

Case – Urothelial carcinoma recurrence presenting with painless cutaneous plaques and papules

Eliana Rohr¹, Alexandra Laverde-Saad², Jessica Lu², May Chergui³, Khue Huu Nguyen²

¹Faculty of Medicine, McGill University, Montreal, QC, Canada; ²Division of Dermatology, McGill University Health Centre, Montreal, QC, Canada; ³Department of Pathology, McGill University Health Centre, Montreal, QC, Canada

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Corresponding author: Dr. Alexandra Laverde-Saad, Division of Dermatology, McGill University Health Centre, Montreal, QC, Canada; Alexandra.laverde-saad@mail.mcgill.ca

INTRODUCTION

Cutaneous metastases are a rare presentation of metastatic urothelial carcinoma and are associated with an accompanying poor prognosis.¹ We describe a case of metastatic urothelial carcinoma presenting as a groin and pubic rash in an 85-year-old man in a presumed remission from his prior bladder and urethral urothelial carcinoma.

CASE REPORT

An 85-year-old man presented to dermatology with a three-month history of a worsening rash on his groin and pubis. His past medical history was remarkable for a remote transitional cell carcinoma of the bladder, for which he underwent a radical cystoprostatectomy with bilateral pelvic lymph node dissection and an ileal conduit. Six years later, he was found to have disease recurrence with carcinoma in-situ of the urethra. He underwent a urethrectomy, and at this time, a second primary malignancy was incidentally found: renal cell carcinoma (RCC) of the left kidney which was treated with a partial nephrectomy and was subsequently deemed to have no evidence of disease. Eleven years later, he presented to the emergency department with pyelonephritis and on imaging, had new right

KEY MESSAGES

- Cutaneous metastases are uncommon in urothelial carcinoma and are associated with a high mortality rate.
- Urothelial carcinoma cutaneous metastases can be below the detection threshold of radiologic investigations, so clinical examination is critical.
- In a patient with a history of urothelial carcinoma presenting with a new onset rash, cutaneous metastasis should be ruled out.

inguinal and mesenteric nodal enlargement, confirmed to be recurrence of his urothelial carcinoma on biopsy. He was treated with radiation therapy and chemotherapy. The patient was closely monitored with serial imaging and felt to be free of disease once again three months following completion of treatment, 17 years after the original diagnosis.

At a routine follow up 5 months after completion of radiation and chemotherapy, the patient reported a two-week history of a pruritic rash over his groin and pubis to his treating team, who initiated a trial of clotrimazole for presumed cutaneous candidiasis. No improvement was seen; thus treatment was changed to hydrocortisone and a barrier cream. During this time, a control PET scan was performed with no FDG avid uptake and was interpreted as showing no evidence of disease. The rash continued to expand however and at a subsequent nephrology follow up, an urgent consult to dermatology was requested.

The patient was seen by our dermatology service on the same day. At this time, 8 months had passed since completion of his treatments and 3 months since the onset of his rash. He was systemically well and denied any night sweats and weight loss. His rash was moderately pruritic but not painful. On exam, an indurated ecchymotic plaque measuring approximately 20x20cm was noted over the right anterolateral thigh, with a few areas of darker purpura on the medial aspect. (Fig. 1A) The rash extended over the scrotum and pubis, which was more erythematous and had overlying firm pink papules in a linear arrangement over the left pubis. (Fig. 1B) The penile shaft was uninvolved, neither was the left thigh or the inguinal fold. No lymphadenopathy was palpated at this time. A high suspicion for cutaneous metastases prompted two biopsies: one of the right medial thigh purpura and a second of a pubic pink papule. Both biopsies showed dermal nests of pleomorphic cells with focal glandular differentiation, prominent nucleoli, and numerous mitotic figures surrounded by desmoplasia, consistent with metastatic urothelial carcinoma. The tumor stained positive for CK7, p40/p63, and GATA3, and was negative for PAX8 and CK20. The specimen from the right medial thigh (Fig 2A and 2B) likely represented lymphovascular invasion, while the tumour burden from the left pubis (Fig 2C and 2D) was more abundant.

The diagnosis of recurrent metastatic urothelial carcinoma was relayed to the patient's treating team, and management options were presented by urology, oncology, and radiation oncology services. The patient ultimately declined further investigations or treatment and transitioned to supportive care exclusively. He passed away 6 months after the diagnosis of this recurrence. A timeline of the patient's disease course is illustrated in Figure 3.

