Case Report

Anorectal melanoma: review of diagnosis and treatment based on a case report

Lúcio Sarubbi Fillmann[1], Érico Ernesto Pretzel Fillmann[1], Henrique Sarubbi Fillmann[1], Jeferson Krawcyk de Oliveira[2], José Francisco Benedetti Parizotto[3], Bruno Lorenzo Scolaro[3], Patrícia Cardoso Motta Lima[3]

[1]Coloproctologist, Service of Coloproctology, Hospital São Lucas da Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS) – Porto Alegre (RS), Brazil; [2]General Surgeon, Hospital São Lucas da PUCRS – Porto Alegre (RS), Brazil; [3]Former residents, Service of Coloproctology, Hospital São Lucas da PUCRS – Porto Alegre (RS), Brazil.

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ABSTRACT: Anorectal Melanoma is a rare and very aggressive tumor that should be part of the range of differential diagnoses of colorectal diseases. Today, the main discussion on the topic is about the best treatment, whether it should be more conservative or more aggressive. In order to review the main points on the subject, the authors report a case of a patient treated at the Coloproctology Service at the São Lucas Hospital, PUCRS.

Keywords: melanoma; neoplasms; anal canal; surgery; neoplasm staging.

RESUMO: O melanoma anorretal é uma patologia de baixa frequência, porém de agressividade expressiva, devendo fazer parte da gama de diagnósticos diferenciais do Coloproctologista. A principal discussão sobre o tema versa hoje sobre a melhor forma de tratamento, seja mais invasivo ou mais conservador. A fim de revisar os principais pontos sobre o assunto, relataremos o caso de uma paciente atendida no Serviço de Coloproctologia do Hospital São Lucas da PUCRS.

Palavras-chave: melanoma; neoplasias; canal anal; cirurgia; estadiamento de neoplasias.

INTRODUCTION

Anorectal melanoma (AM) is a rare malignant tumor of a very aggressive behavior. It represents less than 1% of the anorectal diseases and between 0.4 and 1.6% of melanomas in general[1-3]. Since the first case reported by Moore in 1857, around 600 cases have been described[2,4]. The distribution is similar in men and women, with a slight preference for females, and the mean age of tumor presentation is in the sixth and seventh decades of life. The disease etiology is still uncertain. Common risk factors of cutaneous melanoma, such as sun exposure, seem to have no relation with the development of AM. The disease prognosis is guarded, with survival rates in five years of around 6%, despite the treatment[2]. It is related to the tumor characteristics of fast dissemination and the fact of usually involving late diagnosis, a result of low clinical suspicion. In addition, most patients are suspected of presenting micrometastases at the diagnosis[2,5]. There is no consensus on the best therapeutic strategy, although the early diagnosis seems to be the main factor for a successful treatment.

CASE REPORT

A 64-year old female patient came to the Outpatient Clinic of Coloproctology with a request for a colonoscopy exam due to anemia and weight loss. At the medical appointment, the patient reported to be a former smoker, diabetic, hypertensive, cardiac and obese, with prior history of breast cancer (invasive

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ductal carcinoma – T1N0M0), and she had been submitted to modified radical mastectomy (right side) in 2005; treated today with tamoxifen. She complained of weakness, anorexia and weigh loss – 12 kg in 3 months. She denied any alteration to the bowel habit, bleeding on evacuation, pain or anal itching. She brought laboratorial exams that showed hemoglobin of 11.4 g/dL. At the general physical examination, she presented good physical state, with slightly discolored mucosae and no other significant alteration. At the proctologic examination, the anal inspection and rectal touch showed normal conditions. The anoscopy showed internal hemorrhoidal disease and hyperpigmented papilla at the posterior midline (Figure 1), measuring around 5 mm. Rectosigmoidoscopy was not performed due to the high amount of feces. An excisional biopsy of the papilla was performed, whose initial diagnosis was melanocytic lesion with extensive pigmentary deposit (Figures 3 and 4). After the immunohistochemical study, which showed material with extensive proliferative activity, positive for Melan-A, the surgical excision for a definitive diagnosis was suggested (Figure 2). In staging exams, computed tomography of thorax and abdomen presented normal results. The patient was submitted to wide local excision, with the diagnosis of invasive malignant melanoma, Breslow 2 mm, and free surgical margins as the definitive anatomopathological result. The histological aspect of the lesion, associated with its immunohistochemical profile, enabled a better diagnosis (markers S100, HMB-45, MELAN-A MART 1 and Ki67 (MM1) were positive). In the postoperative period, a magnetic resonance of the pelvis was performed,

