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Metastasis of malignant melanoma to urinary tract: a case report

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Abstract

Introduction Metastasis of malignant melanoma to urinary tract is reported to be rare. According to retrospective analysis of a single center study, improvement of overall survival was observed in patients with metastasis to the gastrointestinal tract that had undergone metastasectomy with curative intent. However, there is no significant evidence regarding resection for metastasis to urinary tract.

Case presentation Case 1: an 86-year-old Japanese man was diagnosed with a small bladder tumor by computed tomography scan during post operative follow-up of malignant melanoma in the choroid of the left eye. Cystoscopy revealed black, nonpapillary tumors, suggesting metastatic malignant melanoma. Because no apparent invasive growth to muscle layer was observed by magnetic resonance imaging, transurethral resection was performed. Pathological appearance was compatible with metastatic malignant melanoma. No recurrence in urinary tract was observed; however, multiple liver metastasis was diagnosed at 3 months after surgery. Case 2: a 57-year-old Japanese man was diagnosed with right hydronephrosis due to ureteral tumor. He had a past history of subungual malignant melanoma to the left thumb 2 years prior to his visit. Right nephroureterectomy was performed, and pathological evaluation revealed metastatic malignant melanoma. He revisited 2 years later due to dysuria, and a large bladder tumor was revealed by ultrasound. Cystoscopy showed black-colored nonpapillary tumor, suggesting malignant melanoma. Total cystectomy was recommended; however, the patient withheld consent. Therefore, we performed transurethral resection. The resulting pathological finding was compatible with metastatic malignant melanoma without invasion to muscle layer. He remained free from local recurrence and metastasis for 22 years after surgery.

Conclusion We successfully performed metastasectomy for bladder and ureteral metastases without recurrence in the urinary tract. Long recurrence-free survival was observed in case 2. Complete resection for metastasis of malignant melanoma may have the potential to improve survival.

Keywords Melanoma, Metastasis, Urinary bladder, Ureter, Metastasectomy

Introduction

Malignant melanoma commonly occurs in the skin and metastasizes to lymph nodes (42–59%), lungs (18–36%), and liver (14–20%) [1]. Although bladder metastasis of malignant melanoma is reported in 14–22% of autopsy cases [2], clinically apparent cases reported in the English-language literature accounted for 31 cases, suggesting that metastatic lesions to the urinary tract are difficult to detect while patients are alive because they are less likely to exhibit symptoms [3–5]. Here, we report

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two cases of malignant melanoma metastasizing to urinary tract that were successfully treated with surgical intervention.

Case presentation

Case 1

An 86-year-old Japanese man underwent left-eye enucleation due to malignant melanoma of the choroid 4 years prior to his visit. After surgery, computed tomography (CT) scan was performed every 6 months to screen for metastasis, with the most recent contrast CT scan revealing a small tumor in the bladder with weak enhancement (Fig. 1A). The patient was then referred to our department, where cystoscopy was performed. The examination showed two black, nonpapillary tumors on the anterior wall of the bladder measuring approximately 5 mm and less than 1 mm, respectively (Fig. 1B). Cytology of the urine was negative. MRI revealed small tumor showing high intensity on T1WI and low intensity on T2WI at anterior bladder wall without apparent invasive growth into the muscle layer (Fig. 1C). Since the size of the tumors was small and less likely to invade the muscle layer, we decided to perform transurethral resection of bladder tumor (TUR-Bt). In the surgery, we incised the bladder mucosa from approximately 1 cm away from the tumors. Histological examination revealed proliferation of atypical cells with rounded hyperchromatic nuclei and intracytoplasmic melanin granules with a nodular appearance at the submucosal layer (Fig. 1D, E). Immunohistochemically, the tumor cells were positive for Melan A and HMB-45 (Fig. 1F). The appearance was similar to primary melanoma (data not shown) and compatible with metastasis of malignant melanoma. No apparent muscular invasion was observed.

The patient recovered without postoperative events. Three months after TUR-Bt, multiple liver metastases were discovered on CT scan. Since genetic analysis revealed no mutation in *BRAF*, treatment by immune checkpoint inhibitor was considered. However, the patient chose best supportive care without additional medical treatment. The general condition remained stable without recurrence in urinary tract at 6 months after surgery.

