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Primary Anorectal Melanoma: Case Report and Literature Review

S Lemsanes , S Harrak , S Najem, S Razine, K Benchakroun, S Lkhoyaali , I El ghissassi, H Errihani.

***Abstract*— Primary Anorectal melanoma (PARM) is a rare and aggressive malignant neoplasm. It accounts for less than two percent of melanomas and it is the third most common location of melanoma, after the skin and retina. There have only been a few cases reported and there is no consensus of treatment. Unlike the generally favorable prognosis of early-stage cutaneous melanomas, the prognosis of anorectal melanoma is extremely poor, with a median survival of less than two years. We report a case of a 77-year-old male metastatic anorectal melanoma patient presenting with progression of disease over 6 months of a PD1 inhibitor treatment course.**

***Index Terms*— Primary anorectal melanoma, rectal examination, Immunohistochemistry, therapeutic challenges.**

I. INTRODUCTION

Melanoma is a malignant melanocytic neoplasm [1]. It arises mainly in the skin, but it can arise rarely as a primary neoplasm in other locations such as uvula of the eye, nervous system, gastrointestinal tract (GIT), and genitourinary tract. Anorectal melanoma (ARM) represents only 1.3% of all melanomas in general [2] and <1% of all colorectal malignancies [1]. It is a highly aggressive tumor with poor prognosis since its 5-year survival rate is <10% [2]. This low survival is due to the late diagnosis of most tumors and aggressive biology of ARM [3]. When these tumors are recognized, they are often misdiagnosed as hemorrhoids or other benign anorectal pathology [4]. National Clinical Cancer Network (NCCN) guidelines on melanoma do not currently include recommendations for treatment of ARM [5]. Without guidelines, and due to the rare nature of the tumor, no clear treatment strategy has emerged as the gold standard for treatment of this rare but aggressive disease.

II. CASE REPORT

We report a case of PARM in a 65-year-old man presenting rectal pain during 3 months with occasional bleeding. The patient was in good condition with no weight loss and past medical and family history unremarkable.

LEMSANES Siham, Department of Oncology, National Institue of Oncology, Rabat, Morocco
HARRAK Soukaina, Department of Oncology, National Institue of Oncology, Rabat, Morocco
NAJEM Salma, Department of Oncology, National Institue of Oncology, Rabat, Morocco

Physical examination revealed a solid polypoid hyperemic palpable mass in the anorectal canal resembling hemorrhoids. Flexible sigmoidoscopy revealed a smooth, 3- × 2-cm dark brown nodule at the anorectal canal.

Excisional biopsy was performed and sent for histopathologic evaluation. Sections of the biopsy specimen demonstrated an ulcerated, multinodular pigmented epithelioid and spindled neoplasm with extensive necrosis involving the anal skin and mucosal interface. Immunohistochemical staining was strongly and diffusely positive for HMB-45 and Melan A and multifocally positive for S100, confirming the diagnosis of malignant melanoma.

Computed tomographic (CT) imaging of the chest, abdomen, and pelvis showed anorectal process (figure 1) and metastasis to the liver and lung. Oncology was consulted and the patient was started on immunotherapy with Pembrolizumab. Unfortunately, the patient succumbed to metastatic disease and passed away in six months.

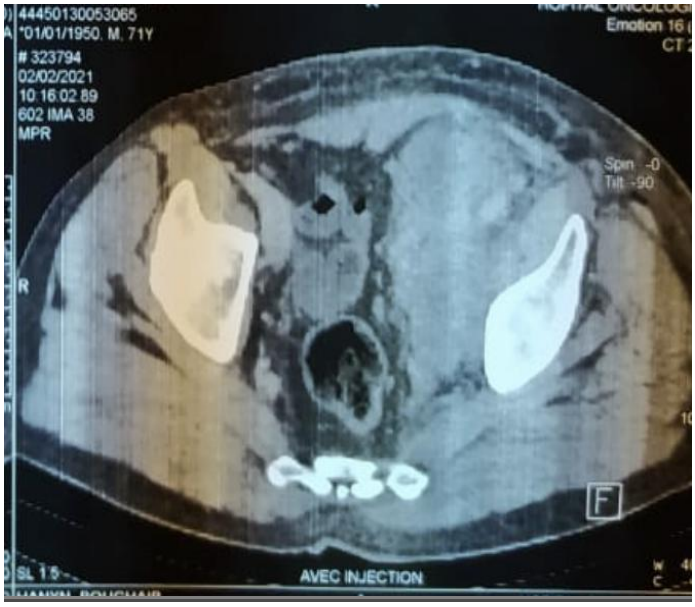

Figure 1: Abdomino-pelvic computed tomography (CT) showing an anorectal process

III. DISCUSSION

Anorectal melanoma is a rare disorder and an extremely aggressive tumor. About 1% of all anorectal carcinomas are melanomas. In fact, it is a fatal disease since the patients have 2-year period and 6-month period mean survival without and

with the presence of metastasis, respectively, regardless of the treatment [1,6]. In most cases, the cause of death is mostly due to the distant metastasis [1]. Mucosal melanoma tends to develop later in life relative to cutaneous melanoma, with a median age at diagnosis of 70 versus 55 years [7-9]. Unlike cutaneous melanoma, the risk factors for anorectal melanoma are largely unknown. Epidemiologic data suggest that there is an increased risk among women, Caucasians, patients with human immunodeficiency virus, activating mutations in KIT, and a personal or family history of melanoma [10,9, 11-13]. Up to 30 percent of anorectal melanomas can be amelanotic and, thus, are often widely metastasized at the time of initial diagnosis [14].

