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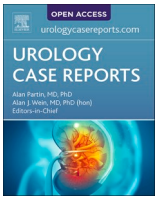

Oncology

# Metastasis of malignant melanoma to the urinary bladder & descending colon: A case report and literature review

Marwin Anandrati [a,*], Vidhi Maini [a], Armand Asarian [b], Philip Xiao [c]

[a] Department of Medicine, St. George's University School of Medicine, True Blue, Grenada, W1, USA
[b] Department of Surgery, The Brooklyn Hospital Center, Icahn School of Medicine at Mount Sinai, Brooklyn, NY, USA
[c] Department of Pathology, The Brooklyn Hospital Center, Icahn School of Medicine at Mount Sinai, Brooklyn, NY, USA

A B S T R A C T

We present a case demonstrating metastases of malignant melanoma (MM) to the urinary bladder (UB) and descending colon (DC). With review of literature, it was determined that the metastases of MM to both the urinary bladder and descending colon in a single case is rare in occurrence.

## 1. Introduction

Malignant melanoma (MM) is exhibiting a notable rise in incidence, especially amongst the caucasian population.[1] MM is characterised by dysplastic proliferation of melanocytes, the pigment-producing cells in the skin, rendering it a form of skin cancer.[2] The diagnosis of melanoma relies on clinical assessment and biopsy of the affected lesion.[2] Cytological features that are prominently seen in MM lesions include an irregular and thick nuclear membrane and the presence of prominent nucleoli.[2] Based on tumor staging, treatment options may entail immunotherapy, gene therapy, and biochemotherapy. However, surgical excision remains the most definitive treatment option and directly correlates with a heightened survival rate.[2]

MM demonstrates a high chance for metastasis, with recent investigations focusing on the role of malignant melanoma stem cells or initiating cells (MMICs) in the metastatic dissemination of the tumor.[3] Based on current literature, MM is prone to metastasize to the skin, lungs, liver and brain 4. In addition, MM also demonstrates a high rate of metastasis to the gastrointestinal (GI) tract.[5] The presentation of melanoma patients varies based on the site of metastasis. Metastasis to the skin typically manifests as skin lesions at sites different from the primary tumor. Metastasis to the bladder may present with hematuria and dysuria. If the malignant cells metastasize to the descending colon, patients may exhibit signs of hematochezia, constipation, and changes to bowel movement.

Here in, we present a unique case of MM metastasizing to the urinary bladder (UB) and descending colon (DC) – both sites are considered rare for MM embedment and metastasis. With the rising number of cases of metastatic melanoma being reported, we hope to better understand the histopathological and clinical implications of our observed pattern of metastasis.

## 2. Case presentation

A 71-year-old Caucasian female with a past medical history of hypertension and MM of the posterior neck presented to the ED with complaints of back pain and hematuria. She underwent a wide local excision with a 2cm margin of the melanotic lesion 9 years ago and had been asymptomatic since. At the time there were no metastatic lesions present. Urinalysis workup at this time yielded negative results for leukesterase and nitrites.

Transabdominal pelvic ultrasound was performed and noted the presence of a bladder mass measuring $3.2 \times 1.7 \times 1.9$ cm with suspicion of potential MM metastasis to the UB (Fig. 1). The patient underwent a cystoscopy revealing a large sessile tumor measuring greater than 3cm located on the right posterior urinary bladder wall with a small 2-3mm lesion just medial to it—these were subsequently resected through a transurethral resection of the bladder. Results from the excisional biopsy demonstrated cells exhibiting pleomorphic characteristics, variable sizes and shapes, along with the presence of atypical mitoses within the cell nuclei and nuclear pleomorphism. The cells within the polyp were strongly suggestive of malignancy, and upon undergoing immunohistological studies were found to be diffusely positive for Melan-A. Similarly, results from a colonoscopy performed 3 months later revealed 3 polyps along the luminal wall of her DC, with the largest one measuring 12mm and demonstrating sloughing and ulceration at the base. Upon immunohistological staining, the colonic polyps were found to be positive for Melan-A as well, indicating the metastasis of MM to both these

* Corresponding author.
*E-mail addresses:* manandra@sgu.edu (M. Anandrati), vmaini@sgu.edu (V. Maini).