Case 2

A 57-year-old Japanese man visited a private clinic with the chief complaint of right abdominal discomfort. Ultrasound examination revealed right hydronephrosis. Because CT scan suggested that the hydronephrosis was due to ureteral tumor (Fig. 2A), the patient was referred to our department. The patient had undergone surgical intervention for subungual malignant melanoma to the left thumb 2 years prior to his visit. Retrograde pyelography showed complete obstruction of upper ureter, and the obstructed portion was matched to the ureteral tumor diagnosed by CT scan. Although urine cytology was negative, CT scan findings were compatible with ureteral carcinoma; therefore, we performed right nephroureterectomy. The resected specimen showed yellow–white and partially black colored pedunculated tumor to the upper ureter, and no satellite tumors were evident in the urinary tract (Fig. 2B). Pathological findings showed submucosal proliferation of polygonal to spindle-shaped cells with oval to irregular-shaped nuclei and intracytoplasmic melanin granules (Fig. 2C). The tumor cells were positive for Melan A and HMB-45, prompting a diagnosis of ureteral metastasis of known malignant melanoma. The patient recovered without postoperative event. A month after surgery, full-body radiological examination by CT scan, MRI, and bone scintigraphy was performed. Results revealed no apparent metastasis. Two years later, the patient revisited with a complaint of dysuria. Ultrasound and CT scan showed bladder tumor measuring approximately 4 cm in diameter (Fig. 2D), and cystoscopy revealed black-colored nonpapillary tumor, suggesting malignant melanoma (Fig. 2E). Because the tumor was large and invasion could not be ruled out, we recommended total cystectomy; however, the patient withheld consent. Therefore, we performed transurethral resection of bladder tumor (TUR-Bt). Pathological diagnosis of the resected specimens was compatible with malignant melanoma similar to the previously resected ureteral tumor (Fig. 2F–H). Fortunately, no apparent invasion to muscle layer was observed, and the patient remained free from local recurrence and metastasis for 22 years after TUR-Bt.

Discussion

Secondary bladder neoplasms have been reported to represent 2–3% of all malignant bladder tumors; however, the majority of these spread directly from adjacent organs, including colon, prostate, rectum, and cervix [6, 7]. In metastatic secondary bladder neoplasm, the most common primary site is stomach (4.3% of all secondary bladder neoplasms), followed by skin (3.9%), lung (2.8%), and breast (2.5%) [6–8]. The most common histological type of secondary bladder neoplasm has been reported to be adenocarcinoma, with malignant melanoma being less common. However, a higher incidence of bladder metastasis of malignant melanoma was reported in autopsy cases. Sheehan *et al.* analyzed 5200 autopsy cases and reported 21 cases of metastatic bladder tumors, with 8 of these (38%) being metastatic malignant melanomas [9]. Bates reported as a possible reason for the frequency of secondary tumors to urinary and male genital tracts being higher in autopsy cases that autopsy cases were

