Metastatic Malignant Melanoma of the Urinary Bladder: A Case Report and Review of Literature

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ABSTRACT

Objective: Metastatic malignant melanoma of the urinary bladder is extremely rare in clinical practice, herein, we review literature to demonstrate epidemiology, management and prognosis of this rare condition.

Case presentation: A 57-year-old male with history of malignant melanoma of left big toe was referred to the urology division with the complaint of intermittent painless gross hematuria. Cystoscopy revealed multiple bladder masses, hence transurethral resection of bladder tumor was performed. Histologic and immunohistochemical examination revealed metastatic malignant melanoma involving urinary bladder mucosa.

Conclusion: Suspicion of metastasis should be raised in a patient with urinary symptom, especially if the history of malignant melanoma is present. Cystoscopy and biopsy is recommended if metastatic disease is suspected. While long-term survival is poor, management should be individualized according to the patient's conditions, symptoms and severity of disease.

Keywords: Malignant melanoma; metastasis; urinary bladder (Siriraj Med J 2018;70: 254-259)

INTRODUCTION

Metastatic malignant melanoma of the urinary bladder is extremely rare in clinical practice with just thirty two confirmed cases reported in English-language literature. However, a study in autopsy series by Dasgupta et al., showed that 18% of patients with melanoma had bladder metastasis.[1] This indicates that the incidence is likely higher than previous thought and may be due to the fact that many patients are asymptomatic. Due to unusual variety in clinical presentation, its diagnosis may be difficult for most urologists. Besides, this metastatic type shows worse prognosis. This poses significant challenges in diagnosis and management. We report a case of metastatic malignant melanoma to the bladder that presented as intermittent gross hematuria. We also review literature of PubMed with a focus on metastatic malignant melanoma to the bladder. To our knowledge, there were a small number of reported cases in Asian population and this is the first reported case in Thailand.

CASE PRESENTATION

A 57-year-old man previously diagnosed with malignant melanoma of left big toe five months ago, had undergone wide local excision and left groin node dissection. The pathologic findings revealed melanoma with 8-mm tumor thickness, Clark's level IV, negative margin and nodal metastasis. He presented with intermittent, painless gross hematuria for 2 months. Computed tomography of the brain, chest and abdomen revealed multiple pulmonary nodules and a 3.2 cm space occupied by lesion/mass at the posterior wall of urinary bladder.

He subsequently underwent cystoscopy, revealing multiple dark blue/black-pigmented solid nodular lesions on the posterior wall, and was treated with complete

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transurethral resection (Fig 1). Pathological examination confirmed it to be malignant melanoma (Fig 2). As a result, diagnosis of stage IV malignant melanoma of left big toe with metastasis to urinary bladder was made. Due to the multi-organ distant metastatic condition of the patient, the multidisciplinary team consensus was palliative chemotherapy. He received 4 cycles of carboplatin and paclitaxel every three weeks. After the fourth cycle, the disease was stable. However, the patient was lost to follow up eight months post diagnosis.

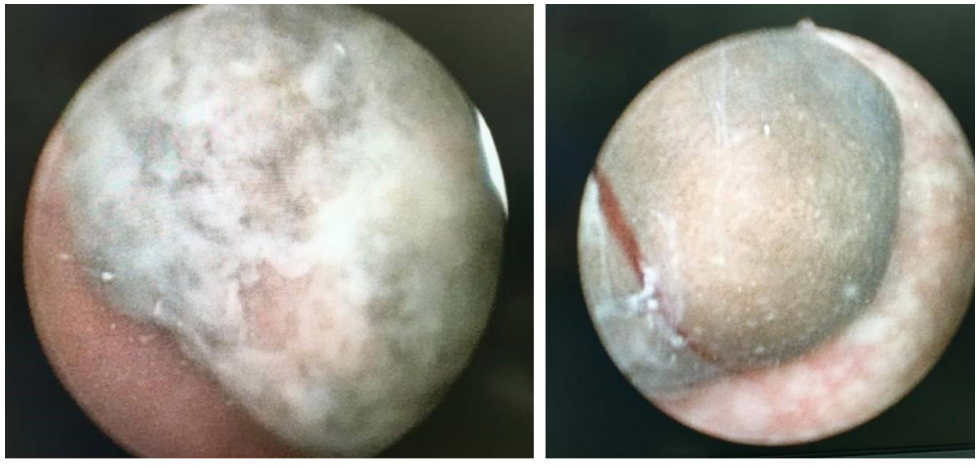

Fig 1. Cystoscopy revealed a large nodular mass (3 cm) with brown pigmentation at right posterolateral wall of bladder (A) and satellite lesion at posterior wall (B).

