CASE REPORT

Primary melanoma of the bladder: case report and review of the literature

Jin-Dong Dai†, Ben He†, Zhi-Hong Liu†, Ming Shi* and Peng-Fei Shen*

Abstract

Background: Primary melanoma of the bladder is extremely rare and has been sporadically reported in case reports. Its incidence, diagnosis, treatment, and outcomes are still unclear.

Case presentation: We report a 67-year-old female patient who presented with hematuria and was diagnosed with primary melanoma of the bladder by transurethral resection. No distant metastasis was detected by fluorodeoxyglucose positron emission tomography-computed tomography (PET-CT). After a multidisciplinary discussion, the patient received laparoscopic radical resection of the bladder tumor. There was no tumor recurrence or distant metastasis after 15 months of follow-up.

Conclusion: Primary melanoma of the bladder is easily confused with urothelium carcinoma in morphology. The immunohistochemical is crucial in diagnosis. Because of a lack of in-depth understanding of primary melanoma of the bladder, the "gold standard" treatment has not been set. We would like to provide some rare information about it and discuss the proper treatment strategy for this rare disease.

Keywords: Melanoma, Bladder tumor, Treatment, Case report

Background

Primary melanoma of the bladder is extremely rare and accounts for less than 0.2% of all reported melanoma cases. It has been reported that 96–95% of all primary melanomas arise from the skin and have a lethal effect on patients. Thus far, up to 30 corresponding cases have been reported [1]. However, no standard treatment has been established for local or advanced primary bladder melanoma.

Transurethral resection (TUR), partial cystectomy (PC), and radical cystectomy (RC) are ordinarily regarded as optional treatments for primary melanoma of the bladder. Although the tumor size and depth of invasion might determine the prognosis in primary disease, the overall survival time is less than 3 years. Because of the risk of recurrence in the bladder or systemic metastasis after local treatment in patients with primary bladder melanoma, RC is recommended in some cases [2]. However, some studies reported that RC did not achieve the expected positive effect on survival [3]. Thus, we report the positive effect of RC on survival in a patient with confirmed primary bladder malignant melanoma.

Case presentation

A 67-year-old female patient with a complaint of gross hematuria underwent a cystoscopy, and a mass lesion approximately 1 cm in size was detected on the left side of the bladder neck. A detailed outpatient consultation revealed that the non-smoker patient had no additional systematic diseases and was not taking any medications. A subtotal hysterectomy has been performed more than 10 years ago due to the myoma of the uterus. In addition, the physical examination did not show...
further positive findings. After all preoperational prepara-
tions were ready, a complete TUR of the bladder
tumor was performed in the primary hospital. Based on
the pathological evaluation by HE (hematoxylin-eosin)
staining, a high-grade urothelial carcinoma was initially
diagnosed (Fig. 1).

To prevent the recurrence of the bladder tumor, a
bladder perfusion with gemcitabine was then per-
formed. The hematuria reappeared after 4 circles of
perfusion of the bladder. After routine laboratory tests,
the following parameters were obtained: hemoglobin
13.7 g/dL; creatinine 49 umol/L; urine analysis, leu-
kocytes 30/HPF; and erythrocytes 9/HPF. After all the
needed preoperational preparations were completed, a
TUR of the bladder tumor was performed again in our
hospital (Fig. 2). After pathological evaluation by the
HE staining method mentioned above, the tumor was
then examined by immunohistochemical (IHC) stain-
ing. Mart-1, HMB-45, and S-100 were positive, while
cytokeratin was negative (Fig. 3). The final pathology
was reported as primary bladder malignant melanoma.

One month after TUR, fluorodeoxyglucose (FDG)
positron emission tomography-computed tomogra-
phy (PET-CT) revealed no distant metastasis in the
body of the patient (Supplemental figure 1). To make a
treatment plan and prognosis assessment, the patient
was discussed by members of the institutional multi-
disciplinary uro-oncologic disease management team,
who proposed a treatment plan. By fully communicat-
ing with the patient and her family members regarding
the patient's condition and treatment plan, a RC with
double cutaneous ureterostomy was performed. Fortu-
nately, no tumor in the bladder was found after path-
ological evaluation (Fig. 4). Follow-up of the patient
lasted 15 months, and no recurrence or metastasis was
found.