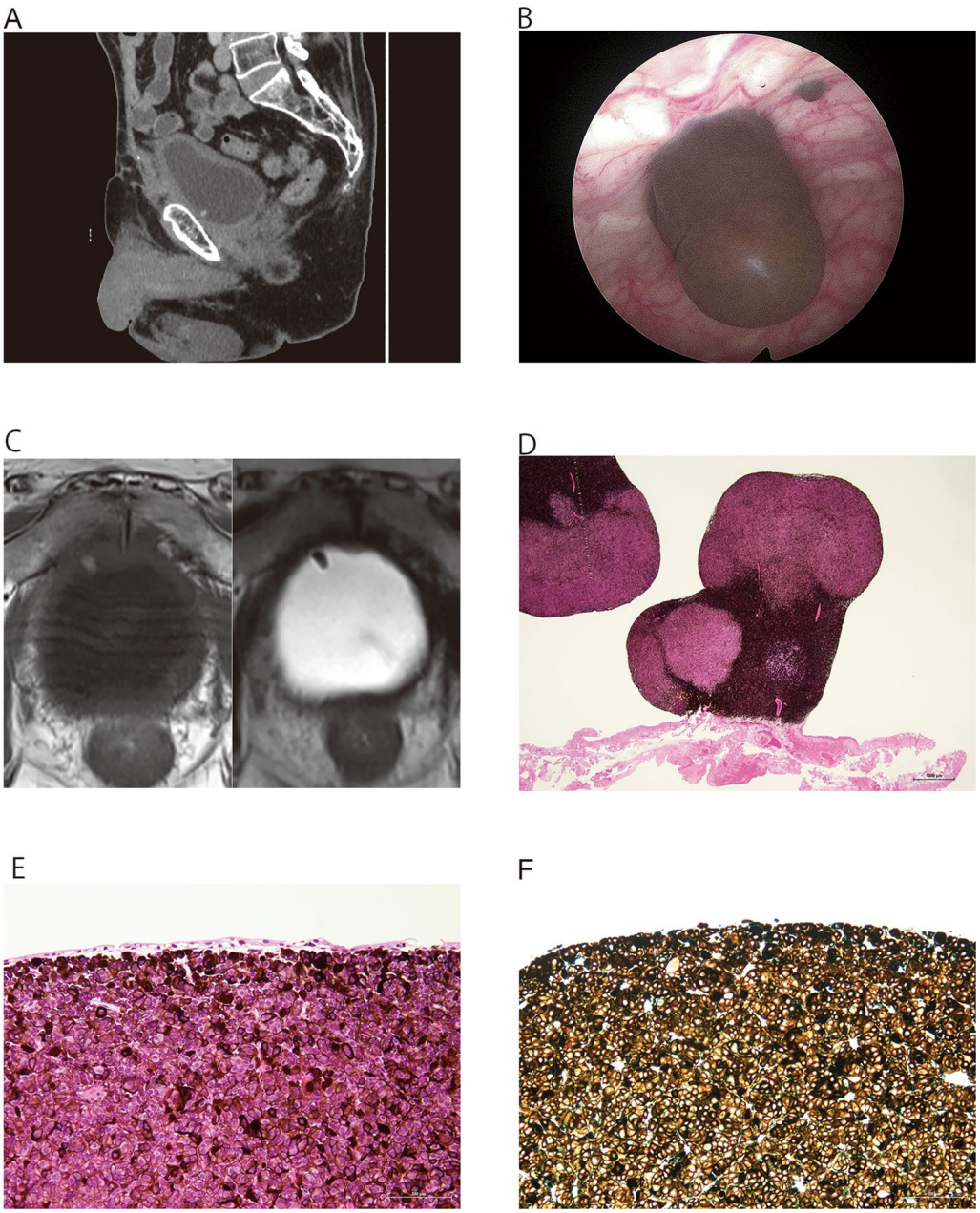

Fig. 1 Clinical and pathological appearance of case 1. Sagittal imaging of contrast computed tomography (nephrogenic phase) is shown (**A**). A small tumor with weak enhancement is suggested on the anterior side of the bladder. Cystoscopic appearance shows two nonpapillary black tumors (**B**). The bladder tumor shows high intensity in T1 weighted image (left), low intensity in T2 weighted image (right). No apparent muscle invasion is revealed in T2 weighted image of magnetic resonance imaging examination (**C**). Histological findings are shown (**D**–**F**). Atypical cells with intracytoplasmic melanin granules proliferate in the submucosal layer (**D**, **E**). The tumor cells are positive for Melan A (counterstaining with Giemsa, **F**)

(See figure on next page.)

Fig. 2 Clinical and pathological appearance of case 2. Contrast computed tomography (early phase) reveals solid mass with weak enhancement in the upper ureter (**A**, white arrow). Macroscopic appearance (cutting surface) of resected right kidney and the ureter is shown (**B**). Yellow–white and partially black colored pedunculated tumor in the upper ureter (yellow arrow). Contrast computed tomography (excretory phase) shows large bladder tumor (**D**), and cystoscopy reveals black-colored nonpapillary tumor (**E**). Histological appearances of ureteral tumor (**C**) and bladder (**F**–**H**) show submucosal proliferation of polygonal to spindle-shaped cells with oval nuclei and intracytoplasmic melanin granules. The tumor cells were positive for Melan A

