

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Metastatic malignant melanoma mimicking urinary bladder mass – a rare presentation

Mirjana Živojinov^{1,2}, Aleksandra Ilić^{1,2}, Tanja Lakić^{1,2}, Ivana Stanišić², Željka Panić³¹University of Novi Sad, Faculty of Medicine, Department of Pathology, Novi Sad, Serbia;²Clinical Center of Vojvodina, Center for Pathology and Histology, Novi Sad, Serbia;³University of Business Academy in Novi Sad, Faculty of Pharmacy, Novi Sad, Serbia**SUMMARY**

Introduction Melanoma is a solid aggressive tumor characterized by the malignant transformation of melanocytes. To date, only about 35 primary and about 30 metastatic malignant melanomas of the bladder have been reported.

Our objective is to report a rare case of secondary tumor of urinary bladder.

Case outline A 57-year-old man presented to the Urologic Clinic due to lower urinary tract symptoms. The urologist indicated transurethral resection (TUR). His medical history was significant for cutaneous malignant melanoma resected 3 years prior, which were localized at scapular region on the left side. Microscopic examination of the TUR specimen showed several fragments of ureter mucosa with presence of tumor and focally with normal urothel. Tumor cells were markedly atypical and polygonal in a solid pattern. The nuclei were large with variation in size and prominent eosinophilic nucleoli. Also, there were present areas with abundant brown pigment. Immunohistochemical analysis of tumor cells showed positivity for Melan A and HMB45 and negativity for GATA3. Molecular analysis showed that *BRAF* was mutated.

Conclusion The incidence of malignant melanoma is high and increasing, but the urinary bladder is a rare location of metastasis. However, both primary and metastatic melanomas can occur in the bladder, so the urologist and the pathologist have to consider it when it is the primary site of onset, or when it represents the first symptomatic metastasis.

Keywords: melanoma; metastasis; urinary bladder

INTRODUCTION

Melanoma is a solid aggressive tumor characterized by the malignant transformation of melanocytes, melanin producing cells in the basal layer of the epidermis. The incidence and mortality rate are high and tend to increase [1, 2].

Overall, metastatic disease to the bladder is unusual, with only 2% of bladder cancer cases representing metastasis [3].

To date, only about 35 primary and about 30 metastatic malignant melanomas of the bladder have been reported [4, 5]. However, on autopsy series of patients with extra-regional disease, 18–37% also had metastases in the bladder [6, 7].

When it occurs, the main complaints are hematuria or lower urinary tract symptoms, urinary retention or dysuria [6, 8, 9].

Our objective is to report a rare case of secondary tumor of urinary bladder.

CASE REPORT

A 57-year-old man presented to the Urologic Clinic due to lower urinary tract symptoms. The urologist indicated transurethral resection (TUR). His medical history was significant for cutaneous malignant melanoma resected three years prior, which were localized at the scapular

region on the left side. The melanoma was 2.8 cm in diameter and 2.6 cm deep (Breslow IV, Clark III). The tumor was widely resected, with negative surgical margins. Thereafter the patient underwent sentinel lymph node biopsy, which proved negative.

Microscopic examination of the TUR specimen showed several fragments of ureter mucosa with presence of tumor and focally with normal urothelium. Tumor cells were markedly atypical and polygonal in a solid pattern. The nuclei were large, with variations in size and prominent eosinophilic nucleoli. Separately, there were polypoid fragments of tumor. Also, there were present areas with abundant brown pigment (Figure 1).

Immunohistochemical analysis of tumor cells showed positivity for Melan-A and HMB-45 and negativity for GATA3 (Figure 2). The patient underwent further imaging studies. Computed tomography of the chest, abdomen and pelvis was negative for dissemination of the disease.

Molecular analysis showed that *BRAF* was mutated.

This case report was approved by the institutional ethics committee, and written consent was obtained from the patient for the publication of this case report and any accompanying images.

