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Case Report / Приказ болесника

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**Metastatic malignant melanoma mimicking urinary bladder mass
– a rare presentation**

Метастаза меланома као туморска маса у мокраћној бешици –
ретка презентација

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Metastatic malignant melanoma mimicking urinary bladder mass – a rare presentation

Метастаза меланома као туморска маса у мокраћној бешици – ретка презентација

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 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

САЖЕТАК

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

Циљ рада је приказати редак случај метастатског тумора мокраћне бешике.

Приказ болесника Мушкарац стар 57 година јавио се на Уролошку клинику због симптома болести доњег уринарног тракта. Уролог је индиковао трансуретралну ресекцију (ТУР). Из његове историје болести сазнали смо да је имао ресекцију кожног малигног меланома пре 3 године, који је био локализован у пределу леве скапуле. Микроскопски преглед узорка ТУР 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 једрима и проминентним еозинофилним нуклеолусима. Такође, била су присутна подручја са обилним смеђим пигментом. Имунохистохемијском анализом, туморске ћелије су показале позитивност на Мелан А и ХМБ45 и негативност на ГАТА3. Молекуларна анализа је показала да је БРАФ 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.

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 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. The melanoma was 2,8cm in diameter and 2,6cm depth (Breslow IV, Clark III). Tumor was widely resected with negative surgical margins. Then patient went sentinel lymph node biopsy which turned out negative.

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. 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 HMB45 and negativity for GATA3 (Figure 2). Patient went further imaging studies. Computed tomography (CT) 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.

DISCUSSION

Malignant melanoma represents 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 skin, lungs, liver and brain while metastasis 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 metastatic disease in the bladder [6, 7].

Meunier *et al* reviewed the published data and confirmed 23 cases of metastatic melanoma which have been reported [11]. However, some authors thought that the reason for this small number data is because metastatic melanoma is often seen at autopsy owing to its asymptomatic nature [3].

A study by Dasgupta and Brasfield in 1964 showed that 18% of patients with melanoma had bladder metastases on autopsy, further validating the notion that secondary melanoma of the bladder might be relatively more common than was originally thought [3, 12].

Diagnosis of metastasis of melanoma of the urinary bladder is based on immunohistochemical confirmation of a morphological suspicion using melanoma tumor markers. Sometimes the haematoxylin 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 and the following criteria have been used: (1) detailed history ruling out cutaneous, regressed, or visceral melanoma; and (2) recurrence pattern that is 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 transurethral resection 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 studies, the BRAF mutation is present in 50% of malignant melanomas and is associated with a bad 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 it when it is the primary site of onset, or when it represents the first symptomatic metastasis.

Conflict of interest: None declared.

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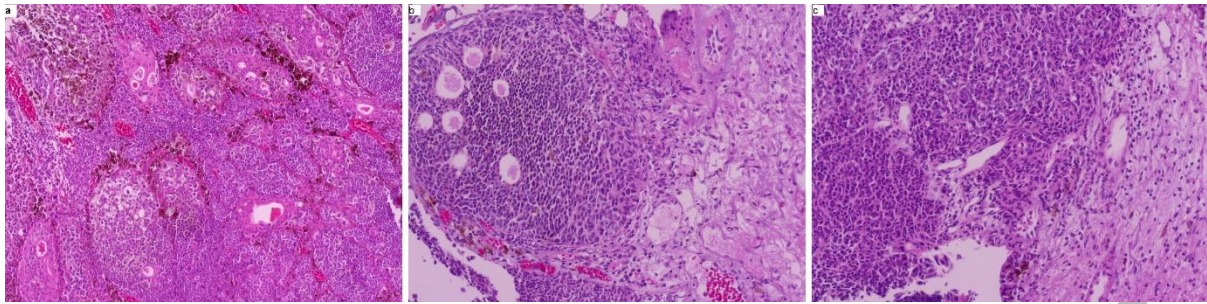


Figure 1. Metastatic malignant melanoma in the urinary bladder, a) H&E; 100 ×; b) H&E; 200 ×; c) H&E; 200 ×.

