

## CASE REPORT

# Anorectal melanoma. Case report and review of the literature

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### Abstract

We report a case of primary anorectal melanoma, a very rare malignant tumor in this localization. The patient, a 57-year-old female, complained for one year of symptoms, which were attributed to hemorrhoids. An abdomino-perineal resection was performed. Pathologic examination revealed an anorectal melanoma with numerous lymph node metastases and an unusual metastatic deposit in a uterine leiomyoma. The pathogenesis, pathology, principles of treatment and prognosis of this entity are briefly discussed.

**Keywords:** anorectal canal, melanoma, clinico-pathologic correlations.

### Introduction

Anorectal melanoma are very rare tumors [1, 2], the larger series having been collected over long periods of time [3–10]. The most common symptom is rectal bleeding, followed by tenesmus, pruritus, proctalgia, changes in bowel habits. The diagnosis is difficult and the disease incorrectly labeled as hemorrhoids or rectal polyps in about 80% of the cases, causing a delay in diagnosis and explaining why the patients present with locally advanced disease and 60–70% of them already have metastases [10–13].

In this paper, we report a new case masquerading as hemorrhoids and discuss the diagnosis and the modalities of treatment of this entity.

### Material and methods

The patient, a 57-year old female complained of rectal bleeding and pain for one year, which were attributed to hemorrhoids. The surgical procedure consisted in abdomino-perineal resection with anorectal amputation, hysterectomy, oophorectomy, omentectomy and removal of regional lymph nodes.

Tumor pieces were fixed in 10% formalin, paraffin-embedded and routinely stained with Hematoxylin–Eosin. Immunohistochemical investigations were done by using antibodies against cytokeratin (CK), leukocyte common antigen (LCA), vimentin, S-100 protein and HMB-45 (Dako).

### Results

Grossly examination revealed a specimen of anorectal amputation having a length of 33 cm, with

several brownish-black nodules, the largest one having 7/5/5 cm, which projected into the lumen. The uterus showed numerous nodules, 0.5–6 cm diameter, with a whorled pattern on cut surface. The largest nodule had a central blackish area. Twenty-nine lymph nodes were dissected and examined.

*Histologically*, the tumor was composed of epithelioid cells with prominent nucleoli, arranged in sheets. There were 22 mitoses figures/HPF, and scattered melanic pigment was present both intracellularly and extracellularly (Figure 1).

Immunostaining for cytokeratin and LCA were negative. Tumor cells were decorated with vimentin, S-100 and HMB-45. The tumor infiltrated the rectal wall extending to a thickness of 7 mm (Figure 2).

The epithelium was largely ulcerated but residual areas showed junctional changes and a pagetoid extension of melanocytes (Figure 3).

All the polypoid nodules showed a similar histopathological picture. Several sections demonstrated that they were in continuity. Twenty-two of the 29 lymph nodes had extensive metastases. There were lymphatic emboli (Figure 4) and perineural extension. The uterine largest nodule was a leiomyoma with metastasis of melanoma (Figures 5, A and B).

### Discussions

Malignant melanoma usually presents like polypoid lesion which projects into the anorectal lumen and progresses rapidly towards the rectal wall, perirectal tissues and pelvic walls. Because the anus has a rich vascular and lymphatic supply, the tumor is often advanced at the time of diagnosis, with metastases in the

regional inguinal and iliac lymph nodes and hematogenic metastases in the liver, bone, brain and lungs [11–13]. The presence of a metastatic deposit in a uterine leiomyoma (“tumor to tumor metastasis”), noted in our case, is quite unusual.

Histologically, epithelioid, spindle cell, lymphoma-like, and pleomorphic subtypes have been described [14]. The diagnosis may be difficult especially in small biopsies of amelanotic or undifferentiated tumors that lack junctional changes. Amelanotic melanoma represents 25–50% of the cases [14, 15].

Poorly differentiated tumors of the anorectal canal, which might raise problem of differential diagnosis, are undifferentiated carcinoma, poorly differentiated squamous cell carcinoma and adenocarcinoma, and lymphoma [16]. Patients who were initially misdiagnosed with “anal carcinoma” received chemotherapy rather than surgery [17].

Metastases of skin melanoma, another problem of differential diagnosis, are usually multiple and submucosal, with normal overlying mucosa. The presence of junctional changes, with atypical intramucosal melanocyte proliferation, may be a useful marker for a primary tumor, but this is often ulcerated [18]. However, metastases may also be solitary and secondarily invade the mucosa.

A correct diagnosis often requires a comprehensive immunohistochemical panel, including vimentin, S-100, HMB-45, tyrosinase and MITF (microphthalmia-transcription factor) [14, 19].

Expression of c-kit was present frequently, including cases with spindle cell morphology, in which it may lead to confusion with gastrointestinal stromal tumors. Some unusual situations – melanotic adenocarcinoma of the rectum [20], synchronous anorectal melanoma and adenocarcinoma [21, 22] – may complicate even more the diagnosis.

The prognosis value of histologic markers is not yet well documented. It seems, however, that there is a trend towards longer survival in patients with an S-phase fraction of <10% [18], and lower Ki-67 and PCNA scores [23].

