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A Case Report of Metastatic Melanoma to the Bladder

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Abstract: *Objective:* The objective of this report is to present the case of metastatic melanoma to the bladder, a rare and underdiagnosed condition due to its often asymptomatic characteristic. *Case presentation:* The case was a 62-year-old female patient, with a history of melanoma at the level of the first toe, with surgical and pharmacological management. The reason for consultation was hematuria. Cystoscopy revealed a single solid, erythematous lesion with necrosis and easy bleeding, and transurethral resection (TUR) was indicated. The pathology found metastatic ulcerated melanoma. Second-line treatment (pembrolizumab) was started and presented progression to the upper limbs and relapse at the bladder level. The patient died a year later. *Discussion:* Melanoma metastases to the genitourinary tract are common, but isolated bladder metastases are rare. Treatment is usually TUR of the lesion, cystectomy, chemotherapy, and radiation therapy. TUR is curative for lesions restricted to the epithelium, although radical cystectomy is usually the therapy of choice in patients with a localized tumor. Pembrolizumab has been shown to increase survival. The prognosis depends on the size and depth of the invasion. *Conclusion:* Metastatic cancer to the bladder is rare and underdiagnosed, it may be present in patients with melanoma, nonspecific urinary irritative symptoms, and hematuria. It tends to have a poor prognosis, and requires surgical treatment associated with systemic management.

Keywords: Melanoma; Neoplasm metastasis; Urinary bladder neoplasms; Hematuria; Urology

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1. Introduction

Melanoma is the best-known presentation of skin cancer. Metastatic melanoma to the bladder is rare, constituting less than 2% of cases [1,2]. However, in autopsies performed on patients with melanoma, bladder metastases have been found in 18–37% of cases [3,4], having the second highest incidence after gastric adenocarcinoma [5]. Metastatic melanoma to the bladder occurs in patients between 44 and 81 years old and no gender prevalence has been demonstrated [6].

Melanoma metastases to the genitourinary tract are frequent, but isolated bladder metastases are rare [7],

which suggests that the incidence is higher than believed. This is explained by the fact that most patients are asymptomatic, although hematuria is present in 15% of cases, being the most frequent form of clinical presentation [8].

The objective of this report is to present the case of metastatic melanoma to the bladder, an infrequent and underdiagnosed condition due to its asymptomatic characteristic.

2. Case presentation

The case was a 62-year-old female patient with a history of melanoma at the level of the first joint of the right foot that required disarticulation in 2011 with subsequent progression to the right thigh, which required inguinofemoral lymphatic draining and pharmacological management in August 2018 with pembrolizumab.

She consulted urology in September 2018 for macroscopic hematuria of one month of evolution. The patient denied having urinary irritative or obstructive symptoms as well as constitutional symptoms and had no significant toxicological history other than those reported for baseline disease.

A urinary tract ultrasound was performed which reported a solid lesion dependent on the right bladder wall measuring 1.5 x 1.5 x 1.2 cm. Cystoscopy showed a single rounded lesion, solid in appearance, at the level of the left lateral wall; the approximately 2 cm lesion was erythematous, with areas of necrosis, very congestive and easy to bleed. Its implantation base was small and not pedunculated.

It was decided not to perform cold forceps biopsy because there was a significant risk of hematuria. Instead, transurethral resection (TUR) of the lesion was indicated. The procedure was performed without complications. **Figure 1** shows the TUR findings.