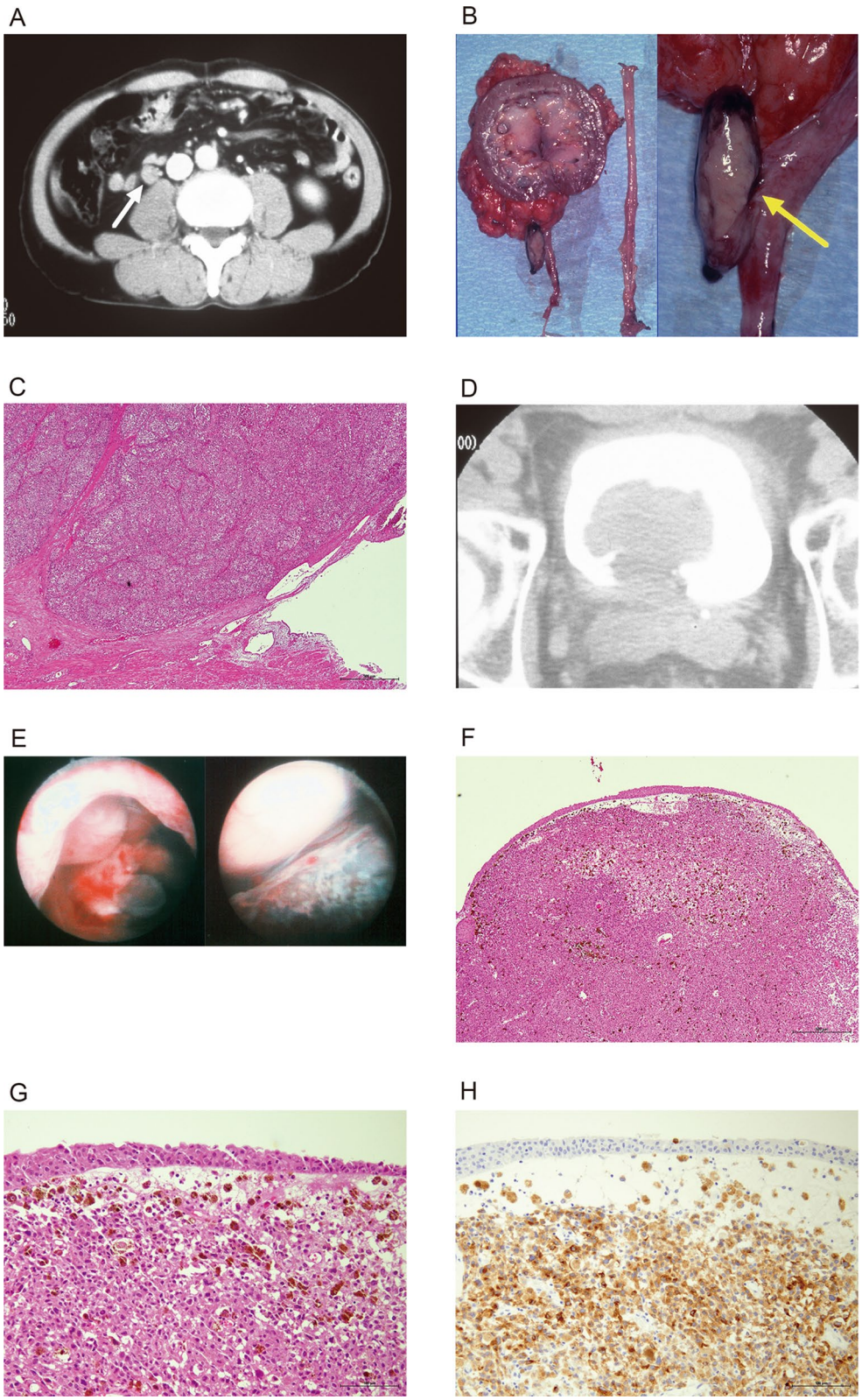

Fig. 2 (See legend on previous page.)

more likely to have disseminated disease [10]. In addition, sampling bias toward unusual lesions and convenience of observation by autopsy for outer layer of hollow organ were discussed with the conclusion that it is simpler to diagnose secondary neoplasia at autopsy than on the basis of biopsy.

