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Version: 2 Date: 4 December 2014

Author’s response to reviews: see over
Cutaneous metastasis of transitional cell carcinoma of the urinary bladder: 8 years after the primary: a case report

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Abstract:

Introduction: Cutaneous metastasis of bladder carcinoma is extremely rare with a limited number of published cases. An awareness of this rare clinical entity and high index of suspicion is needed for diagnosis, as it can occur months or rarely as in this case, even years, after the primary cancer.

Case presentation: An 81-year-old Caucasian male presented with a one year history of increasing left leg swelling and a 2 month history of a macular-nodular rash on the anterior thigh, on a background of high grade transitional cell carcinoma of the bladder in 2006. Following investigations, he was diagnosed as having probable loco-regional recurrence of previously resected urothelial cancer of the bladder with extensive retrograde lymphatic permeation into the left thigh with cutaneous eruptions of malignancy. He completed a planned course of palliative radiation therapy to the left thigh lesions (30Gy divided over 10 fractions) as well as the left pelvic node (Total dose 18Gy divided over 6 fractions). The disease ran an aggressive course and the patient died 6 months after the diagnosis of cutaneous metastases.

Conclusion: Metastatic disease should always be considered in the differential diagnosis in patients with a previous history of bladder cancer who present with cutaneous nodules, even many years after the initial diagnosis at the primary site.

Keywords:

Cutaneous

Metastases
Introduction:

In 2009, there were 2316 new cases of bladder cancer in Australia, accounting for 2% of all new cancers [1]. Bladder cancer is 4 times more common in men than women [1]. However, in 2010, relative survival rates for bladder cancer were higher for men than for women in Australia [2]: the five year relative survival for bladder cancer for the period 2006-2010 was 60.0% for men and 49.6% for women [2]. Approximately 50% of the patients will develop local recurrence and/or metastatic disease after radical cystectomy [3]. Cutaneous metastasis of transitional cell carcinoma (TCC) is rare. The incidence is reported to be less than 1%, and ranges from 0.18% to 2% for TCC of the urinary bladder [4]. Of the cutaneous metastasis from genitourinary organs, TCC of the bladder accounts for 17% of cases [5]. It may occur at the time of diagnosis, or appear months or even years after the primary lesions are found [6]. Rarely, it may present as the first symptom of the disease [7]. We present a rare cutaneous metastasis of TCC in the absence of generalised recurrent disease.

Case presentation:
An 81-year-old Caucasian male presented with a one year history of increasing left leg swelling, initially in the calf and subsequently extending to the thigh. The General Practitioner requested a venous Doppler ultrasound of the left leg and CT of the abdomen and pelvis which failed to discover any underlying cause. He had developed multiple lesions on the left anterior thigh which increased significantly in number and size over 2 months. His past medical history included high grade transitional cell carcinoma of the bladder in 2006 for which he underwent a cystectomy and ileostomy. He did not require adjuvant treatments.

On physical examination there was left lower limb oedema extending to the thigh and a well demarcated macular- nodular rash on the anterior thigh (Figure 1a). There were no palpable masses or nodes in the groin or popliteal fossa bilaterally. The abdomen was soft and non-tender.

Skin punch biopsy demonstrated features favouring metastatic, poorly differentiated non-small cell carcinoma (Figure 2). Immunohistochemical staining (Figure 3) showed strong diffuse positive staining for cytokeratin (CK) 7 and cytokeratin 20 and focal positive staining for cytokeratin CK5/6 and P63. The tumour cells were negative for PSA and TTF-1. The above cytokeratin immunoprofile is consistent with metastatic transitional cell carcinoma showing focal squamoid differentiation. Left lower limb lymphoscintigraphy confirmed severe lymphoedema in the left leg. Contrast-enhanced computed tomography (CT) scan of the chest, abdomen, pelvis and thighs did not demonstrate any mass or adenopathy in the pelvis or left groin to explain the patient’s left leg lymphoedema. There was no other evidence of metastatic disease. Magnetic resonance imaging (MRI) of the spine demonstrated no evidence of metastatic disease to the spine however whole body bone scan found multiple osteoblastic metastases throughout the bony pelvis. Positron Emission Tomography (PET) demonstrated diffuse left leg swelling, likely related to increase tracer activity in a 17mm pelvic lymph node in the left pelvic wall. There were multiple small foci of nodular uptake seen on the anteromedial aspect of the left distal thigh consistent with the known cutaneous metastases. Sclerotic bone lesions with increased uptake on the bone scan were not highly FDG avid in
comparison to the avid pelvic node and thought to be possibly related to an alternative pathology such as prostate cancer. (No PSA on record).

