Anorectal Mucosal Melanoma: A Case Report and Literature Review

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Patient: Female, 81-year-old
Final Diagnosis: Anorectal malignant melanoma
Symptoms: Hematochezia • obstipation • pain • tenesmus
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology • Oncology

Objective: Rare disease
Background: Anorectal mucosal melanoma (AMM) is a rare and aggressive neoplasm, with a 5-year survival rate of 10%. Due to its rarity and nonspecific symptoms, the diagnosis is often made late. Surgical resection remains the criterion standard for treatment of anorectal melanoma.

Case Report: We present the case of an 81-year-old woman presenting with hematochezia, anal secretion, tenesmus, difficulty in defecation, and perianal pain. On physical examination, there was a prolapse of a 5-cm melanocytic nodule in the anal canal, hard on palpation. Biopsy confirmed anorectal melanoma. Staging revealed anal and metastatic disease, with adrenal, lymphatic, and hepatic involvement. As the patient continued to have bleeding, severe pain, and difficulty in defecation, she was submitted to a wide local excision. At 5-month follow-up, the anal lesion had relapsed, and the patient died 10 months after the procedure.

Conclusions: AMM is a rare and extremely aggressive tumor. Symptoms are nonspecific but early diagnosis should be pursued to allow curative treatment. Surgical resection with free margins is the goal of surgical treatment. New therapies are being studied, including immunotherapy, which can improve the dismal prognosis of this rare disease.

Keywords: Colorectal Surgery • Margins of Excision • Melanoma • Rectal Diseases • Treatment Outcome

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Background

Anorectal mucosal melanoma (AMM) is a rare and aggressive neoplasm, with a 5-year survival rate of 10% [1]. It accounts for only 0.4% to 1.6% of all melanoma and 0.5% of all anorectal cancer [1]. Typically, affected patients are older (sixth to eighth decades of life), white, and female [2]. Common presenting symptoms include pain, bleeding, anal mass, tenesmus, or constipation; therefore, it is usually discovered during rectal examination for other suspected anorectal disorders. Due to its rarity and nonspecific symptoms, the diagnosis is often made late, which contributes to the dismal prognosis [3]. AMM is often misdiagnosed as hemorrhoids, polyps, or colorectal cancer [3].

Surgical resection remains the criterion standard for treatment of AMM. The best procedure is still a matter of debate, and both wide local excision (WLE) and abdominal perineal resection (APR) are possible options [4].

We present a case of anorectal melanoma treated with local excision and a literature review of this rare tumor.

Case Report

An 81-year-old woman presented with hematochezia, anal secretion, tenesmus, obstipation, and perianal pain, which started 6 months before. She denied weight loss, diarrhea, pruritus, or inguinal mass. When she noticed the presence of blood in the stool and the appearance of an anal nodule, she went to a general practitioner, when she was diagnosed with thrombosed hemorrhoids.

She had a past medical history of arterial hypertension and type 2 diabetes mellitus. On physical examination, there was a prolapse of a 5-cm melanocytic nodule in the anal canal, hard on palpation, as shown in Figure 1. There was no evidence of inguinal lymphadenopathy or sphincter involvement on digital rectal examination. A biopsy confirmed anorectal melanoma. Complete colonoscopy was performed and ruled out synchronous lesions. Staging with computed tomography of the chest, abdomen, and pelvis was performed and revealed anal disease and metastatic disease, with adrenal, lymphatic, and hepatic involvement (Figure 2).

Figure 1. Prolapsed melanocytic nodule in the anal canal. Physical examination demonstrating a prolapsed melanocytic nodule in the anal canal.

Figure 2. CT scan. Staging CT scan showing a large adrenal metastasis (indicated by the red arrow).

Figure 3. Surgical specimen. Picture of the open surgical specimen showing a partial resection of the anal sphincter, indicated by the red arrow.
As the patient continued to have bleeding, severe pain, and difficulty in defecation, an anal tumor resection was suspected.