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sites.[6]

Following resection of the bladder and colonic masses, patient was started on immunotherapy with Nivolumab 1mg/kg IV every 3 weeks plus Ipilimumab 3mg/kg IV on the same day for a duration of 12 weeks (4 doses)—which she is tolerating well. Subsequently, a positron emission tomography (PET) scan following the second cycle of immunotherapy, and a CT scan of the abdomen and pelvis yielded negative results, thus, suggesting remission (Fig. 2).

## 3. Pathology

Multiple fragments of tan soft tissue were resected from the bladder. Microscopic examination reveals extensive involvement of the bladder wall by sheets of small round blue tumor cells showing cleaved irregular nuclear contours and nucleoli (Fig. 3). Abundant mitosis is present. Tumor cells are positive for S100, SOX10, PRAME, vimentin, focally positive for CD56, AE1/3, CK7, CK20 and p63 (Fig. 4). Ki-67 shows about 25 % positivity. These features are diagnostic of malignant melanoma. Biopsy from the descending colon revealed similar pathological features (Fig. 5). Negative CD45 immunostaining ruled out the possibility of lymphoma.

## 4. Discussion

It is estimated that 30 % of MM cases ultimately develop metastases, with the most common site of embedment being the lungs, skin, brain, or liver.[4] Following a thorough review of current literature, this is ostensibly the first reported case of MM metastasizing to the urinary bladder (UB) and descending colon (DC) in the same patient.

In clinical practice, the metastasis of MM to the UB is extremely rare with roughly 29 cases being reported in English literature over the course of the last 30 years.[7] Though few, this pattern of metastasis carries clinical significance as demonstrated by an autopsy series identifying metastasis to the bladder in 37 % of melanoma patients.[8] Thus, it can be inferred that, there is a high probability of asymptomatic cases which remain undiagnosed. Similarly, the metastasis of MM to the DC remains undocumented. Our literature review yielded no results for this pattern of metastasis, with the closest representation being 2 reported cases of primary MM of the DC.[910] As mentioned prior, the metastasis of MM to the GI tract is not uncommon. However, the large bowel constitutes the least reported incidences with predicted values of 15 % in the colon, 5 % in the rectum, and 1 % in the anus[11].

Aetiology for MM remains unknown, with most data linking sunlight (UVB radiation) as the offending agent. Most theories surrounding the mechanism by which sunlight promotes melanoma remains obscure, however there is great focus on: the action spectrum of human cutaneous MM, the modality and duration of exposure to UVB, and the role

