, pp 143–164.
- 5 Chute DJ, Cousar JB, Mills SE: Anorectal malignant melanoma: morphologic and immunohistochemical features. *Am J Clin Pathol* 2006;126:93–100.
- 6 Chang AE, Karnell LH, Menck HR: The National Cancer Data Base report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the past decade. The American College of Surgeons Commission on Cancer and the American Cancer Society. *Cancer* 1998;83:1664–1678.
- 7 Cheung MC, Perez EA, Molina MA, Jin X, Gutierrez JC, Franceschi D, Livingstone AS, Koniaris LG: Defining the role of surgery for primary gastrointestinal tract melanoma. *J Gastrointest Surg* 2008;12:731–738.
- 8 Roumen RM: Anorectal melanoma in the Netherlands: a report of 63 patients. *Eur J Surg Oncol* 1996;22:598–601.
- 9 McLaughlin CC, Wu XC, Jemal A, Martin HJ, Roche LM, Chen VW: Incidence of noncutaneous melanomas in the U.S. *Cancer* 2005;103:1000–1007.
- 10 Coté TR, Sobin LH: Primary melanomas of the esophagus and anorectum: epidemiologic comparison with melanoma of the skin. *Melanoma Res* 2009;19:58–60.
- 11 Moore R: Recurrent melanosis of the rectum, after previous removal from the verge of the anus, in a man aged sixty-five. *Lancet* 1857;1:290.
- 12 Zhang S, Gao F, Wan D: Effect of misdiagnosis on the prognosis of anorectal malignant melanoma. *J Cancer Res Clin Oncol* 2010;136:1401–1405.
- 13 Hillenbrand A, Barth TF, Henne-Bruns D, Formentini A: Anorectal amelanotic melanoma. *Colorectal Dis* 2008;10:612–615.
- 14 Banerjee SS, Harris M: Morphological and immunophenotypic variations in malignant melanoma. *Histopathology* 2000;36:387–402.
- 15 Gatter KC, Ralfkiaer E, Skinner J, et al: An immunocytochemical study of malignant melanoma and its differential diagnosis from other malignant tumors. *J Clin Pathol* 1985;38:1353–1357.
- 16 Morson BC, Volkstadt H: Malignant melanoma of the anal canal. *J Clin Pathol* 1963;16:126–132.
- 17 Ni S, Huang D, Chen X, Huang J, Kong Y, Xu Y, et al: c-kit gene mutation and CD117 expression in human anorectal melanomas. *Hum Pathol* 2012;43:801–807.
- 18 Slingluff CL Jr, Seigler HF: Anorectal melanoma: clinical characteristics and the role of abdominoperineal resection. *Ann Plast Surg* 1992;28:85–88.
- 19 Ballo MT, Gershenwald JE, Zagars GK, Lee JE, Mansfield PF, Strom EA, Bedikian AY, Kim KB, Papadopoulos NE, Prieto VG, Ross MI: Sphincter-sparing local excision and adjuvant radiation for anal-rectal melanoma. *J Clin Oncol* 2002;20:4555–4558.
- 20 DeMatos P, Tyler DS, Seigler HF: Malignant melanoma of the mucous membranes: a review of 119 cases. *Ann Surg Oncol* 1998;5:733–742.
- 21 Brady MS, Kavolius JP, Quan SH: Anorectal melanoma: a 64-year experience at Memorial Sloan-Kettering Cancer Center. *Dis Colon Rectum* 1995;38:146–151.
- 22 Weyandt GH, Eggert AO, Houf M, Raulf F, Bröcker EB, Becker JC: Anorectal melanoma: surgical management guidelines according to tumour thickness. *Br J Cancer* 2003;89:2019–2022.
- 23 Thibault C, Sagar P, Nivatvongs S, Ilstrup DM, Wolff BG: Anorectal melanoma – an incurable disease? *Dis Colon Rectum* 1997;40:661–668.
- 24 Ross M, Pezzi C, Pezzi T, Meurer D, Hickey R, Balch C: Patterns of failure in anorectal melanoma. A guide to surgical therapy. *Arch Surg* 1990;125:313–316.
- 25 Zhou HT, Zhou ZX, Zhang HZ, Bi JJ, Zhao P: Wide local excision could be considered as the initial treatment of primary anorectal malignant melanoma. *Chin Med J (Engl)* 2010;123:585–588.