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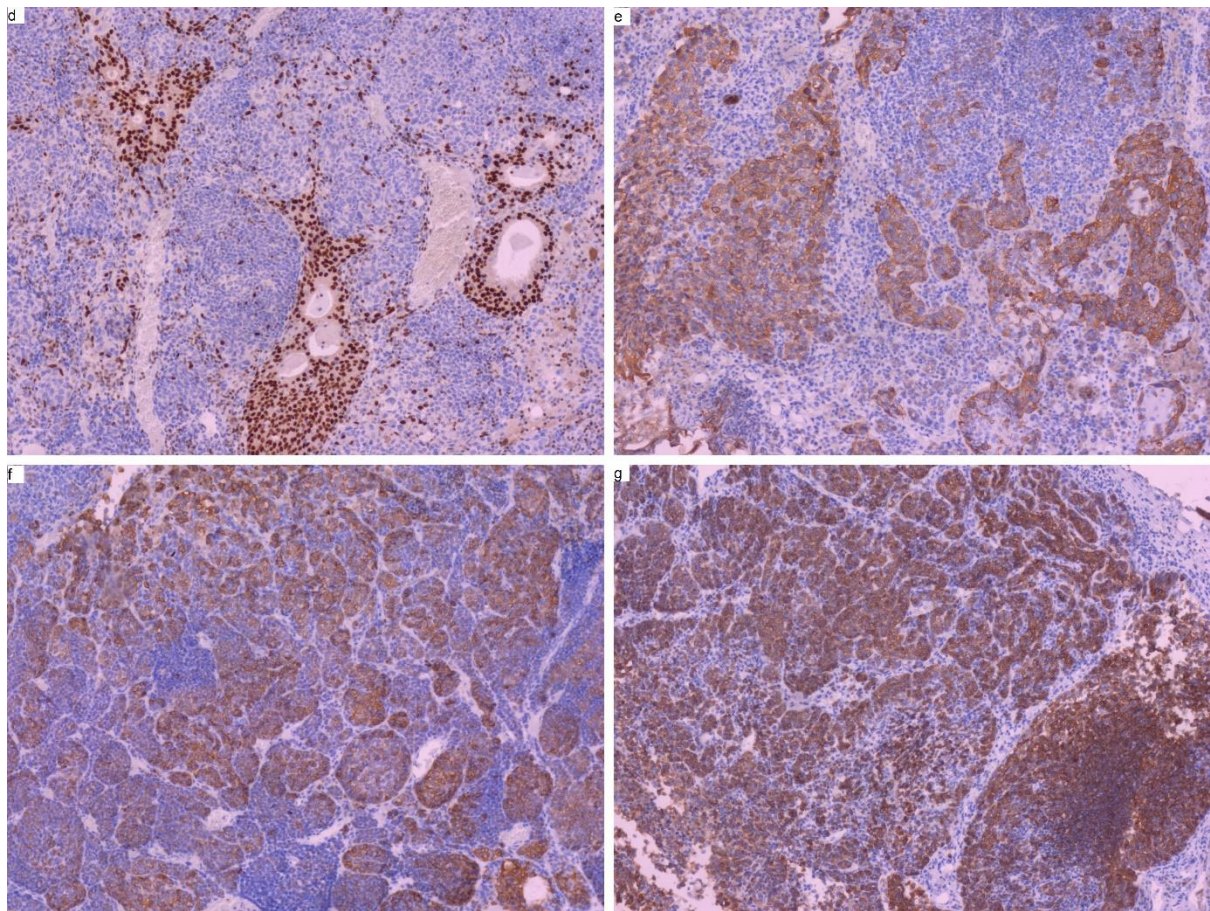


Figure 2. Metastatic malignant melanoma in the urinary bladder: d) GATA 3 immunonegativity in the tumor cells; 100 ×; e) HMB45 immunopositivity in tumor cells, 100 ×; f) HMB45 immunopositivity in tumor cells, 100 ×; g) Melan A immunopositivity in tumor cells, 100 ×