

## Abstract

Melanoma of the skin has an incidence of roughly 23% of all the new US cancer diagnoses in 2018 (1). While majority of melanomas are cutaneous lesions of the skin, only 4-5% melanomas arise extracutaneously (2). One extracutaneous lesion, primary malignant melanoma of the bladder (PMM), represents less than 0.2% of all melanomas (2-5), making this malignancy extremely rare. In regards to bladder tumors, 95% of all bladder tumor are typically urothelial carcinoma, with only 5% representing other rare primary cancers such as gastrointestinal stromal tumors, lymphoma, and neuroendocrine tumors (3). Thus, PMM of the bladder represents both an exceptionally rare melanoma, and also an exceedingly rare bladder tumor.

There are only 30 reported cases of PMM of the bladder in the literature so far. Of those, 17 cases were reported as deceased within 3 years of presentation. Our case reported here is that of a 78-year-old female who presented with new onset of incontinence and intermittent hematuria. She had no evidence of primary melanoma anywhere else in her body. The patient was treated with cystectomy and ileal conduit with plans for adjuvant chemotherapy. Unfortunately, the patient succumbed to her disease with diffuse metastatic involvement and death within 16 months of presentation.

## Introduction

- Extracutaneous melanomas are extraordinarily rare, aggressive, and extremely lethal (2).
- PMM of the bladder typically presents with gross hematuria and/or other voiding symptoms like dysuria or incontinence (2-5).
- There is no apparent risk regarding gender at this time in regards to PMM, affecting both genders equally (3).
- PMM typically presents in people over 50 years old (2) with a mean age of 60.6 years (3).
- At this time, PMM of the bladder has an unknown etiology and risk factors (4).
- Both metastatic malignant melanoma and PMM have similar histopathological features making their distinction and diagnosis difficult (3).
- As of now, the diagnosis of PMM of the bladder is based on ruling out any other area for concern of melanoma presence or prior regression (3).
- First line treatment is surgery including radical/partial cystectomy and transurethral resection of bladder tumor (TURBT). Additional therapies including radiation, chemotherapy, and immunotherapy have been described (2-5).

## Case

A 78-year-old female who initially presented to the emergency department for new onset incontinence and intermittent gross hematuria. Upon initial workup CTU (Figure 1) demonstrated a calcified mass in the bladder along with left hydroureteronephrosis.

@2mo

- OR for TURBT and left stent placement, negative pelvic exam
- Pathology: positive for primary malignant melanoma of bladder (Figure 2)

@3mo

- FDG PET CT (Figure 3): demonstrates uptake of FDG in bladder, chest is negative
- Biopsy of forearm lesion: ruled out melanoma, results showed dermatofibroma

@8mo:

- OR for radical cystectomy with ileal conduit, bilateral pelvic lymph node dissection, lysis of adhesions, removal of left stent, bilateral stent placement, hysterectomy and bilateral salpingoophorectomy, excision of anterior vaginal wall
- Pathology: pT3N0M0 primary malignant melanoma of the bladder

@14mo: abdominal pain

- CTAP: new retroperitoneal lymphadenopathy and infrarenal occlusion of aorta

@15mo

- FDG PET CT (Figure 4): Confluent bilateral adenopathy extends from the aortic hiatus into the pelvis, positive lymph node in chest

- CT guided biopsy of nodes, Pathology: positive metastatic melanoma

@16mo

- Plan to proceed with adjuvant chemo, patient presents to emergency department again with abdominal pain
- Patient succumbs to metastatic disease

Figure 1: Initial CTU during admission for gross hematuria demonstrating presence of bladder mass



