

Metastatic carcinoma of breast in the urinary bladder

MH Wong 王明皓
MK Yiu 姚銘廣
KL Ho 何崑崙

Less than 5% of breast cancers present as metastasis, and urinary bladder secondaries were only sporadically reported in the literature. However, they may even be responsible for the initial presentation, for which reason they can pose a diagnostic challenge. We present here what we believe is the first such case in Hong Kong, with a review of this entity.

Introduction

Carcinoma of the breast is the commonest malignancy in Hong Kong women, and in 2009 it was ranked third as a cause of cancer mortality.¹ The life-time risk for Hong Kong women is 1 in 19 and risk of consequential death 1 in 101. Evidently, 5% of the cases present as metastatic disease, common sites being lymph nodes, lung, liver, and bone.² Metastases to other solid organs such as the urinary bladder are uncommon but have been reported sporadically. Patients with urinary bladder metastasis have very limited survival (about 1 month to 2 years). We present the first reported case of carcinoma of breast with metastasis to urinary bladder in Hong Kong, with a structured review of this entity.

Case report

An 83-year-old woman, with a history of left breast cancer and modified radical mastectomy performed more than 30 years earlier, presented in 2006 with a skin nodule on right chest wall. Biopsy of the right chest wall nodule showed metastatic adenocarcinoma which was oestrogen receptor (ER) positive, progesterone receptor (PR) positive, and c-ERBB2 negative. Metastatic workup revealed diffuse metastases to right chest wall, left breast, left axillary lymph node, bone, adrenal gland, and peritoneal deposit. She received serial hormonal therapy including letrozole and exemestane together with radiotherapy to bony metastasis. Follow-up imaging with positron emission tomography-computed tomography (PET-CT) showed stabilisation of disease and fine-needle aspiration cytology of the left breast lesion only showed mild epithelial hyperplasia. Five years after the diagnosis of metastases, she presented with anaemic symptoms and volunteered a 2-week history of gross haematuria. The CT revealed a contrast-enhancing mass arising from left lateral wall of the urinary bladder. Flexible cystoscopy showed a 25 mm x 25 mm erythematous patch on the left lateral wall with an irregular surface (Fig), which was biopsied with haemostasis achieved by cautery. Histology revealed irregular, solid nests and trabeculae of round-to-polygonal tumour cells. Rare glandular lumens lined by cells possessing a moderate amount of eosinophilic cytoplasm were also noted. On immunohistochemical staining, the tumour cells were positive for CK-7, and negative for CK-20 and GCDFP (gross cystic disease fluid protein). Moreover, ER and PR stains were avidly taken up while the C-ERBB2 score was 2 (ie equivocal). Haemostasis was achieved with electrocautery and no further haematuria was observed. The latest PET-CT showed an interval increase in metabolic activity in most of the metastases, including that in the urinary bladder. The patient continues to receive chemotherapy and hormonal therapy and is currently alive more than 6 years since the diagnosis of metastasis.

Key words

Breast neoplasms; Neoplasm metastasis;
Urinary bladder

Hong Kong Med J 2013;19:455-7
DOI: 10.12809/hkmj133768

Discussion

Urinary bladder secondaries are rare and account for 2% of all bladder neoplasms; most are discovered at autopsy.^{3,4} Known primaries include gastric cancer, melanoma, as well as breast and lung cancer. In a recent clinicopathological study of 11 patients with metastatic lesions in the urinary bladder, most were in women and frequently breast cancer (3/11).⁵ Breast cancer commonly metastasises to lymph nodes, lung, liver and bone, whilst it rarely involves the brain, adrenals, spleen, thyroid, heart, or urinary bladder. In 1980, Haid et al⁶ reported a patient with urinary bladder metastases from breast carcinoma, although

Division of Urology, Department
of Surgery, Queen Mary Hospital,
Pokfulam, Hong Kong
MH Wong, MB, BS, FHKAM (Surgery)
MK Yiu, MB, BS, FHKAM (Surgery)
KL Ho, MB, BS, FHKAM (Surgery)

Correspondence to: Dr MH Wong
Email: edwong56@gmail.com

乳癌細胞轉移膀胱的病例報告

有少於百分之五的乳癌會出現癌細胞轉移，至於癌細胞轉移至膀胱甚為罕見。由於這些轉移的癌細胞可能引致病人出現首發的症狀，因此引致診斷困難。本文報告一宗乳癌轉移到膀胱的病例，並對此等病例進行回顧。我們相信這是香港有關癌細胞轉移至膀胱的首宗病例報告。



FIG. Cystoscopic finding of a urinary bladder secondary

autopsy reports date back to 1956.⁷ To date, there have been at least 40 reported cases of metastatic breast cancer to the bladder.

One postulated mechanism of secondary bladder tumours is from emboli that traverse the pulmonary circulation without causing lung metastasis, but do so upon reaching the urinary bladder haematogenously. Other possible mechanisms are through lymphatic or direct retroperitoneal invasion.⁸

The most common presenting symptom was urinary frequency and gross haematuria. Other presentations include difficulty in voiding, incidental finding on imaging, and/or ureteral obstruction or even urinary incontinence.^{5,9} Less-common findings include pelvic mass and bilateral hydronephrosis, and renal failure.¹⁰ Patients can present concomitantly with the primary tumour, or as a late metastasis, with time lapses exceeding 30 years.² Our case demonstrates one of the longest time lapses between

treatment of the primary tumour and presentation with a metastasis (more than 30 years). Rarely the diagnosis of breast cancer is made after bladder metastasis is discovered.² As in our patient, most cases will have widespread metastases. However, a solitary metastasis to the urinary bladder has also been reported.¹¹

Diagnostic workup requires direct visualisation of the bladder mucosa by cystoscopy, and histological confirmation of a specimen obtained by means of cup biopsy or transurethral resection. Cystoscopic findings vary and include solid tumour, non-specific inflammatory patches, and thickened bladder wall with intact overlying mucosa (Fig). Upper urinary tract imaging is indicated when there is evidence of renal impairment suggesting obstructive nephropathy. Screening by means of magnetic resonance imaging or PET-CT may reveal other metastases.

