Cutaneous Metastases from Urothelial Carcinoma of the Bladder A Rare Presentation and Literature Review

I Agarwal¹, GF Bruney¹, C Sands¹, G Shirodkar², M Recine³

ABSTRACT

With the advances in imaging, earlier detection of recurrence and metastatic disease is possible. However, there are limited data on the metastatic pattern of bladder cancer. In addition, cutaneous metastases from primary genitourinary malignancies are rare and, in spite of advances in imaging which detect smaller lesions, the patterns of metastases from bladder cancer have not been well described. Very few cases of skin metastasis from urothelial carcinoma have been reported in the past. We present a case of primary bladder transitional cell carcinoma in which a cutaneous metastasis was the initial presentation.

Keywords: Bladder, cutaneous, metastases, transitional cell carcinoma

Metástasis Cutáneas del Carcinoma Urotelial de la Vejiga Una Manifestación Rara y una Revisión de la Literatura

I Agarwal¹, GF Bruney¹, C Sands¹, G Shirodkar², M Recine³

RESUMEN

Con los avances en imaginología, es posible una detección más temprana de las recidivas y las enfermedades metastásicas. Sin embargo, los datos existentes acerca del patrón de metastásico del cáncer de vejiga, son limitados. Además, las metástasis cutáneas de las malignidades genitourinarias primarias son raras, y a pesar de los avances en la obtención de imágenes que detectan lesiones más pequeñas, los patrones de metástasis del cáncer de vejiga no han sido bien descritos. Muy pocos casos de metástasis de piel del carcinoma urotelial, han sido reportados en el pasado. Presentamos un caso de carcinoma primario de células transicionales de la vejiga, en el cual una metástasis cutánea fue la manifestación inicial.

Palabras claves: Vejiga, metástasis cutáneas, carcinoma de células transicionales

INTRODUCTION

Bladder carcinoma is one of the common malignant diseases but data on its metastatic pattern are limited. One should be familiar with the common and uncommon sites of metastases as their detection is important to guide appropriate treatment selection and has a marked influence on prognosis. The incidence of cutaneous metastases from all urologic malignancies is 1.1% to 2.5% (1). Metastases to the skin from renal cell carcinoma are the most common (3.4% to 4.0%), West Indian Med J 2014; 63 (5): 548

followed by bladder (0.84 to 3.6%), prostate (0.36 to 0.7%) and germ cell tumours [0.4%] (2). The index patient had transitional cell carcinoma of the bladder and presented with a large subcutaneous flank mass which led to the diagnosis of the primary tumour.

CASE REPORT

The patient was a 49-year old male who presented with a 12 x 8 cm flank mass of two months (Fig. 1). Initial history revealed haematuria and non-specific symptoms of fatigue. The flank mass was biopsied. Initial morphologic features revealed an undifferentiated carcinoma with clear cell features (Figs. 2 and 3); immunohistochemistry showed strong positivity for cytokeratin (CK) 7, CK20 (Fig. 4), keratin cocktail (AE1/AE3) and tumour protein p63 (Fig. 5),

From: ¹Department of Pathology, ²Department of Radiology, Princess Margaret Hospital, Nassau, Bahamas and ³Department of Pathology, Mount Sinai Medical Centre, Miami Beach, Florida, USA.

Correspondence: Dr I Agarwal, Department of Pathology, Princess Margaret Hospital, Nassau, Bahamas. E-mail: induinpath@yahoo.co.in



Fig. 1: Large right flank mass. Note bilateral hydronephrosis on noncontrast computed tomography scan.



Fig. 2: Haematoxylin and eosin (H&E) sections showing nests of transitional cell carcinoma infiltrating the dermis (10x).



Fig. 3: Tumour cells infiltrating the fibrous tissue (H&E, 10x).

Fig. 4: Positive staining for cytokeratin (CK) 7 and CK20, supporting urothelial differentiation.

Fig. 5: Positive staining for p63, supporting urothelial differentiation.

and negativity for CK5/6, placental alkaline phosphatase (PLAP), napsin, thyroid transcription factor-1 (TTF-1), cluster of differentiation (CD) 117 and homeobox protein CDX-2. A diagnosis of undifferentiated carcinoma favouring metastatic urothelial carcinoma was made. Work-up for haematuria showed a large bladder mass with bilateral hydroureteronephrosis (Fig. 6). There was a large liver mass suspicious for a metastatic lesion. In addition, there were multiple right adrenal masses, peritoneal nodules, largest in the left subphrenic region, several other smaller soft tissue nodules in the posterior abdominal wall and gluteal region, and bilateral axillary, pelvic and inguinal lymphadenopathy.

Serum creatinine and blood urea nitrogen (BUN) levels were elevated (2.2 mg/dL and 23 mg/dL, respectively). Hyperkalaemia (serum potassium 5.9 mg/dL) and deranged serum protein profile were noted. Serum alpha fetoprotein (AFP) levels were normal and mild elevation of gammaglutamyl transpeptidase (GGT) was noted (113 U/L). Serum

Fig. 6: Large bladder mass with bilateral pelvic lymphadenopathy on magnetic resonance imaging scan (T2 weighted image).

lactate dehydrogenase (LDH) level was 429 U/L. Urinalysis showed a large amount of blood.