The patient underwent a wide local excision of the tumor, with a 0.5-cm radial margin, which required partial resection of the anal sphincter. She had an uneventful recovery, and was discharged on the second day after the procedure. A surgical specimen is shown in Figure 3. In the outpatient follow-up, the patient reported a significant improvement in symptoms.

The pathological examination demonstrated a pT4b melanoma, with a Breslow index of 28 mm, ulceration, microsatellitosis, vascular and perineural invasion, invasion of rectal mucosa, and 10 mitoses/mm², as shown in Figure 4. Immunohistochemistry staining was positive for S-100 and HMB-45.

Consultation with the clinical oncology team led to a decision not to proceed with chemotherapy, due to absence of performance status and considering the patient's advanced age, comorbidities, and metastatic disease with poor response rate. After 5 months, the anal lesion relapsed and the patient developed anal bleeding. One session of hemostatic radiation therapy (800 cGy) was performed in the anal canal for palliation. Death occurred 10 months after the surgical procedure, due to liver failure related to multiple liver metastases.
Discussion

Pathophysiology

AMM is a malignant neoplasm originating from melanocytic cells in the anorectal mucosa. Mucosal melanomas (MM) originate from melanocytes located in the mucous membranes of any part of the mucosal surface, most commonly in the mucosa of the oral cavity, pharynx, vulvovaginal, anorectal, and urinary tract.

MM has different somatic mutation profiles compared to cutaneous melanoma (CM); BRAF mutations are rare in MM, while mutations related to cell surface receptor tyrosine kinase activity (c-KIT) are identified more frequently [5].

Clinical Picture

The symptoms are nonspecific, generally common to several anorectal disorders, such as hemorrhoidal disease, polyps, and squamous cell carcinoma, delaying the diagnosis and early treatment, as occurred with our patient. Zhang et al, in a Chinese study with a case series that included 79 patients with AMM, reported that in 46 patients the initial diagnosis was a benign anorectal disease [6]. Symptoms are usually more evident in larger tumors with deeper tissue penetration [1], and include pain, bleeding, anal mass, and constipation. The average time between the onset of symptoms and confirmation of the diagnosis varies between 4 and 8 months.

Differential diagnoses include hemorrhoids, polyps, and colorectal cancer. Hemorrhoids do not usually present with dark color at inspection. Polyps can present with an aspect and color similar to the normal mucosa, and colorectal cancer presents with an ulcerated friable mass. Although the differences can be remarkable, in some cases the melanoma does not present its characteristic dark color (amelanotic melanoma). In these cases, the differential diagnosis is far more challenging, and histopathological evaluation is essential.

Diagnosis and Staging

Histology and immunochemistry are required to confirm the diagnosis of AMM. Mucosal melanomas show high pleomorphism in the nucleus, are epithelioid spindle-shaped, and they often present melanin granules, as well as the proliferation of atypical junctional melanocytes and atypical melanocytic cells in the basal layer in the superficial epithelium [7]. Proteins S-100, HMB-45, and Melanin A are useful to confirm the diagnosis and help to differentiate it from other tumors [8] such as gastrointestinal stromal tumors (GISTs) and sarcomas. Either endoscopic ultrasound or pelvic magnetic resonance imaging should be used for local staging [5]. Systemic staging should be performed with head, thorax, abdomen, and pelvis CT scans. Complete colonoscopy is indicated to rule out synchronous lesions. Endoscopic findings include nodule with black pigmentation, with friability and ulceration. The endoscopic appearance can help the differential diagnosis with adenocarcinomas and hemorrhoids [9,10].

The staging of AMM is divided into 3 stages: I, local disease; II, local disease with regional lymph nodes; and III, with distant metastasis [6]. The primary site for metastasis is the liver, followed by the lungs and bones [5]. The stage of melanoma is an independent factor for overall survival [11,12].