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Correspondence to:

Aleksandra Ilić
Hajduk Veljkova 3
21000 Novi Sad, Serbia
aleksandra.m.ilic@mf.uns.ac.rs

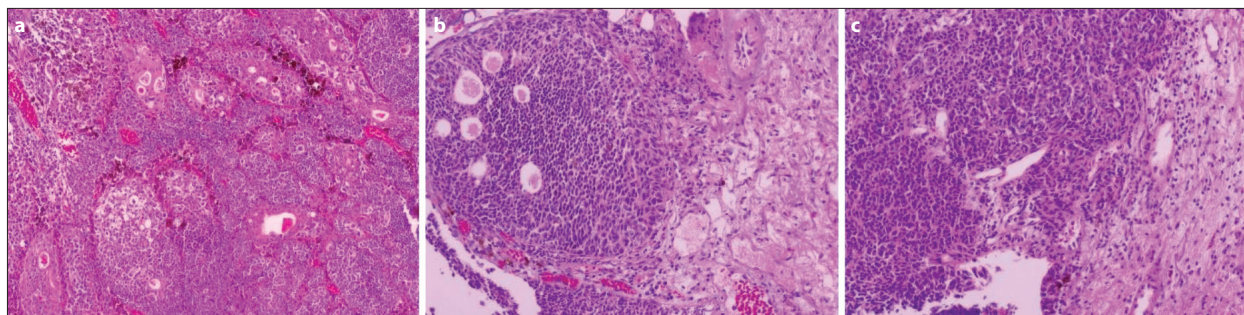


Figure 1. Metastatic malignant melanoma of the urinary bladder; a) H&E; 100 ×; b) H&E; 200 ×; c) H&E; 200 ×

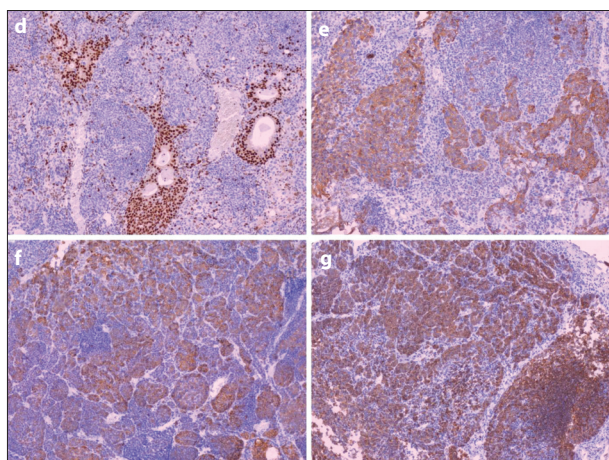


Figure 2. Metastatic malignant melanoma of the urinary bladder; d) GATA3 immunonegativity in the tumor cells; 100 ×; e) HMB-45 immunonegativity in the tumor cells, 100 ×; f) HMB-45 immunopositivity in the tumor cells, 100 ×; g) Melan-A immunopositivity in the tumor cells, 100 ×

DISCUSSION

Malignant melanoma is a highly aggressive tumor with an incidence that continued to rise in the past 30 years. It is the deadliest skin cancer, accounting for up to 60% of skin cancer-related deaths, primarily due to rapid proliferation and metastasis [10].

Melanoma can metastasize to any part of the body, but it has predilection for the skin, the lungs, the liver, and the brain, while metastases to the bladder in clinical series appear to be rare, with only about 30 reported cases in the literature [3, 4, 6]. In contrast, autopsy series indicate an 18–37% incidence of the metastatic disease in the bladder [6, 7].

Meunier et al. [11] reviewed the published data and confirmed the previously reported 23 cases of metastatic melanoma. However, some authors consider that the reason for this small number of cases is due to the fact that metastatic melanoma is often seen only at autopsy, as a result of its asymptomatic nature [3].

A study by Dasgupta and Brasfield [12] from 1964 showed that 18% of patients with melanoma had bladder

metastasis on autopsy, further validating the notion that secondary melanoma of the bladder might be relatively more common than was originally thought [3].