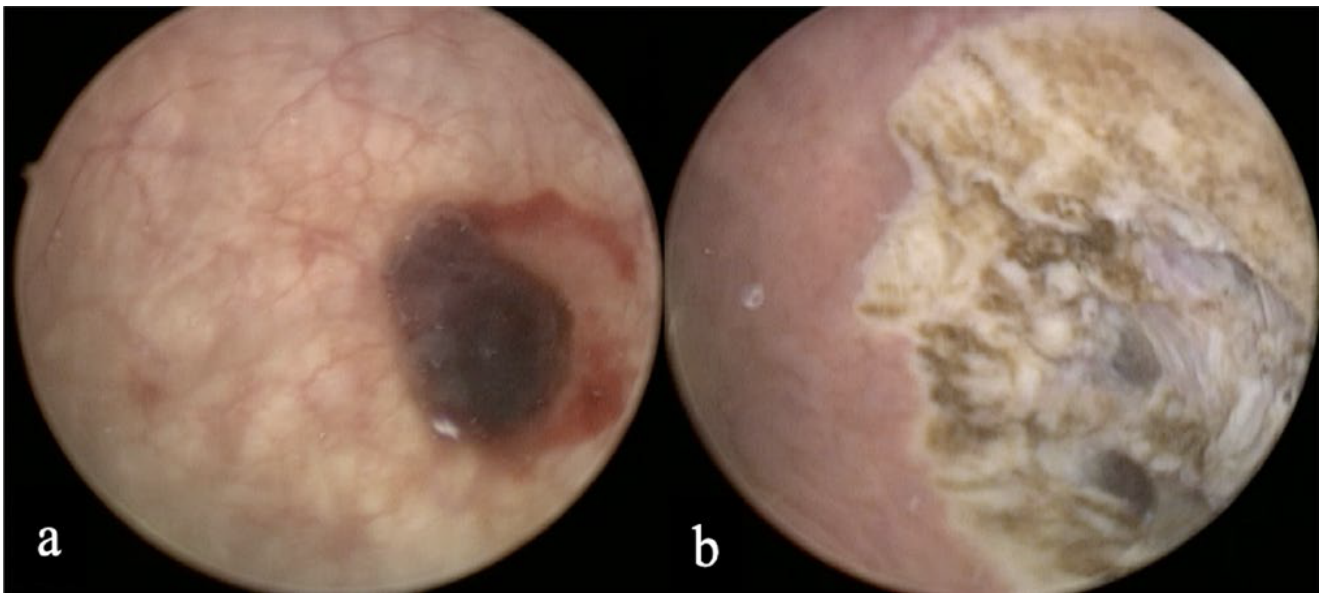

Figure 1. TUR findings a) Pre-resection with a single rounded lesion of solid appearance at the level of the left lateral wall; it was approximately 2 cm, erythematous, with areas of necrosis, very congestive, with easy bleeding, small implantation base, and not pedunculated. b) Post-resection of the lesion.

The pathology report demonstrated pathologic findings of a malignant tumor lesion, consisting of cells with atypical vesicular nuclei, prominent nucleolus, and intracytoplasmic melanic pigment. The lesion ulcerated the urothelium (**Figure 2**).

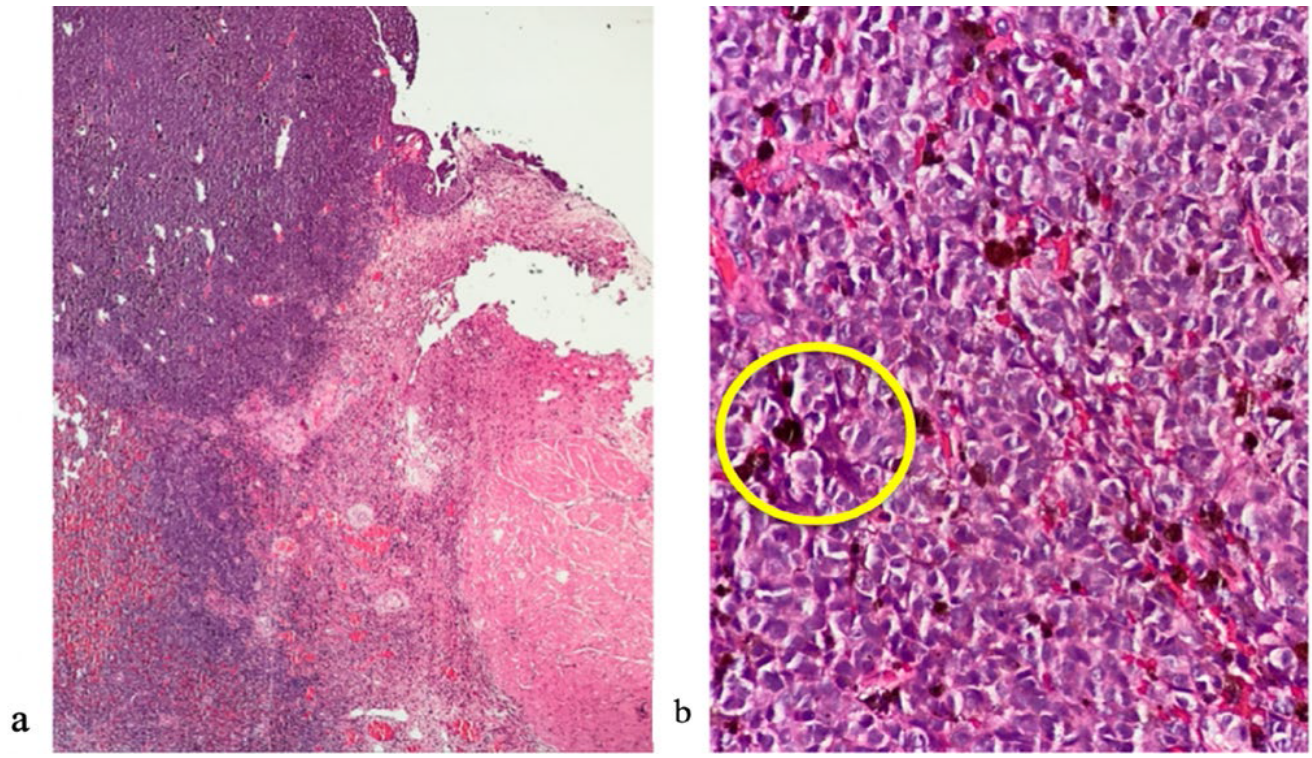

Figure 2. Histopathologic findings a) Hematoxylin & eosin 4x. There is urothelium and muscularis propria on the right side, and a malignant tumor lesion that ulcerates the epithelium on the left. b) Hematoxylin & eosin 40x. Tumor lesion is constituted by cells of atypical vesicular nuclei with prominent nucleolus and intracytoplasmic melanic pigment (yellow circle).