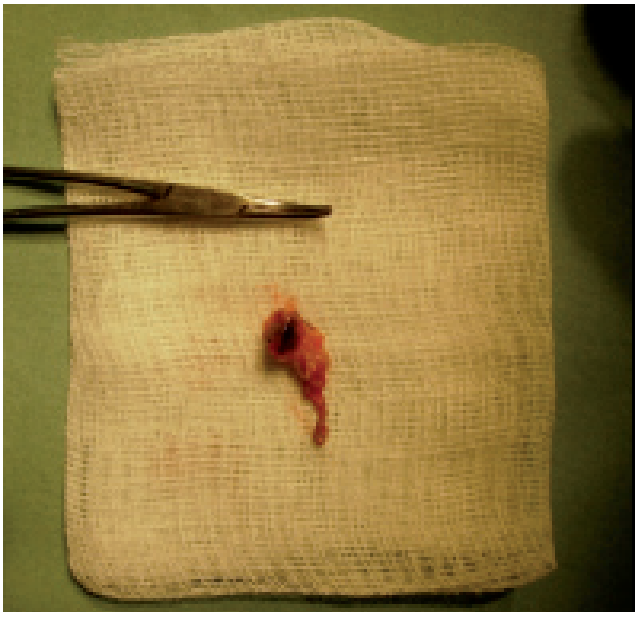

Figure 2. *Specimen from the surgical excision for a definitive diagnosis.*

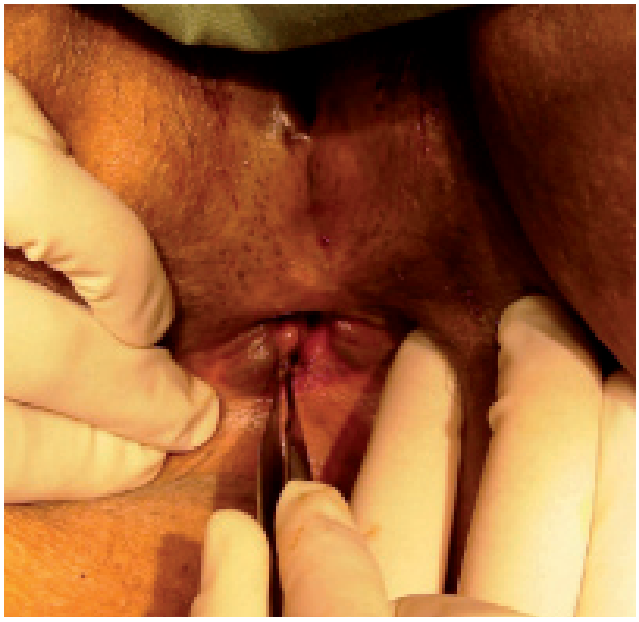

Figure 1. *Hyperpigmented anal papilla at the posterior midline.*

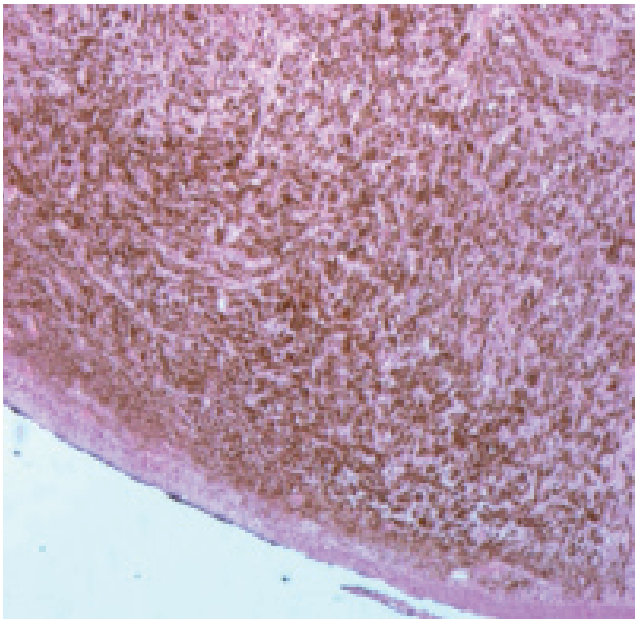

Figure 3. *Melanocytic lesion with extensive pigmentary deposit. HE 50x.*

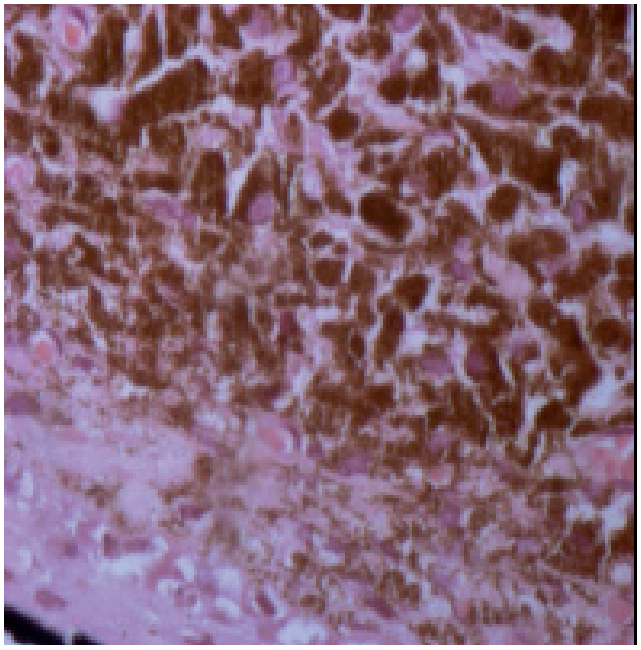

Figure 4. *Melanocytic lesion with extensive pigmentary deposit. HE 100x.*

which did not present lesion in the anal canal of rectum, but the presence of nodular images of 0.6 and 1.5 cm close to the bifurcation of iliac vessels on the left and pre-sacral region, respectively, which could correspond to grafts with melanin or hemorrhage, as well as bilateral inguinal ganglia, with conglomerates of 3.7 cm on the left. After that, the patient was submitted to a lymphoscintigraphic analysis, with injections of 99 m Tc-Phytate in the anal region close to the surgical scar. The result was absent sentinel lymph node in the inguinal region and small hyperabsorption of deep aspect in the bladder area, left to the midline, a finding considered inconclusive. It was decided to place the patient under observation. She remains under outpatient supervision, now asymptomatic, without signs of disease progress since she was submitted to the surgery, in November 2009.

DISCUSSION

Malignant melanoma, a neoplasm of neuroectodermal origin, has the skin as its main primary site, although it may appear in other regions, such as retina, oral cavity, genitourinary tract and others[4,6-8]. It occurs because the tumor transformation starts with the precursor cells of melanocytes (melanoblasts), which are present in the most varied types of epithelium, including the mucous surface[4,9]. This is the case of the anorectal region, characterized by the diversity of coatings. The rectum has a typically glandular epithelium. On the other hand, the anal canal, below the pectineal line, is covered by a squamous epithelium. Right above the pectineal line is the transition zone, where both glandular and squamous cells are present. Melanocytes may appear in the three regions (rectum, anal canal and transition zone), although the occurrence of melanoma is more frequent in the transition zone and squamous epithelium[1-8].