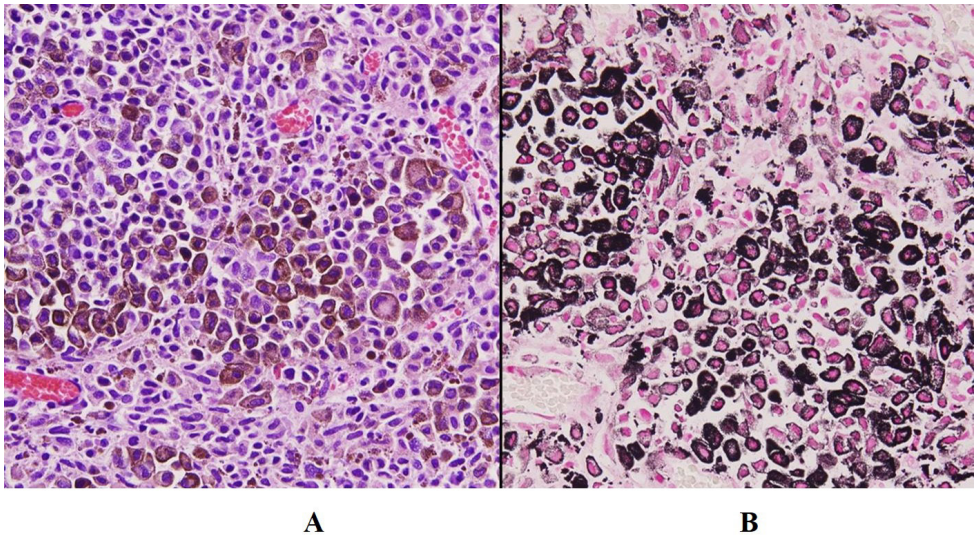

Fig 2. (A) H&E section shows pleomorphic cells with granular eosinophilic cytoplasmand hyperchromatic nuclei. Many cells contain dark brown pigments. (x40) (B) Masson-Fontana stainhighlights melanin pigments in black color. (x40)

DISCUSSION

Metastatic tumors to the urinary bladder are rare; with accounts only about 2 %.[2] They are often categorized as direct extension of tumor from surrounding organs, distant metastasis, and infiltration by lymphoma/leukemia. The most common primary sites of metastasis are prostate, colorectum and cervix. Breast, lung, and skin primaries are less common sources. Primary malignant melanoma is known to occur very rarely in the urinary tract, especially in the bladder. However, metastases of malignant melanoma to the genitourinary tract are relatively common. Therefore, it is very important to distinguish primary from secondary melanomas of the bladder. No evidence of other melanomas and presence of atypical melanocytes at the bladder margin are diagnostic criteria for primary bladder tumor. Metastatic malignant melanoma of the bladder is a rare occurrence in clinical practice with only thirty two other cases of this diagnosis which have been reported in the English literature (Table 1). However, the autopsy series of metastatic melanoma

TABLE 1. Review of English-language literature of metastatic melanoma to the bladder.