Figure 3: FDG PET prior to cystectomy no areas of metastatic concern at 3mo



Figure 2: TURBT specimen stains + for HMB-45 and S-100

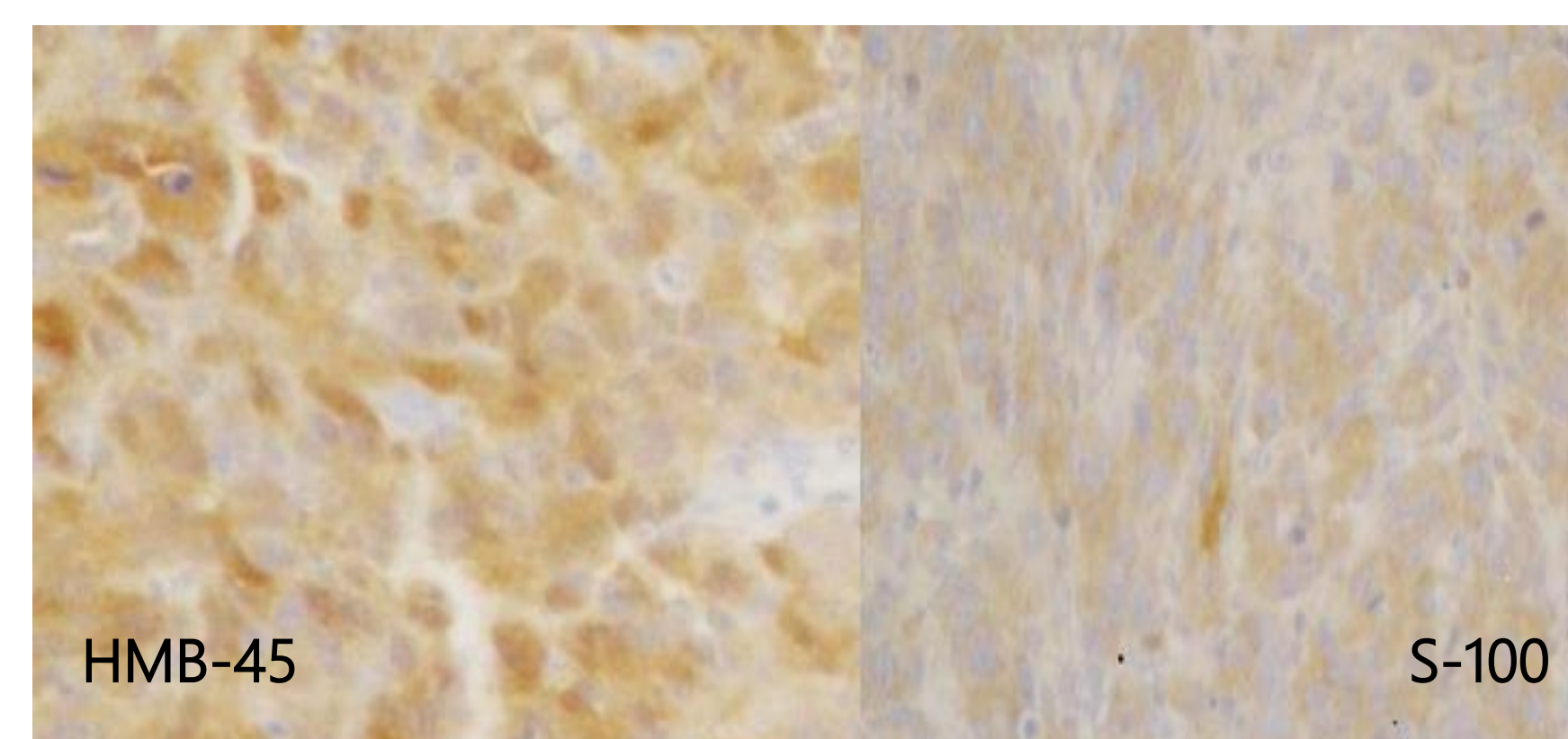
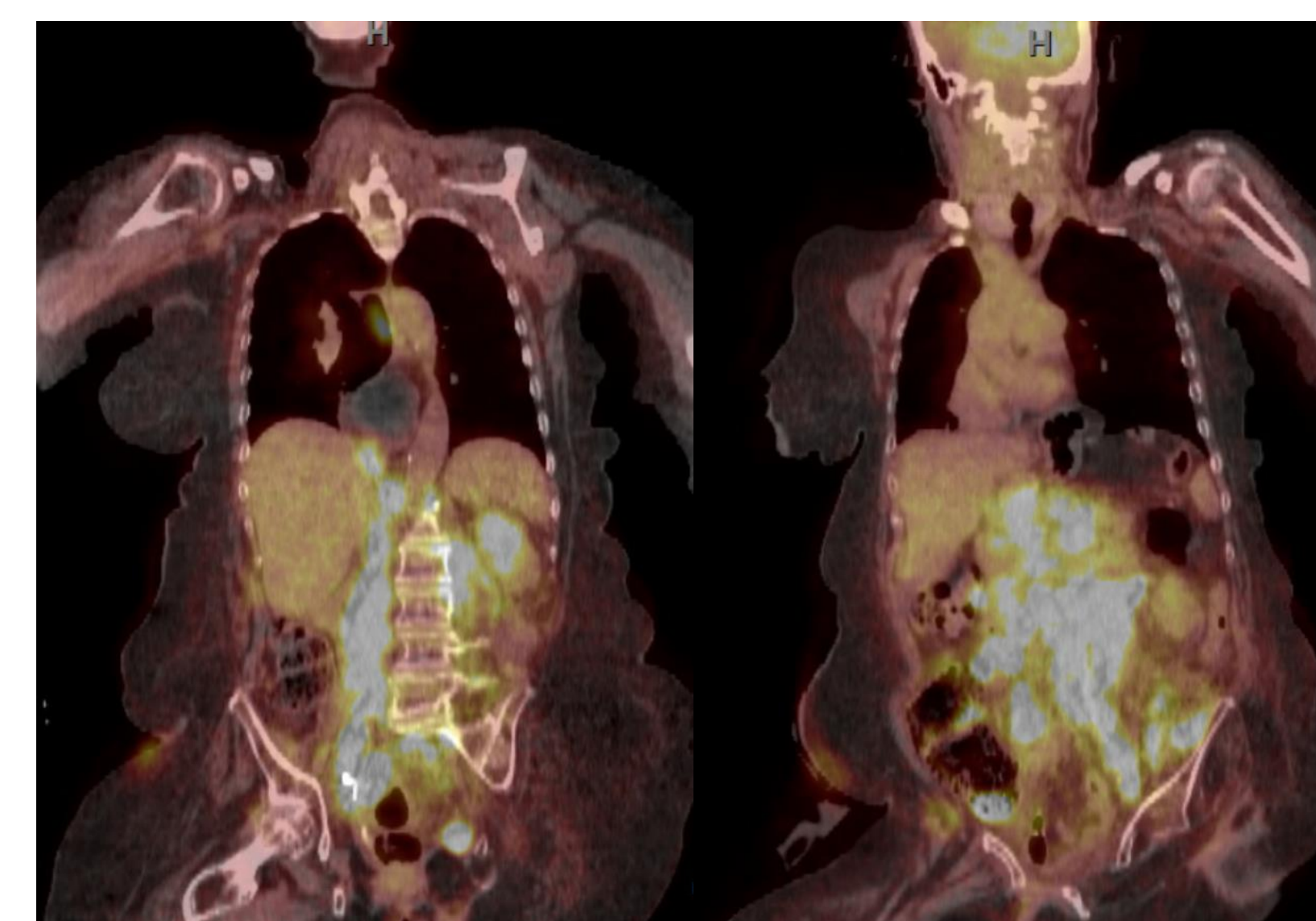