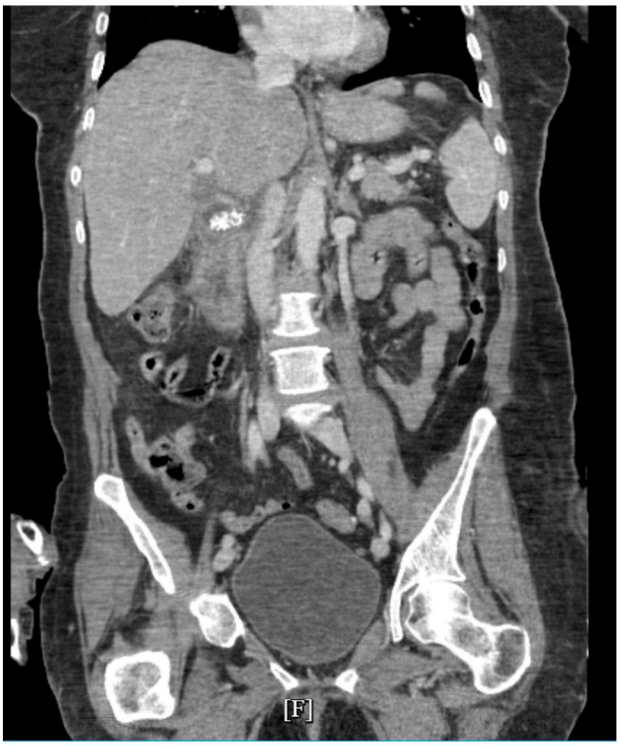


**Fig. 2.** CT scan of the abdomen and pelvis revealing an unremarkable urinary bladder.

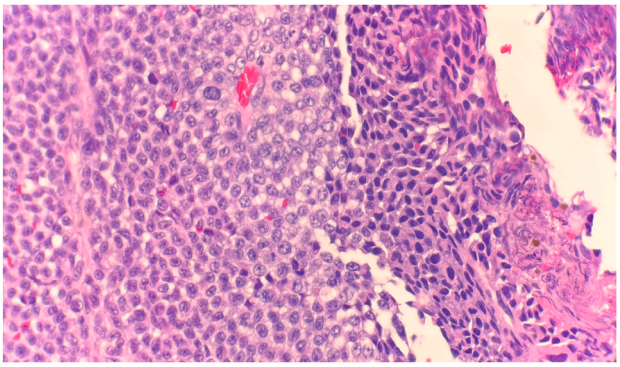

**Fig. 3.** Microscopic examination reveals sheets of malignant cell adjacent to unremarkable urothelium epithelium. H&E stain 40x

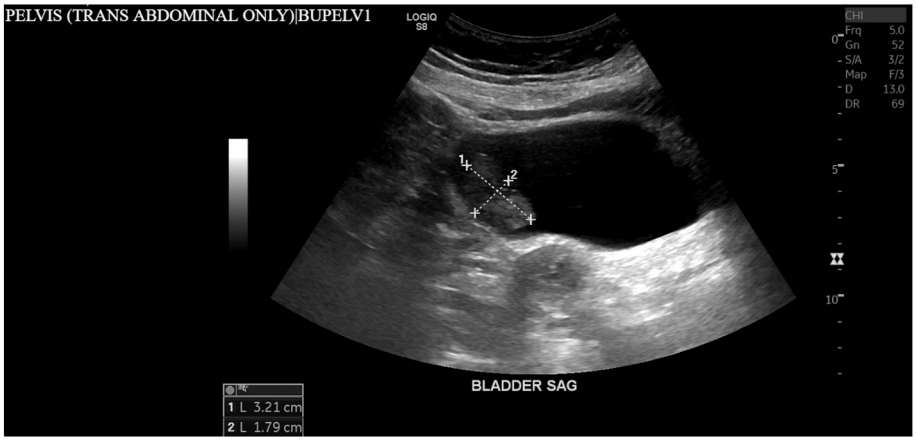


**Fig. 1.** Transabdominal ultrasound of the pelvis revealing an incidental finding of a bladder mass measuring 3.2 cm in size.