Authors	Year	Age	Sex	Primary site	Presenting symptom	Synchronous metastasis	Treatment	Survival
Amar[6]	1964	33	M	Neck	Hematuria	Maxillary lesions	Partial cystectomy	NR
Bartone[7]	1964	70	F	Thumb	Hematuria	Lymph nodes	Partial cystectomy	Died within 2 months
Weston and Smith[8]	1964	69	M	Eyelid	Urinary retention	Widespread	None	Died 5 days after diagnosis
Dasgupta[9] (2 patients)	1965	35	M	Unknown	Hematuria	Axillary lesion	Transurethral fulguration	Died within 4 months
		35	F	Unknown	Hematuria	Inguinal nodes	Tumor cryotherapy and partial cystectomy	NR
Meyer[10] (3 patients)	1974	69	M	Unknown	Incidental	Widespread	Chemotherapy	NR
		60	F	Arm	Hematuria	Unknown	Partial cystectomy	Died 16 month after resection
		42	M	Upper Back	Incidental	Lungs	TUR	Died 2 months after resection
Silverstein et al[11]	1974	56	M	Unknown	Hematuria	Lymph nodes	Intratumor injection of BCG vaccine followed by partial cystectomy	Alive at 8 months follow-up
Tolley et al[12]	1975	48	F	Vulva	Hematuria	Absent	Radical cystectomy	NR
Chin et al,[13]	1982	70	F	Unknown	Hematuria, voiding symptoms, suprapubic pain, fatigue	Bowel	Partial cystectomy Colectomy	NR
Stein and Kendall[3]	1984	50	M	Arm	Hematuria	Absent	TUR, chemotherapy	Alive at 2 year follow-up
Arapantoni-Dadioti et al[14]	1995	28	F	Unknown	Dysuria	Brain, Skin, Lungs lymph nodes	Incomplete TUR	2 months after resection
Ergen et al[15]	1995	65	M	Unknown	Hematuria, Flank pain	Renal pelvis, Stomach	Biopsy	Died within 1 week
Demirkesen et al[16]	2000	45	F	Heel	Hematuria, urinary frequency	Widespread	TUR, chemotherapy	NR
Lee et al[17]	2003	46	M	Back	Hematuria	Widespread	TUR and high-dose IL-2 immunotherapy	NR

Abbreviations: TUR= Transurethral resection; SBRT= Stereotactic body radiotherapy; NR= Not reported

TABLE 1. Review of English-language literature of metastatic melanoma to the bladder.

Authors	Year	Age	Sex	Primary site	Presenting symptom	Synchronous metastasis	Treatment	Survival
Fink et al[18]	2003	38	M	Upper leg	Hematuria	Tonsil Lymph nodes Esophagus Stomach, skin	Embolization of nutrient vessels	NR
Martinez-Giron[19]	2008	49	M	Back	Hematuria	NR	NR	NR
Efesoy and cayan[20]	2011	60	F	Middle finger	Hematuria, weight loss	Lungs	TUR	Died 7 months after resection
Nair et al[21]	2011	54	M	Conjunctiva	Hematuria	Widespread including ureteral and renal pelvic tumors	TUR and laser ablation of ureteral and renal pelvic tumors, Chemotherapy	Died within 3 months of TURBT
Charfi et al[22]	2012	54	M	Esophagus	Unknown	Lymph nodes	TUR	Died within 1 month
Paterson et al[23]	2012	84	M	Upper back	Incidental	No other metastatic lesions	None	NR
Wisenbaugh et al[24] (4 patients)	2012	81	M	shoulder	Hematuria and voiding	Solidary	TUR	Alive at 10 months
		84	M	Skin	symptoms	Small bowel	TUR	Died at 4 months
		85	M	Shoulder	Incidental	Widespread	TUR	Died within 4 months
		62	F	Eye	Hematuria	Lymph node,	TUR	Died within 5 months
					Incidental	small bowel, widespread		
Rishi et al[25]	2014	61	F	Back	Hematuria, dysuria	Brain Lung Skin	TUR Brain radiotherapy High-dose interferon Temozolomide	Died with 2 months
Meunier et al[26]	2015	55	F	Thigh	Hematuria	Liver Spleen Lung	Checkpoint inhibitor	Died
Topal et al[27]	2016	70	F	Eye	Hematuria	NR	TUR,Chemotherapy	Alive at 8 months
Shukla et al[28]	2016	60	M	Thigh	Hematuria	Widespread	TUR	Alive at 1 year follow-up
Krishnan[29]	2017	83	M	Back	Dysuria	Liver, Lymph node, wide spread	Biopsy	NR
Patil[30]	2017	49	F	Flank	Hematuria	Brain	Brain SBRT, checkpoint inhibitors	-
Current report	2017	57	M	Big toe	Hematuria	Lung Lymph nodes	TUR,Chemotherapy	Alive at 8 months