- 26 Iddings DM, Fleisig AJ, Chen SL, Faries MB, Morton DL: Practice patterns and outcomes for anorectal melanoma in the USA, reviewing three decades of treatment: is more extensive surgical resection beneficial in all patients? *Ann Surg Oncol* 2010;17:40–44.
- 27 Kim KB, Sanguino AM, Hodges C, Papadopoulos NE, Eton O, Camacho LH, Broemeling LD, Johnson MM, Ballo MT, Ross MI, et al: Biochemotherapy in patients with metastatic anorectal mucosal melanoma. *Cancer* 2004;100:1478–1483.

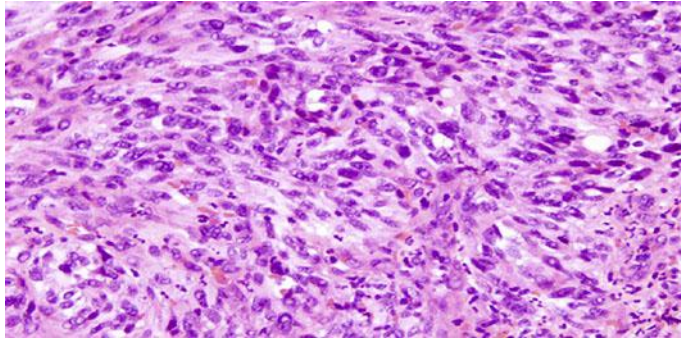


Fig. 1. Anorectal mass, biopsy specimen: hematoxylin and eosin stain ($\times 20$) showing an atypical spindle cell proliferation with mitotic activity and without melanin. The neoplastic spindle cells have increased nuclear/cytoplasmic ratios and nucleoli.

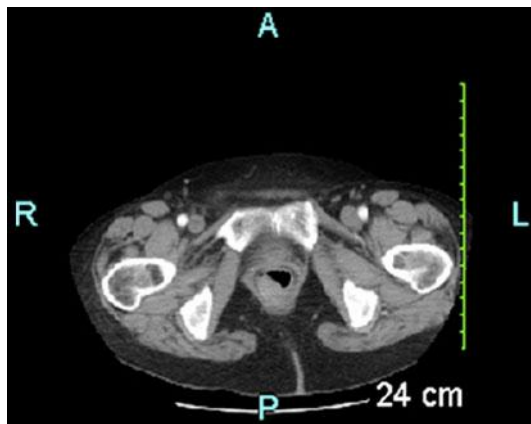


Fig. 2. CT scan of the abdomen and pelvis showing an abnormal soft tissue mass occupying the anorectal junction, extending to the right lateral wall of the rectum.

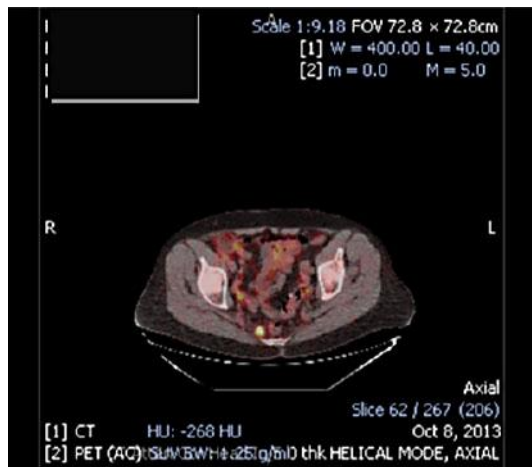


Fig. 3. PET/CT scan showing a 1-cm metabolically active, precoccygeal lymph node.

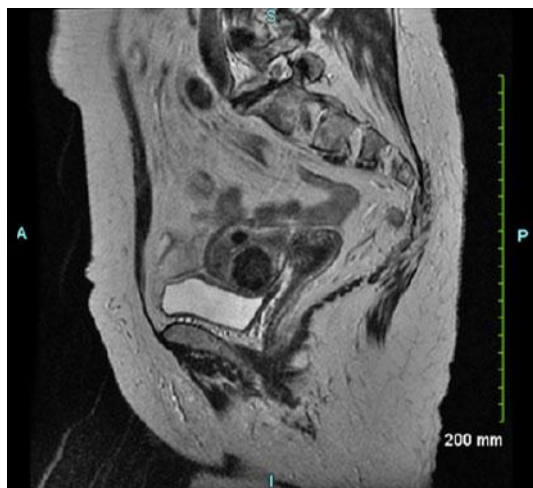


Fig. 4. MRI of the pelvis showing a thickening of the anal wall and a mild surrounding soft tissue enhancement.