Discussion and conclusion
Primary bladder malignant melanoma is extremely rare
in the genitourinary tract, especially in the bladder. Since
Wheelock and colleagues reported the first case of pri-
mary bladder malignant melanoma of the bladder in
1942, approximately 31 cases of primary bladder mela-
noma have been reported in the authoritative medical
literature. All the reported cases are listed in Table 1. The
median age of patients was 61 (from 7 to 87) years old,
and 17/31 patients were male. In addition, the follow-
up time varied from 0.5 to 144 months (a median of 14
months), during which only 13/31 (41.9%) patients were
still alive. It has been reported that bladder metastasis of malignant melanoma is more common than primary bladder malignant melanoma. Furthermore, renal and bladder metastases have been reported in 45% and 18% of patients dying of melanoma, respectively [2].

The symptoms caused by this tumor vary and depend on its location [32]. The patient in our report complained of hematuria for 1 month. Gross hematuria is one of the most frequent presenting symptoms, depending on the size and location of the tumor in the bladder. It was reported that recurrent urinary tract infections might be an initial symptom in some patients with primary bladder melanoma [32].

In ordinary clinical practice, the diagnosis of primary melanoma of the bladder is complicated. In this case, the tumor was originally misdiagnosed as a high-grade urothelial carcinoma. IHC staining is crucial to make an accurate diagnosis of this disease, and immunohistochemical staining such as HMB-45, Melan-A, and S-100 are helpful in diagnosis during the pathological examination. Thus far, some diagnostic criteria for primary melanoma in the bladder have been established as follows [30]: (1) absence of any previous skin lesions, (2) cutaneous malignant melanoma, (3) primary visceral malignant melanoma, (4) recurrence pattern showing consistency with the primary tumor diagnosis, and (5) atypical melanocytes at the tumor margin upon microscopic examination.

It is generally known that no standard treatment has been established for primary melanoma in the bladder. The PC, RC, and TUR were potential surgical plans. TUR was always considered a conservative treatment for some patients. The tumor is apt to recurrence, and metastasis after TUR, therefore, refers to the treatment of urothelium carcinoma; BCG instillation was used to decrease the recurrence of carcinoma after TUR. There was only one patient treated with Bacillus of Calmette Guerin (BCG) after TUR; however, its effect after TUR still requires further explore [22]. Some case studies revealed that chemotherapy could be considered a therapy for patients after surgery. For the two patients without distant metastasis, they were treated with chemotherapy after TUR, and the patients died after 18 and 6 months, respectively [14, 30]. RC was carried out on 10 patients, and the survival rate was 60% (6/10) at a median follow-up of 15.5 months.

Two patients with suspicious distant metastasis received immune checkpoint inhibitors (ICIs) after surgery, and one of the patients who received Nivolumab after RC was alive at 16 months [29]. Nivolumab plus Ipilimumab or Nivolumab alone, blocking the interaction between the programmed cell death PD1, and its ligand PD-L1 have been reported to be effective
in antitumor response in melanoma [31, 33, 34]. ICIs might be considered for the primary bladder melanoma patients with distant metastasis after surgery.

In this case report, the patient was informed regarding all corresponding treatment options in advance and was managed in a pre-emptive manner by carrying out RC following transurethral resection of the bladder tumor.

In conclusion, primary melanoma of the bladder is easily confused with urothelium carcinoma in morphology. The IHC is crucial in diagnosis. Because of the lack of adequate evidence about the treatment of patients with primary melanoma of the bladder, no “Gold standard” treatment has been set. We would like to provide some rare information about primary bladder melanoma and discuss the appropriate treatment strategy for this rare disease.

**Abbreviations**

BCG: Bacillus of Calmette Guerin; FDG: Fluorodeoxyglucose; PET-CT: Positron emission tomography-computed tomography; H&E staining: Hematoxylin-eosin staining; IHC: Immunohistochemical; PC: Partial cystectomy; RC: Radical cystectomy; TUR: Transurethral resection; ICIs: Immune checkpoint inhibitors.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12957-022-02753-5.

**Additional file 1: Supplemental Figure S1** The patients’ preoperative PET/MRI scan. The red arrow marks the point of the tumor in neck of bladder.