Bilateral ureteric stents were inserted. Later, transurethral resection of bladder tumour (TURBT) for the bladder mass and the flank mass resection were done (Fig. 7).

Fig. 7: Gross specimen of right flank mass.

The urinary bladder mass was noted to be sessile and involved the left base and lateral wall. The histology confirmed it to be urothelial carcinoma (transitional cell carcinoma). The patient had chronic renal insufficiency and anaemia. Later, he also developed balanitis and lower urinary tract symptoms during the postoperative period, for which he was treated. Multiple packed red blood cells (PRBC) units were transfused and there was some improvement in the patient's haemoglobin levels. The patient received one cycle of chemotherapy including gemcitabine, cisplatin and carboplatin; however, he died seven weeks after receiving the chemotherapy and 17 weeks after the initial presentation.

DISCUSSION

Chung *et al* described a case of urothelial carcinoma of the bladder that metastasized to the brain and abdominal skin (3). Akman *et al* have described a rare case of extensive skin metastases of transitional cell carcinoma as the initial presenting feature (4). Chang *et al* reported a patient with bladder urothelial carcinoma presenting with cutaneous metastases initially and bladder tumour was the incidental finding (5). Shinagare *et al* have published a study that evaluated the metastatic pattern of muscle invasive bladder cancer from a clinic population of 392 patients. The most common sites were lymph nodes (69%), bone (47%), lung (37%), liver (26%), peritoneum (16%), pleura (11%), soft tissue including subcutaneous tissue (9%), adrenal (7%), brain (5%), urethra (3%), intestine (3%) and spleen [1%] (6).

Cutaneous metastasis from internal malignancies is a rare clinical entity and may be the first sign of an advanced disease. In a meta-analysis performed by Krathen et al, it was found that the overall incidence of cutaneous metastases was 5.3% among 20 380 cancer patients (7). Breast cancer was the most common origin of cutaneous metastases and the most common affected sites were the chest and the abdomen. Due to the limited number of patients with cutaneous metastases of bladder cancer and their subsequent poor survival, management strategies have not been clearly defined. Treatment options are often limited and palliative due to the patient's advanced age and the disease stage, resulting in poor prognosis. The treatment of choice for metastatic bladder cancer is chemotherapy, which is rarely curative. Currently, the combination of gemcitabine and cisplatin and the MVAC scheme (methotrexate, vinblastine, doxorubicin and cisplatin) are established treatments with reported tumour remission rates up to 70% (8, 9). Prognosis, however, is poor.

In conclusion, we presented a rare case of cutaneous metastases from urothelial carcinoma of the bladder. Metastatic disease should always be considered in the differential diagnosis in patients who present with malignant appearing skin nodules and a search should be done to identify the primary tumour, if not diagnosed previously. Urothelial carcinoma, although rare, can be a source of metastasis to the subcutaneous tissues. Due to advanced stage of the disease in most cases, treatment is mainly supportive and the prognosis is poor.

ACKNOWLEDGMENT

We would like to thank Dr Olga Stokes and Dr Wesley Francis for their invaluable input and information.

REFERENCES

- Ugurluer G, Dogan E, Turan N. Cutaneous metastasis from transitional cell carcinoma of the bladder (in a case with two primaries). Erciyes Tip Dergisi 2010; **32**: 127–30.
- Chuang K-L, Liaw C-C, Ueng SH, Liao S-K, Pang S-T, Chang Y-H et al. Mixed germ cell tumor metastatic to skin: Case report and literature review. World J Surgl Oncol 2010; 8: 21.
- Chung JH, Lee JY, Pyo JY, Oh YH, Lee SW, Moon HS et al. Brain and skin metastasis from urothelial carcinoma of bladder. Korean J Urol 2013; 54: 66–8. doi: 10.4111/kju.2013.54.1.66. Epub 2013 Jan 18.
- Akman Y, Cam K, Alper M. Extensive cutaneous metastasis of transitional cell carcinoma of the bladder: case report. Int J Urol 2003; 10: 10–4.
- Chang CP 1st, Lee Y, Shih HJ. Unusual presentation of cutaneous metastasis from the bladder carcinoma: case report. Chin J Cancer Res 2013; 25: 362–5. doi: 10.3978/j.issn.1000-9604.2013.06.08.
- Shinagare AB, Ramaiya AH, Jagannathan JP, Fennessy FM, Taplin ME, Van den Abbeele AD. Metastatic pattern of bladder cancer: correlation with the characteristics of the primary tumor. AJR Am J Roentgenol 2011; 196: 117–22. doi: 10.2214/AJR.10.5036.
- Krathen RA, Orengo IF, Rosen T. Cutaneous metastasis: a metaanalysis of data. South Med J 2003; 96: 164–7.
- Svatek RS, Siefker-Radtke A, Dinney CP. Management of metastatic urothelial cancer: the role of surgery as an adjunct to chemotherapy. Can Urol Assoc J 2009; 3 (6 Suppl 4): S228–S231.
- Jakse G, Stockle M, Lehman J, Otto T, Krege S, Rubben H. Metastatic bladder carcinoma. Dtsch Arztebl 2007; 104: A1024–8.