Most patients do not present symptoms, but, when present, they are: bleeding, pain, pruritus, anal secretion, alteration to bowel habit or bulging sensation[4]. The association of this clinical presentation with anorectal benign pathologies can cause confusion and delayed diagnosis. A polypoid lesion can be taken for a hemorrhoidal thrombus[1] and 15 to 40% of the lesions can be amelanotic, which does not contribute to easy detection. Some cases have been reported with incidental findings at the anatomopathological analysis of post-hemorrhoidectomy and lateral internal sphincterotomy specimens[6]. The coloproctological examination with inspection, rectal touch and proctoscopy is extremely important, as it provides data such as size, consistency, fixation and invasion of sphincter or adjacent structures[1].

Most tumors have nodular, polypoid and ulcerated macroscopic presentation. The histological pattern at microscopy is similar to that found in cutaneous melanoma: melanoma cells larger than normal melanocytes, with large and irregular nuclei, well or poorly clustered into nests. The higher the number of mitoses, the worse the diagnosis. In case of doubt or amelanotic lesions, the immunohistochemical analysis is used: the expression of S-100 and HMB-45 antibodies confirm the diagnosis of melanoma[1].

AM can appear in three forms: limited to the primary site, disseminated to regional lymph nodes or with distant metastases. The dissemination can be local or via lymphatic or hematogenic pathways. In lymphatic dissemination, the lymph nodes most commonly affected are those from the inguinal, obturator, mesenteric and para-aortic chains[5,6,8]. In hematogenic dissemination, the most frequent sites are: liver, lungs,

brain and bones. Around 40% of the patients may have metastatic disease at the diagnosis[1].