The presence of two distinct melanic tumors in the anorectal region has recently been described [24]. This case may represent multiple synchronous primary melanomas, but the possibility that one of the lesions is primary melanoma and the second one is a satellite lesion cannot be excluded. The case that we have studied also showed several discrete nodules, but a careful examination of the intercalated intestinal segments revealed the continuity of the lesion.

The histogenesis of anorectal melanoma has been a subject of dispute for a long time. As the presence of melanocytes was demonstrated not only in the squamous zone and transitional zone, but also in the colorectal mucosa, it became clear that malignant melanoma may originate not only below, but also above the dentate line [25, 26].

Ultraviolet light, a major carcinogen in skin melanoma, cannot obviously be involved in this peculiar anatomic localization (“where the sun never shines”, as Miller BJ *et al.* [27] said).

Cagir B *et al.* [28] noted a changing epidemiology in the San Francisco area, where the incidence in young males aged between 25 to 44 years tripled when compared with others locations. The authors suggested that there is indirect evidence that implicates human immunodeficiency virus infection as a risk factor. Helmke BM *et al.* [29] did not confirm the possible intervention of the tumorigenic human herpes virus type 8.

The prognosis of anorectal malignant melanoma is extremely severe. Two recent reviews reported 5-year survivals of 17.8% [8], and 9.8%, respectively [30]. The tumor size, the depth of invasion [19], the status of lymph nodes [10], and the stage [5] influence the prognosis.

Surgery remains the primary treatment, but the choice of procedure – abdomino-perineal resection (APR) vs. local excision (LE) remains a matter of debate. Most authors did not notice significant survival advantage of the radical procedures [4–6, 9, 11, 15, 17, 18, 31].

Brady MS *et al.* [8] reported more favorable outcome for the patients who underwent APR than that for patients who underwent LE only, although the difference was not statistically significant. Based on there data the authors stated that APR should be considered in patients with localized melanoma, particularly those with smaller tumors and no evidence of nodal metastases. The rate of local recurrences is slightly higher in patients who had LE [17, 32] but, as most patients do not survive, local recurrences rarely require re-intervention. Lymph node dissection is indicated only in cases with clinical invasion [33].

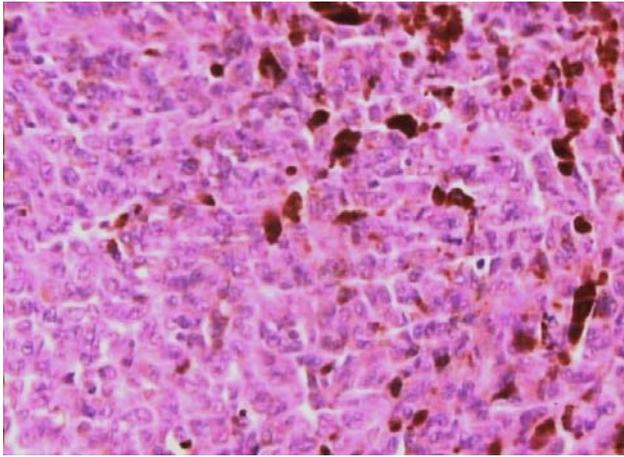
Radiation therapy has been applied in a few cases [34–36]. Brachytherapy may reduce the rate of recurrence [37, 38].

In the study of Moozar KL *et al.* [17], comparison of the survival in patients who had surgery alone or surgery in combination with radiotherapy did not demonstrate significant differences. Several authors reported favorable results of chemotherapy. Based on a larger experience, Kim KB *et al.* [39] suggested that biochemotherapy should be considered in the treatment of metastatic melanoma disease.

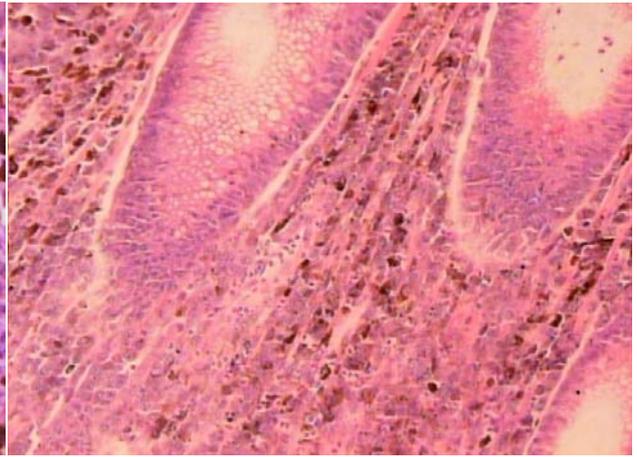
It is improbable, however, that anorectal melanoma could be cured with available procedures and efforts should be made for the detection of this disease in early stage.