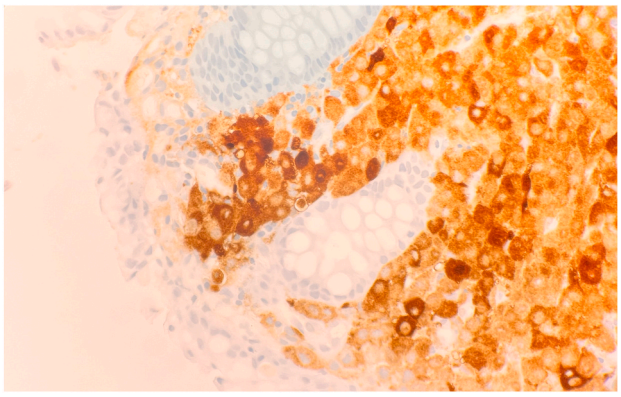

**Fig. 4.** Microscopic examination shows that sheets of malignant cells are positive for S100. IHC stain 40x

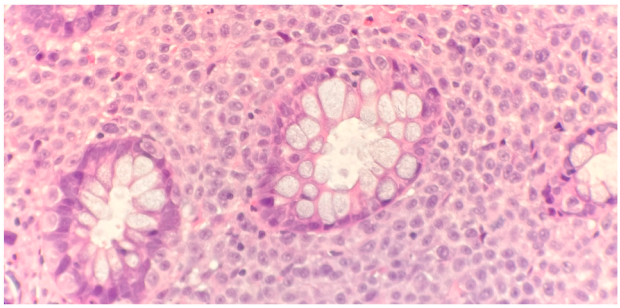

**Fig. 5.** Microscopic examination reveals sheets of malignant cells between unremarkable colonic crypts. H&E stain 40x

of UV-related and UV-unrelated genetic damages in melanocytic cells.[12] The most common symptoms in patients with metastasis of MM to the UB is painless gross hematuria, with back pain and fatigue being quite rare occurrences.[13] Furthermore, as demonstrated in our patient, the concurrence of metastasis to the DC may skew the clinical picture with additional symptoms such as anaemia, weight loss, bowel obstruction, and abdominal pain. It is of note that symptomatic cases are directly correlated with a poorer prognosis.[14]

Despite the multisystemic pattern of metastasis, surgical intervention is the most definitive treatment modality for MM of the UB and DC. Focusing on the UB, treatment options require a multidisciplinary approach which could vary from transurethral resection of the bladder, cystectomy (partial or radical), radiotherapy, or immunotherapy. Initial treatment is dependent on tumor size and would utilise either a cold cup bladder biopsy or a transurethral resection of the bladder tumor (a diagnostic and therapeutic intervention).[15]

Similarly, surgical resection is considered the criterion standard for MM of the DC as it is not only palliative but may positively influence long-term outcome.[16] An outcome analysis was performed to assess the survival outcomes of patients with metastatic MM of the colon, comparing operative and non-operative treatment. The findings revealed that colonic resection was significantly more effective with a mean survival time of 27.5 months following their surgery, contrary to the non-operative candidates who had a mean survival time of 7.8 months following their diagnosis.[17] Although chemotherapeutic agents have demonstrated limited clinical efficacy in the past, novel agents have shown a more favourable toxicity profile and greater efficacy, henceforth, improving the management of non-resectable tumours. The most prominent drug classes include antibodies directed towards the cytotoxic T-Lymphocyte-associated antigen (CTLA4) such as Ipilimumab, and monoclonal antibodies against programmed cell death protein 1 (PD-1) such as Pembrolizumab or Nivolumab.[18,19]

As this is, to our knowledge, the first reported case of the metastasis of MM to the UB and DC, there is insufficient data outlining the expected long-term outcomes. As such, careful monitoring and close follow-up with patients are needed to appropriately outline the disease prognosis. Metastases to each of these sites are already deemed rare, therefore, having both in the same case accentuates the likelihood of recurrence and alludes to poor prognosis. To date, no patient who has undergone resection of metastatic MM of the UB or the DC has survived more than 3 years.[9,10,20]

## 5. Conclusion

Malignant melanoma (MM) represents a significant health concern globally, as it is one of the leading causes of fatality due to a dermatological pathology. Characterised by its aggressive nature, MM is known to metastasize to various sites in the body mainly the skin, liver, and brain. In this case report, we presented a patient with a history of MM with symptoms concerning for UB and DC involvement. Based on histological examination, the presence of atypical melan-A positive cells with nuclear pseudoinclusions were confirmatory of MM metastasis to the bladder.

As discussed in this report, there are multiple therapeutic modalities including pharmacological agents such as monoclonal antibodies against PD-1 or CTLA4, chemotherapy or radiotherapy, available for treating MM. Treatment options can be selectively chosen based on the site of metastasis. Nonetheless, surgical resection remains the foremost definitive treatment, notable for its ability to decrease recurrence and reduce the risk of further metastasis. Surgical intervention is particularly preferred, as demonstrated in the case presented in this report. Based on recent literature, there are not many cases of MM that metastasize to the bladder or the descending colon. Considering the rising incidence of MM and the demonstrated unique metastatic potential observed in the presented case, this study carries substantial implications for both clinical practice and ongoing research endeavours.

## CRediT authorship contribution statement

**Marwin Anandrati:** Writing – review & editing, Writing – original draft, Data curation. **Vidhi Maini:** Writing – review & editing, Writing – original draft, Data curation. **Armand Asarian:** Supervision, Conceptualization. **Philip Xiao:** Writing – review & editing, Supervision, Conceptualization.

## Consent

Non-written consent was documented and witnessed, and all personal identifiers were redacted in the publication of this report.

## Declaration of competing interest

None declared.

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