Metastatic malignant melanoma of the bladder is typically reported to present as asymptomatic macroscopic hematuria and diagnosed by cystoscopy and histopathological features considered with clinical history of previous melanoma. Diagnostic criteria to determine whether malignant melanoma of the bladder is a primary tumor include (1) absence of any previous skin lesions, (2) absence of cutaneous malignant melanoma, (3) absence of primary visceral malignant melanoma, (4) absence of recurrence pattern showing consistency with the primary tumor diagnosis, and (5) atypical melanocytes at the tumor margin upon microscopic examination [9]. In our two cases, each patient had an apparent past history of primary melanoma, and the bladder tumor was pathologically compatible with primary tumor. Therefore, we diagnosed metastatic malignant melanoma of the bladder in both cases.

Ureteral metastasis of malignant melanoma is extremely rare. To the best to our knowledge, this is the ninth case report [11–14]. In addition, malignant melanoma occurred in the bladder metachronously. Because the tumor was located in the submucosal region (not the superficial region), metastasis was considered rather than intraluminal seeding from ureteral melanoma. Although all tumors were located in the submucosal area, no apparent muscle invasion was observed. Therefore, the tumors were completely resected without local recurrence.

When distant multiple metastases are discovered in patients with malignant melanoma, surgical intervention may be less indicated. However, complete resection may have the potential to improve overall survival (OS) in some cases. Deutsch *et al*. reported the patients with abdominal visceral metastases undergoing surgical resection had superior overall survival compared with patients treated with medical agents only, including new agents (18 months versus 7 months; $P < 0.001$) [15]. The study included 366 cases with metastasis in the gastrointestinal tract, 697 cases in the liver, 138 cases in the adrenal glands, 38 cases in the pancreas, 109 cases in the spleen, and 305 cases with multiple sites. Patients with metastasis to the gastrointestinal tract undergoing complete curative resection had the greatest benefit from metastasectomy (median OS of 64 months). However, no apparent benefit for OS was observed in patients receiving palliative surgery. The study included a large number of cases and yielded significant results; however, a limitation is that it was a retrospective analysis. Further prospective study is recommended to clarify the significance of metastasectomy.

Although there was no metastasis in another organs at surgery (complete metastasectomy was performed in this period), liver metastasis appeared at 3 months after TUR-Bt in case 1. On the other hand, long-term disease control (22 years) was observed in case 2 by complete resection. According to literature, complete curative metastasectomy may have benefit for patient survival, especially in metastasis to gastrointestinal tract; however, there was no evidence of metastasectomy in patients with metastasis to urinary tract. Therefore, accumulation and analysis of the cases with urinary tract metastasis will be necessary to clarify the benefit of metastasectomy.

On contrast CT scan, metastatic melanoma usually manifested as hyper vascular mass [16]. MRI showed high intensity on T1WI and low intensity mass on T2WI [17]. In our cases, weak enhancement was observed by contrast CT scan in both cases. In addition, MRI appearance of the bladder tumor on MRI was consistent with that of conventional malignant melanoma in case 1. Although no reports described the specific appearance of metastasis to genitourinary systems, appearance in the current cases was similar to that of metastasis to other organs. MRI may be useful in developing a differential diagnosis for bladder metastasis because common urothelial carcinoma revealed iso-intensity on T1WI and iso- to slightly high-intensity compared with the muscle layer on T2WI [17, 18].

As follow-up, imaging examination at every 3–12 months for 2 years, then every 6–12 months for another 3 years was recommended for patients with stage IV NED with cutaneous melanoma [19]. Screening for metastasis was performed by CT scan at every 6 months in case 1, and bladder metastasis manifested as small tumors. Postoperative (after nephroureterectomy) follow-up was insufficient in case 2, and larger bladder melanoma was found, suggesting the significance of sufficient follow-up by routine imaging examination.

Conclusion

Metastatic malignant melanoma to the urinary tract has been reported as a rare secondary tumor. We successfully performed metastasectomy for bladder and ureteral metastases without local recurrence. In addition, long recurrence-free survival was observed in case 2. Complete resection for metastasis of malignant melanoma may have significant potential to improve survival.