The universal classification of TNM established by the AJCC (American Joint Committee on Cancer) has been increasingly been used to classify melanomas[4,10-12]. The presence of ulceration, the mitotic index and Breslow index are used in the staging and evaluation of tumor (T) extension, classifying the tumor at different levels, according to the lesion depth (Box 1). The tumor thickness seems to be the most important predictive factor for recurrence[1].

Imaging exams complement the diagnostic investigation. Endoanal ultrasound, when available, may help in the surgical planning, as it evaluates the lesion extension, structures invaded and the level of sphincter involvement, as well as the chain of regional lymph nodes[2,4]. Magnetic resonance imaging of the pelvis enables to study the involvement of lymph nodes and the local extension of the disease[4,13,14]. Computed tomography of abdomen and thorax is used to detect the organs most affected by distance metastases: liver and lungs.

The sentinel lymph node analysis, although not standardized, is feasible and can prevent unnecessary ganglion emptying. It can also prevent substaging of those patients who are clinically node-negative, but that, at the specimen analysis, are pathologically node-positive[2].

After staging, the most difficult part is performed: the selection of the best therapeutic strategy. Many comparative studies have been conducted to establish a standardized treatment, but, due to the low incidence of an aggressive behavior of AM, no consensus has been reached in the literature.

The surgical treatment with curative intent should be proposed, considering the disease stage and the clinical conditions of each patient[1]. Most frequent approaches include: Abdominoperineal Amputation (APA) and Wide Local Excision (WLE). For a long time, the APA was considered the standard therapy, but several studies have demonstrated no significant difference in survival when comparing it to more conservative approaches (APA *versus* WLE)[1-8,15]. Such evidence is supported by the fact that the recurrence is almost always systemic, regardless of the initial surgical approach, reinforcing the idea that a high number of patients already presented the micrometastatic disease at the initial diagnosis[2]. Local recurrence is usually associated with the presence of metastasis in lymph nodes[1-8]. After reviewing some cases, Homsi et al. concluded that, when technically viable, WLE should be the initial treatment of choice for patients without evidence of metastasis[5]. APA should be performed in case of larger tumors, recurrences, disease with locoregional invasion or when a good local control is required. Weyandt et al.[6,12,16] proposed a scheme in which the surgical approach is selected according to the tumor thickness, the Breslow Index[6] (Table 1). Prophylactic inguinal emptying has no indication and involves high morbidity[1,4]. Lymph node emptying should be performed only if the lymph nodes are clinically affected and when a complete resection (R0) is possible[1].

Melanomas are characteristically radioresistant, but radiotherapy can be used in the palliative treatment for a better locoregional control. Chemotherapy can be applied as neoadjuvant or adjuvant therapy[1-8]. Most common drugs are cisplatin, vinblastine, dacarbazine, interferon and interleukin-2. Although increasingly used, therapies with immunostimulants such as interferon, vaccines and monoclonal antibodies have not shown high gains in survival[4,17].

Despite the treatment options and attempts, the prognosis remains guarded, with survival rates in five years as low as 6% and mean survival of 25 months[1-8,9], regardless of the treatment type[18,19]. It shows an intrinsically aggressive and rapidly fatal disease, resulting in a limited number of cases with successful therapy.

Box 1. *Breslow Index, according to the American Joint Committee on Cancer[11].*

<1 mm	1–2 mm	2.1–4 mm	>4 mm

Table 1. *Surgical treatment according to Weyandt et al[6,16].*

LESION THICKNESS	TYPE OF SURGERY
Breslow <1 mm	WLE with preserved sphincter and margins of 1 cm.
Breslow of 1–4 mm	WLE with preserved sphincter and margins of 1 cm.
Breslow >4 mm	APA or neoadjuvant therapy followed by WLE if viable.

WLE: Wide Local Excision; APA: Abdominoperineal Amputation.

CONCLUSION

AM is a rare and challenging pathology. The fast tumor dissemination associated with late diagnosis results in a dismal prognosis, with low cure rates and disease control. So far, the evidences are not enough to establish advantages of more aggressive surgical approaches over more conservative options in terms of survival. However, surgery is the only option of curative-intent treatment. The selected procedure should enable complete resection of the disease and be adapted to the functional characteristics of the patient's quality of life.

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Correspondence to:
Patrícia Cardoso Motta Lima
Av. Protásio Alves, 7355, 904, Bloco 4
CEP: 91310-003 – Porto Alegre (RS), Brazil
E-mail: patriciamottalima@gmail.com