DISCUSSION

Cutaneous spread from internal solid visceral tumors is a rare phenomenon, with an incidence of approximately 5.3%.² The presence of cutaneous involvement reflects widespread metastatic disease and holds a poor prognostic indication with a median survival of less than one year.¹ The most common cancers to metastasize to skin are breast for women and lung for men, and they carry an anatomical predilection for the chest and abdomen, respectively.³

Primary urological malignancies tend to spread primarily to the lymph nodes, bones, liver, and lungs. Cutaneous metastases occur in 1.1% of cases of urological malignancies, and for patients diagnosed with transitional cell carcinoma (TCC) bladder cancer, 0.84% will experience skin metastases.⁴ This invasion is thought to be secondary to four different routes: direct tumour invasion, hematogenous spread, lymphatic spread, or from iatrogenic implantation of tumour cells.⁴ In a mini-review by *Wolfson and Shvero*, the time interval between diagnosis of the original tumor and skin metastasis ranged between 3 weeks and 8 years.⁵ In our patient, cutaneous metastases appeared approximately 7 months after the original diagnosis of Stage IIIB urothelial carcinoma metastatic to lymph nodes.

The appearance of cutaneous metastases of genitourinary malignancies may mimic other dermatologic conditions such as angiosarcoma or herpes zoster.⁶⁻⁸ Hence, trials of ineffective therapies for unsuspected tumoral processes often lead to delays in diagnosis.⁴ Clinical manifestations are grouped into three main categories according to morphology: nodular, inflammatory and fibrotic. The most prevalent manifestation is the nodular type, characterized by an acute aggregation of discrete, firm, fixed nontender nodules. The inflammatory type typically occurs on the anterior chest wall and is manifested with erythema, swelling, and tenderness. Lastly, the fibrotic or sclerodermoid type is predominantly found on the scalp, exhibits a round or oval morphology with a smooth surface, distinctive red-pink hues and is characteristically nontender and non-pruritic.³

Although our patient had a prior history of both RCC and urothelial carcinoma, our clinical suspicion was lower for RCC given that cutaneous metastases of RCC have a predilection for the scalp and usually present as vascular nodules.⁹ On the other hand, metastases of urothelial carcinoma, like those of most genitourinary cancers, most commonly involve the abdominal skin.⁴ Furthermore, the ecchymotic indurated aspect of the right thigh raised the differential diagnosis of post-radiation angiosarcoma; however, this disease process has a mean latency period of 12 years following radiation, a much longer time frame than the one-year period for our patient.¹⁰

Cutaneous metastases are the presenting feature of urologic malignancies in roughly 1% of cases,⁴ but it is unclear how frequently they are a manifestation of recurrent disease. For several internal malignancies, we rely on imaging to reflect disease burden. Our case shows that urothelial carcinoma cutaneous metastases, however clinically significant, may be below the detection threshold of conventional PET scans. Some cancers are known to be less readily detected by PET scans, such as necrotic, cystic, mucinous, or low-grade tumours which have less FDG avidity.¹¹ Studies have shown that the sensitivity of PET for smaller cutaneous lesions is poor and can lead to false negatives in the context of micrometastasis, as seen in the context of metastatic melanoma amongst others.¹² Furthermore, as our patient had a prior cystectomy and ileal conduit, the excretion of the tracer through the stoma could have obscured the detection of clinically significant disease near the site of cystectomy.¹¹ Hence, thorough regular physical

exams and a high index of suspicion are critical in patients with a history of cancer presenting with new onset cutaneous lesions.

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CONCLUSIONS

Cutaneous metastases are a rare presentation of metastatic disease and even more so in the context of urothelial carcinoma. Physicians should maintain a high index of suspicion when faced with a patient with a known history of malignancy and new cutaneous lesions.

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FIGURES AND TABLES

Figure 1. Clinical photographs of lesions at presentation to dermatology. (A) Ecchymotic plaques over the right thigh. (B) Linear arrangement of pink papules clustered over the left lateral pubis on a background of violaceous to red discoloration.



Figure 2. Hematoxylin and eosin histopathology of skin biopsies. (A) and (B) are biopsies of the right medial thigh ecchymotic plaques at 2x and 20x magnification respectively, where deeper dermal nests of carcinoma can be seen, likely representing lymphovascular invasion. (C) and (D) are biopsies of the left pubic papules at 2x and 10x magnification respectively. Nests of pleomorphic cells with focal glandular differentiation, prominent nucleoli, and numerous mitotic figures surrounded by desmoplasia, consistent with metastatic urothelial carcinoma.