Abbreviations: TUR= Transurethral resection; SBRT= Stereotactic body radiotherapy; NR= Not reported

patients demonstrated an 18%-37% rate of metastatic disease to the bladder, indicating that many patients with this condition remain undiagnosed.[1,3] In addition, the incidence of melanoma has increased faster than any other cancers and accounts for 4% of all newly diagnosed cancers, according to cancer register in the United States.[4] These data suggest that this condition should receive more concern.

The genitourinary tract is a common metastatic site of melanoma. However, isolated metastatic disease to the bladder is relatively rare. The majority of cases are asymptomatic and the most common presenting symptom is hematuria. Other symptoms can mimic infection and benign prostate hyperplasia. When the patient presents with urinary tract symptoms and has a clinical history of previous malignant melanoma, appropriate workup is warranted. As in our patient, the urinary bladder lesions were incidental detected by computed tomography two months after the clinical diagnosis of hematuria. It is important to consider less common causes, such as malignancy in this scenario. The diagnosis of metastatic melanoma to the bladder requires cystoscopy and biopsy. Histopathologic examination should reveal atypical melanocytic cells morphologically similar to the primary tumor. In some cases, like this one, the tumor cells contain melanin pigments; therefore, only compatible morphology and Masson-Fontana positive brown pigments are sufficient to make a diagnosis. However, in cases of amelanotic melanoma, melanoma markers such as S100, HMB45 and melan-A immunostains, are beneficial adjunctive tools.

Several treatments have been proposed to deal with metastatic malignant melanoma including TUR, partial or radical cystectomy, chemotherapy and radiation. Once metastasis occurs, treatment options are limited and survival is generally poor, reflecting a lack of effective systemic therapy. The question for urologists is "Does surgery play a role in the management? If so, should management be transurethral resection (TUR) or cystectomy?" Similar to genitourinary malignancy, metastasectomy for malignant melanoma is controversial, but retrospective data suggested that metastasectomy may be associated with improved overall survival compared to systemic therapy alone.[5]

The choice of surgical strategy should be based on overall prognosis, the patient's health status, presence of local symptoms attributable to bladder metastases, invasiveness of approach, and quality of life factors. Bladder metastasis results in hematuria and voiding symptoms that can sometimes be managed by TUR, although TUR may not be sufficient to remove the entire tumor in many cases. Partial or radical cystectomy seems to be the treatment of choice in potentially curable patients with solitary metastasis. Radical cystectomy is theoretically the first priority of the treatment that would achieve a good tumor control. However if patient has only a single metastatic bladder lesion and denied total cystectomy, partial cystectomy could be recommended with informed risk of tumor recurrence. Up to date, patients have survived less than three years in literature, indicating the aggressive natural history and ominous prognosis of this disease. However, recent literatures have reported that patients were alive at 8-12 months of follow up, even though they had vital organ metastases and underwent TUR for urinary bladder lesion. This surgical treatment was similar to the previous reports, therefore improving systemic chemotherapy trends to be a major role for longer survival. Our patient had concomitant multiple lung metastases and hematuria which was first managed by Transurethral resection of bladder tumor (TURBT). Unfortunately, after 4 cycles of systemic chemotherapy, the patient refused further treatment and was lost to follow up.

CONCLUSION

Reported cases of metastatic melanoma to the bladder are rare. The majority of cases are reported in western countries and also in Japan. To our knowledge, this is the first reported case in the Southeast Asian population. Our case demonstrates the importance of considering a rare diagnosis in a patient with urinary symptom, especially if the history of malignant melanoma is present. Cystoscopy and biopsy are recommended if metastatic disease is suspected. While long-term survival is poor, management should be individualized according to the patient's conditions, symptoms and severity of disease.

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