Abbreviations

CT	Computed tomography
MRI	Magnetic resonance imaging
TUR-Bt	Transurethral resection of bladder tumor
NED	No evidence of disease

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Author contributions
TU drafted the manuscript, performed the examination, observation, and approved the final version of the manuscript. HB, KI, TM, MF, and TN performed examinations, surgery, and cared for the patient and approved the final version of the manuscript. TK (Takumi Kiwaki) diagnosed and reviewed the pathological specimens and approved the final version of the manuscript. SM, AS, and TK (Toshiyuki Kamoto) drafted the report and contributed the final version of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The supporting data and materials for this report are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
This case report was approved by the Ethics Committee of Miyazaki University (approval number: C-0172). Consent to participant was obtained from the patient.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal.

Competing interests
The authors declare that they have no conflict of interest.

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References

1. Fink W, Zimpfer A, Ugurel S. Mucosal metastases in malignant melanoma. Oncology. 2003;26:249–51.
2. Stein BS, Kendall AR. Malignant melanoma of the genitourinary tract. J Urol. 1984;132:859–68.
3. Lee CS, Komenaka IK, Hurst-Wicker KS, *et al*. Management of metastatic malignant melanoma of the bladder. Urology. 2003;62:351.
4. Patil RV, Woldu SL, Lucas E, *et al*. Metastatic melanoma to the bladder: case report and Review of the Literature. Urol Case Rep. 2017;10(11):33–6.
5. Ogunremi O, Sirjuesingh D, Deshpande A. Metastatic melanoma to the urinary bladder: a rare cause of visible haematuria. Case Rep Urol. 2024;1:5516547.
6. Bates AW, Baithun SI. Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumours: clinicopathological and histological features of 282 cases. Histopathology. 2000;36(1):32–40.
7. Velcheti V, Govindan R. Metastatic cancer involving bladder. A review Can J Urol. 2007;1:3443–8.
8. Goldstein AG. Metastatic carcinoma to the bladder. J Urol. 1967;98:209–15.
9. Sheehan EE, Greenberg SD, Scott R. Metastatic neoplasms of the bladder. J Urol. 1963;90:281–4.
10. Bates AW, Baithun SI. The significance of secondary neoplasms of the urinary and male genital tract. Virchows Arch. 2002;440(6):640–7.
11. Stoykov B, Velev D, Ali A, *et al*. Adrenal and ureteral metastasis of malignant melanoma: a case report and review of the literature. Urol Case Rep. 2022;45: 102286.
12. DeSanto M, Strait R, Zopp J, *et al*. Metastatic melanoma to the proximal ureter. Urol Case Rep. 2023;50: 102543.
13. Macneil J, Hossack T. A case of metastatic melanoma in the ureter. Case Rep Urol. 2016. https://doi.org/10.1155/2016/1853015.
14. Nair BC, Williams NC, Cui C, *et al*. Conjunctival melanoma: bladder and upper urinary tract metastases. J Clin Oncol. 2011;29(9):e216–9.
15. Deutsch GB, Flaherty DC, Kirchoff DD, *et al*. Association of surgical treatment, systemic therapy, and survival in patients with abdominal visceral melanoma metastases, 1965–2014: relevance of surgical cure in the era of modern systemic therapy. JAMA Surg. 2017;152:672–8.
16. Barat M, Guegan-Bart S, Cottereau AS, *et al*. CT, MRI and PET/CT features of abdominal manifestations of cutaneous melanoma: a review of current concepts in the era of tumor-specific therapies. Abdom Radiol (NY). 2021;46(5):2219–35.
17. Patnana M, Bronstein Y, Szklaruk J, *et al*. Multimethod imaging, staging, and spectrum of manifestations of metastatic melanoma. Clin Radiol. 2011;66(3):224–36.
18. Caglic I, Panebianco V, Vargas HA, *et al*. MRI of bladder cancer: local and nodal staging. J Magn Reson Imaging. 2020;52(3):649–67.
19. Swetter SM, Thompson JA, Albertini MR, *et al*. NCCN guidelines insights: melanoma: cutaneous, version 2.2021. J Natl Compr Canc Netw. 2021;19(4):364–76.

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