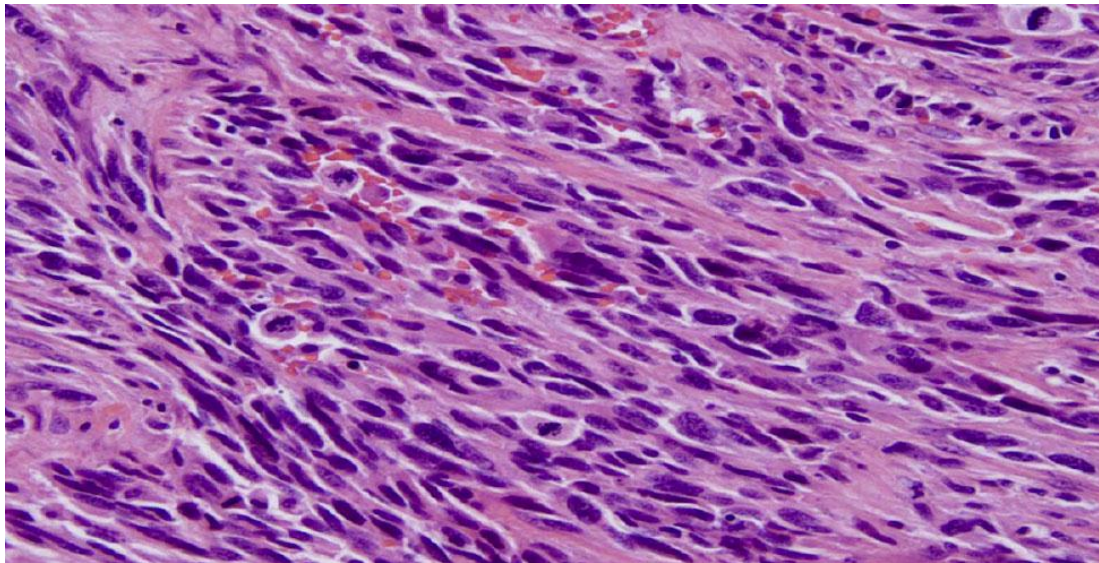


Fig. 5. APR specimen: hematoxylin and eosin stain showing spindle cells with marked nuclear pleomorphism and abnormal mitotic activity.

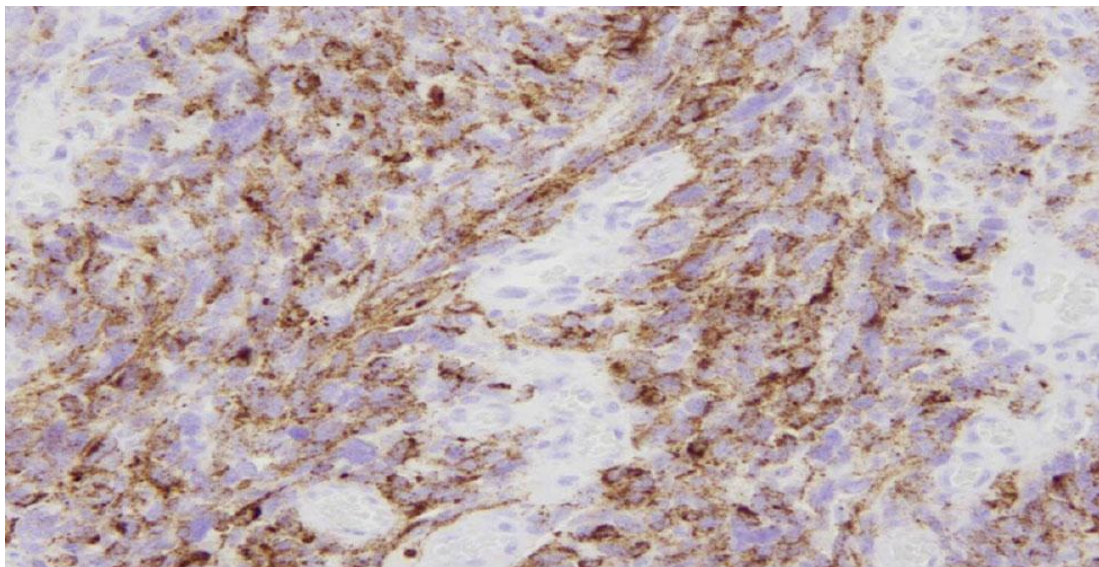


Fig. 6. APR specimen: immunochemical stain for HMB45 is diffusely positive, confirmatory of malignant melanoma.