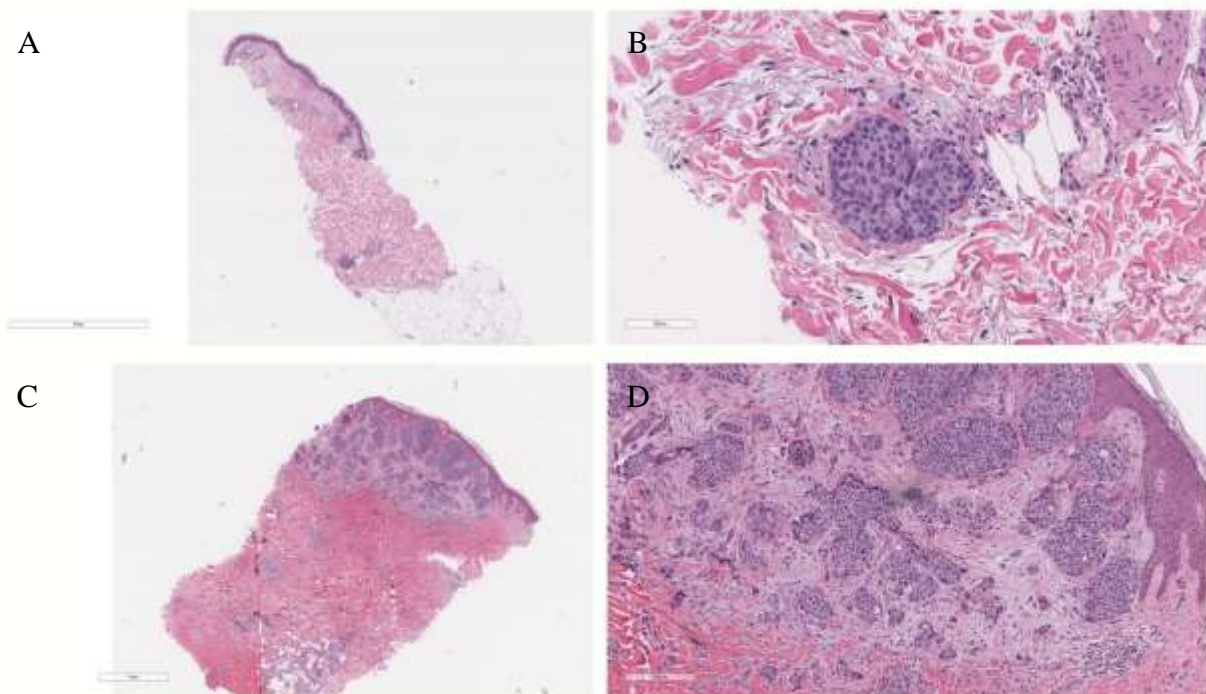
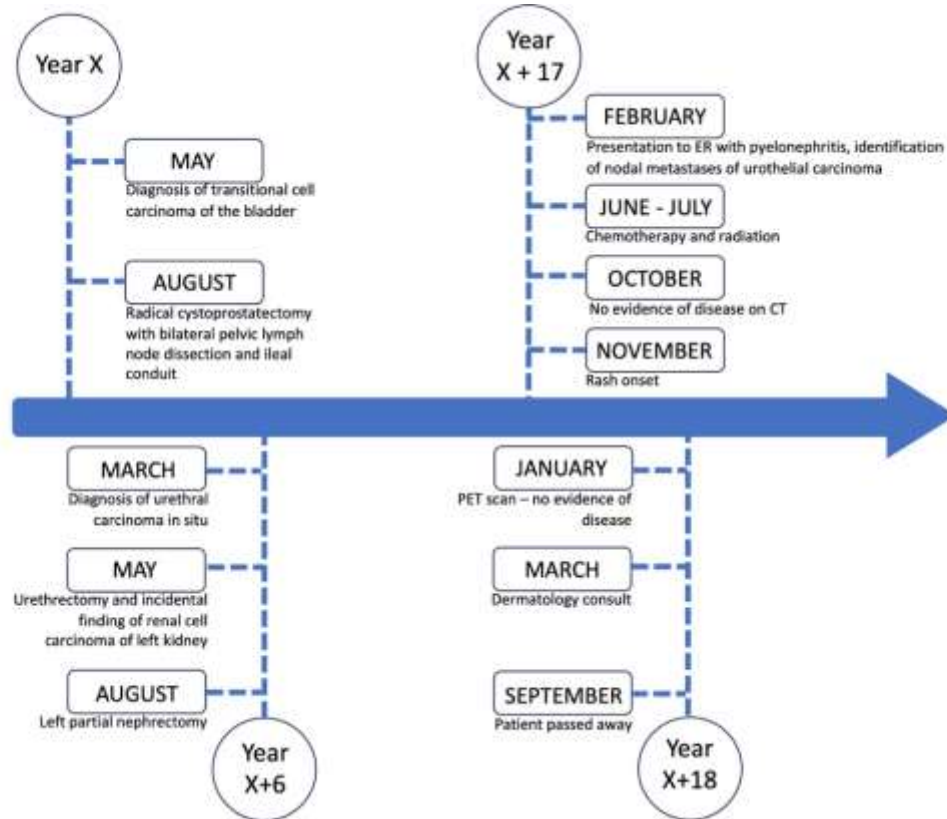


Figure 3. Timeline of disease course. ER: emergency room; CT: computed tomography; PET: Positron emission tomography.



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