With these findings, it was decided that clinical oncology would manage the case, which decided to initiate second-line therapy with pembrolizumab. Despite this management, the patient presented with progression of the disease to upper limbs and recurrence at bladder level at 7 months postoperatively. She did not present new episodes of hematuria and died in August 2019 due to metastatic involvement of the disease. The patient died outside the institution, so communication was maintained with her relative who confirmed her death due to sequelae of the disease.

3. Discussion

Metastatic melanoma to the bladder is a rare and underdiagnosed condition because not all patients present associated symptoms that allow suspicion of metastatic involvement in the bladder, as in the previously reported case.

Dasgupta and Brasfield found that, in autopsies of 125 patients with melanoma, there was 18–37% of metastatic disease to the bladder [4]. Likewise, Ganem and Batal reviewed 80 cases of metastatic spread to the bladder from distant foci and found that 22.5% were secondary to melanoma, with melanoma being second in incidence only to gastric adenocarcinoma [3].

To date, less than 20 cases of primary bladder melanoma have been reported in the literature [6,8]. Regarding symptomatology, it is known that most patients are asymptomatic and only 15% present hematuria, its most frequent form of presentation [5,9]. For this reason, for patients with a previous history of melanoma who develop

voiding syndrome (dysuria, difficulty urinating, urinary urgency, pollakiuria or nocturia) and hematuria, it is recommended that endoscopic studies be performed to exclude metastatic involvement at the bladder level [8-11]. Autopsy studies have shown that up to 18% of patients with metastatic disease have unknown bladder involvement [12]. No information or studies based on Colombian or Latin American population were found within the selected articles.

At the time of cystoscopy, a single lesion with an implantation base or several lesions such as small, pigmented, and elevated nodules covering the urothelium, as found in the patient, may be evidenced [10,13]. Histopathologically, atypical melanocytic cells similar to the primary tumor are evident. The diagnosis can only be confirmed with the morphology and the positive brownish Masson-Fontana pigments [1,14].

The treatment proposed for these cases is transurethral resection of the lesion, partial cystectomy, radical cystectomy, chemotherapy, and radiotherapy. TUR is curative for lesions restricted to the epithelium [14,15], although most authors conclude that radical cystectomy is the therapy of choice for a patient with a localized tumor, since this type of tumor tends to recur after local excision [16].

PD-L1 (programmed death-ligand 1) is an immune checkpoint protein with PD-L1 and PD-L2 ligands that interact on the lymphocyte membrane and suppress T-cell activity. Two anti-PD-1 monoclonal antibody drugs (nivolumab and pembrolizumab) have been developed and are used as second-line treatments, which have demonstrated immune modulation that can translate into objective tumor responses in 30% of patients and long-term benefit in responders [17]. Pembrolizumab has been shown to improve survival in patients with metastatic melanoma who have not responded to other treatment schemes [17-19].

The choice of treatment should be based on prognosis, health status, presence or absence of local symptoms, and depth and size of the lesion. In the present case, apart from TUR, clinical oncology decided to initiate second-line treatment with pembrolizumab, since the patient presented tumor relapse while on nivolumab.

The prognosis depends on the size and depth of the invasion [14], the mean survival is usually between 6 and 7.5 months and never exceeds 3 years [8,20]. The patient presented progression of the disease to the upper limbs and recurrence at the bladder level in 7 months, with death 12 months after consulting urology.

4. Conclusion

Metastatic melanoma to the bladder is a rare and underdiagnosed disease, since very few patients present with associated symptoms. It should always be suspected in patients with a history of melanoma and non-specific urinary irritative symptoms and hematuria. For this reason, cystoscopy is recommended in all symptomatic patients with a history of melanoma. Metastatic melanoma to the bladder usually has a poor prognosis and requires surgical management with TUR (as in the reported case) or cystectomy, associated with systemic management.

Primary melanoma of the genitourinary tract is extremely rare and represents 0.2% of all melanomas. Less than 20 cases of primary melanoma of the bladder have been reported in the literature up to 2013. Its diagnosis must be confirmed with immunohistochemistry, and its treatment consists of radical cystectomy. However, it has a poor prognosis, with a high mortality rate within the first 3 years.

Disclosure statement

The authors declare no conflict of interest.

Consent for participation

The patient's authorization was obtained by means of an informed consent form.

Consent for publication

For the publication of this article, the patient authorized the manipulation of the data for academic research purposes according to resolution 8430 of 1993.

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