He completed a planned course of palliative radiation therapy to the left thigh lesions (30Gy divided over 10 fractions) as well as the left pelvic node (Total dose 18Gy divided over 6 fractions). Methotrexate was excluded as a treatment option in our patient in light of the potential for accumulation in the ‘third space’ comprising the lymphoedema in his left leg. The patient became too unwell to undergo a subsequent planned course of chemotherapy (Carboplatin and Gemcitabine). The disease ran an aggressive course and the patient died 6 months after the diagnosis of cutaneous metastases.

**Discussion:**

Since the first recorded case of cutaneous metastases in 1909 [8], infrequent reports have reached the world literature. Skin metastases may occur at any time after the initial diagnosis at the primary site [9]. From the published literature, cutaneous metastases most often occur within eighteen months of the primary diagnosis, and only one documented case occurring ten years after the primary diagnosis [10]. Urologic malignancies most commonly metastasize to regional lymph nodes, liver, lung and bones [5, 11]. Metastatic infiltration of the skin or subcutaneous tissues can occur due to direct tumour invasion, haematogenous or lymphatic spread, or as a result of iatrogenic implantation of tumour cells [5]. Gross appearance of cutaneous metastases is not distinctive and may mimic many common dermatologic disorders [12,13]. These lesions can be solitary or multiple in appearance [11,14,15]. Brownstein et al. described 3 clinical features of metastatic cutaneous lesions, including a nodular type, inflammatory type, and sclerodermoid type [16]. In addition, a rarer zosteriform lesion has also been documented [17-19]. Metastatic skin lesions from
genitourinary TCC are reported to be always located on the head, face, neck, trunk, abdomen, suprapubic region or extremities, as well as occasionally on scrotal skin and ocular region [9].

Diagnosis requires clinical suspicion of metastases as well as histological evaluation. Diagnosis is usually established by microscopic examination of excisional biopsy specimens [9]. Among reported cases, cutaneous metastases of TCC almost exclusively show high-grade differentiation of histological grading at the primary genitourinary sites [9]. Wang et al discovered that coordinate expression of cytokeratins 7 and 20 are positive in 89% of transitional cell bladder cancer [20].

The prognosis for patients with cutaneous transitional cell carcinoma is typically poor, with a median survival of fewer than 12 months [13]. However, very rare cases of extended survival (up to 23 years) have been reported [21]. The treatment of choice for metastatic bladder cancer is either chemotherapy, with the combination of gemcitabine and cisplatin or the MVAC scheme (methotrexate, vinblastine, doxorubicin, and cisplatin); or palliative care [22]. Chemotherapy has reported tumour remission rates up to 70% [22], but survival does not exceed 14 months [3]. Symptomatic patients may benefit from surgical resection of metastases in terms of tumour-related symptoms and performance status [23]. Local radiation therapy has also been reported to resolve cutaneous lesions which did not respond to chemotherapy [13].

**Conclusion:**

This is a rare case of late presentation cutaneous metastasis of transitional cell carcinoma. Metastatic disease should always be considered in the differential diagnosis in patients with a previous history of bladder cancer who present with cutaneous nodules. This disease has a broad clinical impact across medicine, in particular for urologists, dermatologists, medical and radiation oncologists, general physicians, geriatricians and palliative care specialists. In many cases, as in this patient, treatment is mainly supportive and prognosis is poor. Due to its rarity and poor survival rate, management strategies have been difficult to define. Therefore it is important for the medical
community to have access to each case, through case reports, so as to advance our understanding of this particular disease.

(Patient’s perspective and list of abbreviations: not applicable)

Consent:

Written informed consent was obtained from the patient for publication of this case report and accompanying images (prior to the patient’s death). A copy of the written consent is available for review by the Editor-in-Chief of this journal. Consent has also been obtained from their next of kin.

Competing interests:

The author declares that they have no competing interests.

Author’s contributions:

AL was the only contributor in writing the manuscript, and read and approved the final manuscript.
Author’s information:

AL: Staff Specialist Geriatrician: FRACP, MBChB, BHB

Acknowledgements:

We thank:

- The patient on whom the case report is based, and his wife

- Shaun Donovan, Staff Specialist Pathology, Royal Hobart Hospital, for the photographs of the histology

(Endnotes: not applicable)

References:


Figure legends:

Figure 1: Photograph of left thigh cutaneous metastases: [Figure 1A] at presentation; [Figure 1B] 1 month later; [Figure 1C] 3 months later, post radiotherapy to left leg.

Figure 2: Histology showing extensive infiltration from a high-grade urothelial carcinoma (H-E stain, x100)

Figure 3: Photomicrograph of skin punch biopsy: CK-7 [Figure 2A] and CK-20 [Figure 2B].