Prognosis

The anatomical location of AMM, whether anal, anorectal, or rectal, does not appear to influence disease-free survival or overall survival [13]. The main recurrence factors for MM are perineural invasion and tumor thickness [14,15].

The Breslow index measures the thickness of the lesion in millimeters, from the epidermis to the deepest tumor cells in the skin. The more superficial the lesion on removal, the better the prognosis [1].

Up to one-third of these patients already have metastasis at the time of diagnosis [4]. The prognosis of AMM is poor, which is partially attributed to the late detection of this rare entity.

Our patient had a tumor located in the anal region, and the pathological examination demonstrated a pT4b melanoma, with a Breslow index of 28 mm, ulceration, microsatellitosis, vascular and perineural invasion, invasion of rectal mucosa, and 10 mitoses/mm², as well as metastasis to the liver.

Despite our patient presenting several poor prognostic factors, local resection was indicated due to the difficulty in defecation, pain, and bleeding, and was then sent for adjuvant therapies.

In up to one-third of MM patients at the time of diagnosis, the disease is in an advanced stage, and the surgical strategy (WLE or APR) may not influence the natural history of the disease, its clinical course, and overall survival [4,16,17].

Treatment

The treatment of choice for localized disease is surgical resection, either by wide local excision (WLE) or abdominoperineal resection (APR). The standard surgical procedure is yet to be established. Despite the greater radicality of APR, results have not demonstrated improved survival. WLE is a feasible procedure when sphincter involvement it not a concern, and it minimizes the morbidity associated with the surgical procedure. Thibault et al reviewed 50 patients with AMM, and reported...
that the 5-year survival and recurrence rates for local excision and abdominoperineal resection did not differ [4]. Given that WLE is associated with less morbidity, with comparable survival, it is reasonable to consider it as the initial treatment choice. Palliative surgery may also be performed, such as a diverting colostomy in the setting of bowel obstruction [3].

In past decades, several adjuvant therapeutic options such as immunotherapy with alfa interferon, brachytherapy with 117-Caesium, and chemotherapy with dacarbazine, vincristine, and nimustine hydrochloride were developed. Alfa interferon is used particularly in patients with positive lymph nodes, and demonstrates a significant prolongation of overall survival and relapse-free survival [18]. The role of pelvic radiation has not been systematically examined [19]. Radiation can be used with a palliative intent for bleeding control, such as in the present case. Metastatic melanoma can be managed with dacarbazine in combination with interleukin-2, although the responses rates are very poor [3]. Patient performance status, comorbidities, and expectations must be considered to pre-scribe adjuvant therapy for metastatic AMM.

Immunotherapy is a promising strategy to treat advanced mucous melanoma [3]. Ipilimumab is an anti-CTLA-4 (cytotoxic T-lymphocyte antigen 4) monoclonal antibody that has an effect on T-cell-mediated antitumor immune response [20]. Nivolumab and Pembrolizumab are anti-PD1 (programmed-death) monoclonal antibodies that also target the T-cell-mediated antitumor immune response [3]. Nivolumab and Ipilimumab can be used in combination, with improvement of progression-free survival in patients with advanced melanoma [21]. KIT-mutated metastatic melanomas are susceptible to therapy with specific inhibitors. Hodi et al reported favorable results in patients with KIT-mutated rectal melanoma [22]. Complete remission was reported in patients with KIT-mutated melanoma who underwent treatment with sunitinib [23].

The literature suggests that AMMs are extremely heterogeneous in their mutations, and studying this variable tumor biology may allow the discovery of new target molecules with therapeutic implications.

Conclusions

AMM is a rare and extremely aggressive tumor. Surgical resection with free margins should be achieved either by wide local excision or abdominoperineal resection. For locally advanced disease, palliative treatment is indicated for debilitating symptoms. New therapies are being studied, including immunotherapy, which may improve prognosis.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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