### Table 1  Primary melanomas of the bladder reported in literature

| Reference          | Year | Age (year) | Gender | Treatment                                         | Follow-up (Months) | Outcomes |
|--------------------|------|------------|--------|---------------------------------------------------|--------------------|----------|
| Wheelock [4]       | 1942 | 67         | Female | Partial cystectomy                                | 36                 | Died     |
| Su and Prince [5]  | 1962 | 61         | Female | None                                              | 2                  | Died     |
| Ainsworth et al. [6]| 1976 | 65         | Female | Radical cystectomy                                | 17                 | Alive    |
| Willis et al. [7]  | 1980 | 57         | Female | Radical cystectomy                                | 36                 | Died     |
| Anichkov and Nikonov [8]| 1982 | 48     | Male   | Partial cystectomy                                | 12                 | Died     |
| Anichkov and Nikonov [8]| 1982 | 46     | Male   | Radical cystectomy                                | 3                  | Alive    |
| Ironside et al. [9]| 1985 | 56         | Male   | None                                              | 8                  | Died     |
| Goldschmidt et al. [10]| 1988 | 53     | Female | Partial cystectomy                                | 7                  | Died     |
| Goldschmidt et al. [10]| 1988 | 56     | Female | None                                              | 6                  | Alive    |
| Philippe et al. [11]| 1989 | 77         | Male   | TUR                                               | -                  | -        |
| Van Ahlen et al. [12]| 1992 | 81         | Female | Radical cystectomy, radiotherapy, interferon-alpha| 24                 | Died     |
| Lund et al. [13]   | 1992 | 81         | Female | Local excision, radiotherapy, chemotherapy        | 15                 | Alive    |
| Kojima et al. [14] | 1992 | 63         | Female | TUR + Chemotherapy                                | 18                 | Died     |
| Lange-Welker et al. [15]| 1993 | 75   | Male   | Partial cystectomy                                | 3                  | Died     |
| Mourad et al. [16] | 1993 | 34         | Male   | Radical cystectomy                                | 12                 | Alive    |
| Niederberger and Lome [17]| 1993 | 53     | Male   | Radical cystectomy                                | 18                 | Alive    |
| De Torres et al. [18]| 1995 | 44         | Male   | Radical cystectomy                                | 14                 | Died     |
| Tainio et al. [19] | 1999 | 52         | Male   | TUR                                               | 8                  | Died     |
| Garcia Montes et al. [20]| 2000 | 44     | Female | TUR                                               | 144                | Alive    |
| Khalbuss et al. [21]| 2001 | 82         | Female | Radiotherapy                                       | 16                 | Died     |
| T. Hsu and Y. Hsu [22]| 2002 | 73         | Male   | TUR + intravesical BCG and ReTUR at 2-7-9 months  | 16                 | Alive    |
| Baudet et al. [23] | 2005 | 7          | Female | Partial cystectomy                                | 84                 | Alive    |
| Pacella et al. [24]| 2006 | 82         | Male   | TUR                                               | 9                  | Died     |
| Sandersingh et al. [25]| 2011 | 56     | Male   | Radical cystectomy and pelvic excision four months later | 10                | Alive    |
| El Ammari et al. [26]| 2011 | 71         | Male   | TUR                                               | 5                  | Died     |
| Truong et al. [27] | 2013 | 84         | Female | TUR + Ipilimumab                                   | -                  | -        |
| Otto et al. [28]   | 2017 | 52         | Male   | TUR + Interferon/dacarbazine                       | 18                 | Died     |
| Barijarlo et al. [29]| 2018 | 72         | Male   | Radical cystectomy + Nivolumab                    | 16                 | Alive    |
| Bumbu GA, et al. [30]| 2019 | 80         | Male   | TUR + Chemotherapy                                | 6                  | Died     |
| Monica K, et al. [31]| 2019 | 87         | Female | None                                              | 0.5                | Died     |
| Mercimek MN, et al. [2] | 2019 | 39        | Female | Partial cystectomy + BPLND                        | 52                 | Alive    |

TUR, transurethral resection; BCG, Bacillus of Calmette Guerin; BPLND, bilateral pelvic lymph node dissection
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