Diagnosis of metastasis of melanoma of the urinary bladder is based on immunohistochemical confirmation of a morphological suspicion using melanoma tumor markers. Sometimes the hematoxylin and eosin appearance can be very deceptive; for example, melanotic malignant melanoma of the bladder can have many features in common with a high-grade urothelial carcinoma, leading to misdiagnosis. Also, it is important to differentiate metastatic melanoma of the bladder from primary melanoma of the bladder, for which the following criteria have been used: (1) detailed history ruling out cutaneous, regressed, or visceral melanoma; and (2) recurrence pattern consistent with the primary origin of melanoma [3, 4, 13].

On the other hand, lesions that can mimic melanoma of the bladder both clinically and cystoscopically include melanosis and pseudomelanosis (lipofuscinosis and hemosiderosis) of the bladder, which can be differentiated only by careful histological examination [4].

Several treatments for malignant melanoma metastatic to the bladder are available, considering the performance status of the patient, the anatomic location of the metastases, the existence of bladder symptoms, and the life expectancy. Radical cystectomy is an aggressive approach, while conservative options include TUR and partial cystectomy. Also, systemic chemotherapy is reported as an adjunct to endoscopic resection and should be limited to patients with good performance status [9].

According to some studies, *BRAF* mutation is present in 50% of malignant melanomas and is associated with poor prognosis. Targeted therapies, including *BRAF* inhibitors, have been shown to improve response rates, but not durably [5, 14, 15].

The incidence of malignant melanoma is high and increasing, but the urinary bladder is a rare location of metastasis. However, both primary and metastatic melanomas can occur in the bladder, so the urologist and the pathologist have to consider when it is the primary site of the onset and when it represents the first symptomatic metastasis.

Conflict of interest: None declared.

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Метастаза меланома као туморска маса у мокраћној бешици – редак случај

Мирјана Живојиновић^{1,2}, Александра Илић^{1,2}, Тања Лакић^{1,2}, Ивана Станишић², Жељка Панић³

¹Универзитет у Новом Саду, Медицински факултет, Катедра за патологију, Нови Сад, Србија;

²Клинички центар Војводине, Центар за патологију и хистологију, Нови Сад, Србија;

³Универзитет Привредна академија у Новом Саду, Фармацеутски факултет, Нови Сад, Србија

САЖЕТАК

Увод Меланом је солидан агресивни тумор који настаје малигном трансформацијом меланоцита. До данас је забележено само око 35 примарних и око 30 метастатских малигнух меланома мокраћне бешике.

Циљ рада је приказати редак случај метастатског тумора мокраћне бешике.

Приказ болесника Мушкарац стар 57 година јавио се на Клинику за урологију због симптома у доњем уринарном тракту. Уролог је индиковио трансуретралну ресекцију. Из његове историје болести сазнали смо да је имао ресекцију кожног малигнух меланома пре три године, који је био локализован у пределу леве скапуле. Микроскопски преглед узорка трансуретралне ресекције показао је неколико фрагмената слузнице уретера са присуством тумора и фокално

са нормалним уротелом. Туморске ћелије су биле изразито атипичне и полигоналне, са великим и плеоморфним једрицама и проминентним еозинофилним нуклеолусима. Такође, постојала су подручја са обилним смеђим пигментом. Имунохистохемијска анализа туморских ћелија показала је позитивност на Мелан А и *HMB45* и негативност на *GATA3*. Молекуларна анализа је показала да је *BRAF* мутиран.

Закључак Иако је инциденца меланома висока, са тенденцијом пораста, мокраћна бешика је веома ретка локализација метастаза. Међутим, како се и примарни и метастатски меланоми могу јавити у бешици, уролог и патолог треба да размотре да ли је примарна болест или представља први симптом метастатске болести.

Кључне речи: меланом; метастаза; мокраћна бешика