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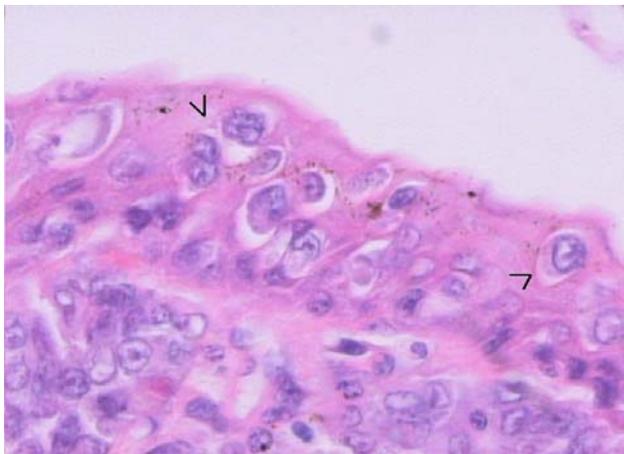
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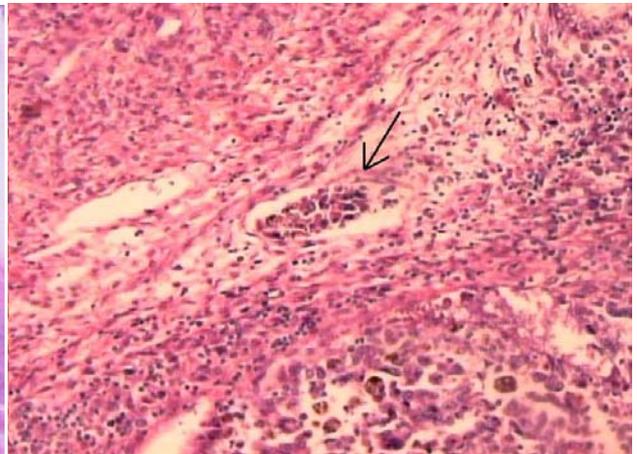
**Figure 1** – Tumor area showing a dense proliferation of malignant cells with prominent nucleoli. A large number of cells are heavily pigmented (H&E stain, 50×)



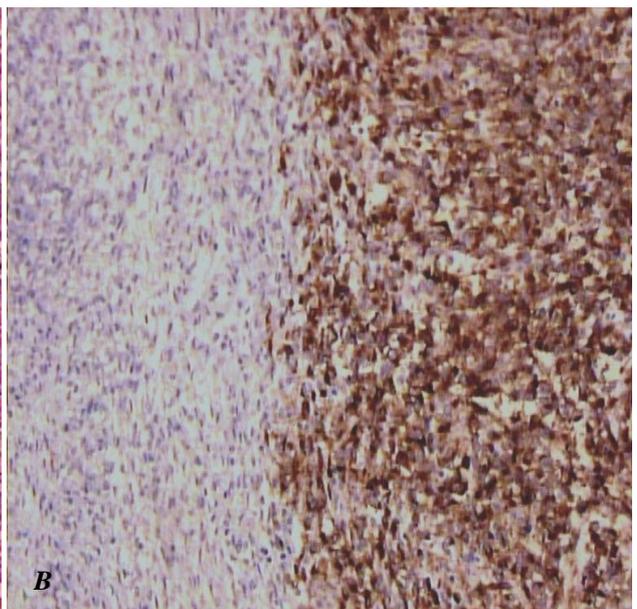
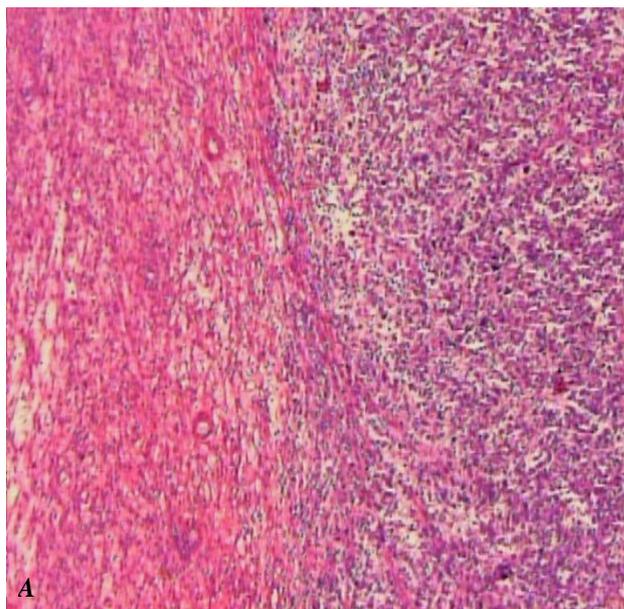
**Figure 2** – Pigmented melanoma cells infiltrating between the crypts of the rectal mucosa (H&E stain, 25×)



**Figure 3** – Pagetoid extension of tumor cells (arrowheads) into the anal squamous epithelium (H&E stain, 100×)



**Figure 4** – Tumor embolus lying within a lymph vessel (arrow) (H&E stain, 25×)



**Figure 5** – Metastatic deposit of melanoma cells (the right side of the picture) into a leiomyoma (the pink nodule on the left): A. H&E stain, 10×; B. Malignant cells stained brown, positive for melanoma markers (HMB-45 stain, 10×)

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Received: June 20<sup>th</sup>, 2007

Accepted: July 25<sup>th</sup>, 2007