Lymphatic spread to the inguinal, inferior mesenteric, hypogastric or para-aortic nodal is common [13]. Most patients with distant metastases have hepatic metastases, followed by pulmonary and bone metastases [15,16].

Clinically, most of the anorectal melanoma cases are presented with bleeding per rectum [1,17]. Other signs and symptoms include anorectal pain, tenesmus, pruritus, changes in bowel habits, and sings and symptoms related to the metastasis [1,2,4]. Since anorectal melanoma share the same signs and symptoms of some common inflammatory and neoplastic anorectal lesions [1,2,17], the diagnosis of such disease is extremely difficult and needs a high index of suspicion [1,18].

The initial evaluation of patients with anorectal melanoma should include a total body skin check to rule out a primary cutaneous melanoma that has metastasized [3]. A careful rectal examination should be performed.

Radiological studies are helpful tools in evaluating the original neoplasm, the presence of possible metastasis, and the therapeutic response of the neoplasm to the treatment; however, it cannot be used to confirm the diagnosis [2].

Endoscopically, most of the cases arise at the transitional zone between the rectum and the anal canal [1] and there is no major difference between those originate from the rectum, and those originate from the anal canal regarding the survival rate [19].

Grossly, the tumor is usually present as a large, expensive nodular mass with variable involvement of anal squamous epithelium and rectal mucosa [20]. The presence of melanin pigment may help in the diagnosis histologically and both pigmented and amelanotic melanoma are reported in the literature [21−24]. Variable histomorphology like epithelioid, spindle-cell, pleomorphic, and small round cells either alone or in combination are reported [25,22, 24].

Hence, routine haematoxylin & eosin (H&E) stain may not be determiner enough to reaffirm the diagnosis of ARM [22]. 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 [26,21,25,22-24].

The various mimickers of ARM can be epithelioid sarcoma, spindle cell sarcoma, gastrointestinal stromal tumor, lymphoma, small round cell sarcoma, and undifferentiated adenocarcinoma [21,25, 22,24].

Patients without lymph node metastasis have a survival advantage with a 5-year survival rate of 20 versus 0% in patients with metastasis. Survival of patients with recurrent or metastatic disease is <10 months [27]. There is an important deterioration of the prognosis for tumors superior to 20 mm. A worse prognosis was also associated with tumour thickness, tumour necrosis and perineural invasion [28]. An amelanotic lesion has a worse prognosis [29].

Sarac et al observed that genital mucosal melanomas had the most favorable and ARM had the worst outcome [30]. 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 [30].

The management plan is different from case to case since there is no specific guideline for those conditions due to their rarity [2]. Different treatment modalities were used in those patients, including surgery (both wide local excision and abdominoperineal resection), chemotherapy, radiotherapy, and targeted therapy, but none of them shows improvement regarding to the survival of the patients [1,2].

At the time of diagnosis, up to one-third of patients have metastatic disease [31]. For these patients, treatment with radiation or chemotherapy might be an option.

There is currently no standard systemic chemotherapy regimen that exists for metastatic anorectal melanoma.

The use of targeted therapy has revolutionized the treatment of cutaneous melanoma. As in cutaneous melanoma, 3 to 15 percent of mucosal melanomas harbor the BRAF V600 mutation, and thus, might respond well to combined BRAF and MEK inhibition [32].

There are limited data on the use of immunotherapy in patients with anorectal melanoma. In a retrospective study using National Cancer Database (NCDB) data from 2004 to 2015, two-year overall survival was significantly improved for patients receiving immunotherapy versus not (49.21% vs. 42.47%; p=0.03), but the percentages of patients alive at five years were not significantly different between the two groups [33]. Furthermore, a retrospective study by Shoushtari et al [34] showed that response rates to programmed cell death receptor (PD-1) blockades in patients with mucosal melanomas were comparable to the response rates observed for cutaneous melanoma. There have not yet been studies looking at PD-1 blockade usage specifically for anorectal melanomas, but the response rates for other mucosal melanomas is promising.

IV. CONCLUSION

Anorectal melanoma is an extremely rare subtype of melanoma with a poor prognosis. This disease entity presents significant diagnostic and therapeutic challenges. To avoid diagnostic pitfalls, early detection is key and should always be in the differential diagnosis of benign and malignant lower gastrointestinal disorders. Without good evidence to drive treatment decisions, surgical and non-surgical management remains highly variable across the world. With the use of personalized molecular analysis, all patients with anorectal melanoma should have their tumors assayed for the presence of gene mutations. In the future, randomized controlled studies comparing different treatment modalities for anorectal melanomas are needed to determine optimal management and therapeutic protocols.

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