Figure 4: FDG PET s/p cystectomy demonstrating diffuse metastasis at 16 months



## Discussion and Conclusion

Extracutaneous lesions of melanoma as discussed are very rare. Most cutaneous melanomas typically arise from genetic alterations of the melanocyte precursors due to direct UV radiation exposure. These melanocyte precursors are however, also found in areas of squamous covered mucous membranes, like the respiratory and urogenital tracts (4). Mucosal melanomas have been described, but only account for 1.3-1.4% of all melanomas. Incidence of mucosal melanomas of the vagina represent 7.4%, penis 3.3%, urethra 1.8%, and bladder 0.2% of the cases (4). Since these squamous covered mucous membranes are typically not exposed to UV radiation, at this time, the histopathogenesis and etiology of PMM of the urogenital bladder remains unknown (3, 4).

To differentiate metastatic melanoma of the bladder from PMM of the bladder the following criteria have been used: 1) detailed history ruling out cutaneous, regressed, or visceral melanoma, 2) recurrence pattern that is consistent with the primary origin of melanoma (2-5). Histological and immunohistochemistry can help confirm diagnosis of primary melanoma but due to its highly variable morphological appearance, these methods themselves may not be definitive. A review of cases shows that positive expression of S-100, HMB45, and Melan-A can help identify the bladder melanoma (4). Further investigation and characterization of its morphological variability and cellular patterns (nested, spindle cell, small cell variants) is needed so PMM of the bladder is not missed.

Primary malignant melanoma of the bladder has a poor prognosis because it presents at an advanced stage, has ambiguous pathological features making it difficult to diagnose, and is very aggressive with two thirds of patients succumbing to metastatic disease by 3 years (4,5). In addition, there is lack of data suggesting best treatment options for this rare cancer. First line therapy is surgery with cystectomy or TURBT (2), but for those with poor performance, evidence for alternatives is sparse. It appears that tumor stage and mitotic activity can aid in prognosis and some authors suggests identifying if the malignancy contains a BRAF activating mutation for therapeutic targeting may be of benefit (3, 4). Others have suggested immunotherapy after cystectomy with Nivolumab as successful treatment (2). Overall, we have yet to define the best treatment regimen.

In conclusion, due to the rarity of primary malignant melanoma of the bladder, evidence regarding etiology, risk factors, histopathological diagnosis, and treatment options still remains in question. Further analysis of all reported cases and head to head trials is warranted to adequately identify these unknowns.

## References

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