Although ductal breast carcinoma is more common than the lobular subtype, infiltrating lobular carcinoma accounts for the majority of metastases to the bladder.² The latter tends to occur as a diffuse thickening of mucosa rather than a discrete nodule.¹² To differentiate histological variants of primary bladder tumour from secondaries, absence of bladder mucosa alterations/lesions can be helpful. There may also be unusual monomorphic growth patterns without accompanying conventional urothelial carcinoma features, and the tumour can appear to invade towards the luminal surface from the outside.¹¹

Additional means of avoiding diagnostic confusion is the utilisation of immunohistochemical staining for various markers. Common screening markers include cytokeratin, CK-7, CK-18, CK-19, CK-20, as well as ER/PR expression for tumours of suspected endometrial and breast origin. Other typical urothelial markers include p63, Ker903, thrombomodulin, GATA3, and CK5/6. Other markers to screen for cancers include prostate-specific antigen for prostate, thyroglobulin for thyroid, uroplakin III for urothelium, and HepPar I for hepatocellular origin.⁵

Treatment of metastatic breast cancer involves a combination of chemotherapy and hormonal treatment, mainly anti-oestrogens. Local resection is mainly reserved for diagnostic purposes and amelioration of local symptoms. It is not curative, as the deposit is muscular rather than mucosal, and ER- and PR-positive tumours are more responsive to hormone therapy than their negative counterparts that have longer disease-free survivals.¹³ However, not uncommonly the ER/PR status of the metastatic lesion differs from that of the original tumour, and one study reported that the discordance rate was as high as 24%.¹⁴ Patients whose tumour status changed from positive to negative (positive/negative) have

shorter median survivals than positive/positive or negative/negative patients.¹⁵ In our case the original ER/PR status was unknown as the primary treatment was performed more than 30 years ago. Also, HER2-positive breast cancer tends to be more aggressive and less responsive to hormone treatment than other breast cancers. In cases of obstructive uropathy, percutaneous drainage via ureteric catheterization should be performed to optimise renal function before initiation of chemotherapy. In terms of survival, there are reports of survival for more than 5

years after diagnosis of bladder metastasis, but most patients die within 1 year.⁵ Our case is currently alive and receiving further hormonal manipulation.

The urinary bladder is an uncommon site of metastasis from breast cancer. Although routine screening of the lower urinary tract is not warranted for all patients, women with a history of breast cancer who present with urinary symptoms should be investigated to exclude such a bladder lesion. However, if the presence of a metastasis is confirmed, early initiation of appropriate treatment is warranted.

References

- Hong Kong Cancer Registry. Hospital Authority; 2009.
- Feldman PA, Madeb R, Naroditsky I, Halachmi S, Nativ O. Metastatic breast cancer to the bladder: a diagnostic challenge and review of the literature. *Urology* 2002;59:138. [crossref](#)
- Bates AW, Baithum SI. Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumours: clinicopathological and histological features of 282 cases. *Histopathology* 2000;36:32-40. [crossref](#)
- Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma: analysis of 1000 autopsied cases. *Cancer* 1950;3:74-85. [crossref](#)
- Xiao GQ, Chow J, Unger PD. Metastatic tumor to the urinary bladder: clinicopathologic study of 11 cases. *Int J Surg Pathol* 2012;20:342-8. [crossref](#)
- Haid M, Ignatoff J, Khandekar JD, Graham J, Holland J. Urinary bladder metastases from breast carcinoma. *Cancer* 1980;46:229-32. [crossref](#)
- Ganem EJ, Batal JT. Secondary malignant tumors of the urinary bladder metastatic from primary foci in distant organs. *J Urol* 1956;75:965-72.
- Ponte JE, Oldford JR. Metastatic breast carcinoma to the bladder. *J Urol* 1970;104:839-42.
- Massoud W, Ferlicot S, Hajj P, et al. Metastatic breast carcinoma to the bladder. *Urology* 2009;74:785-6. [crossref](#)
- Forster J, Agrawal V, Anathhanam AJ, Spencer N, Biyani CS. Breast carcinoma metastasizing to the urinary bladder presenting as bilateral hydronephrosis treated with ureteral stenting and chemotherapy. *Urol Oncol* 2006;24:33-5. [crossref](#)
- Zagha RM, Hamawy KJ. Solitary breast cancer metastasis to the bladder: an unusual occurrence. *Urol Oncol* 2007;25:236-9. [crossref](#)
- Ryan PD, Harisinghani M, Lerwill MF, Kaufman DS. Case records of the Massachusetts General Hospital. Case 6-2006: A 71-year-old woman with urinary incontinence and a mass in the bladder. *N Engl J Med* 2006;354:850-6. [crossref](#)
- Lin WC, Chen JH. Urinary bladder metastasis from breast cancer with heterogeneous expression of estrogen and progesterone receptors. *J Clin Oncol* 2007;25:4308-10. [crossref](#)
- Iguchi C, Nio Y, Itakura M. Heterogeneous expression of estrogen receptor between the primary tumor and the corresponding involved lymph nodes in patients with node-positive breast cancer and its implications in patient outcome. *J Surg Oncol* 2003;83:85-93. [crossref](#)
- Lower EE, Glass EL, Bradley DA, Blau R, Heffelfinger S. Impact of metastatic estrogen receptor and progesterone receptor status on survival. *Breast Cancer Res Treat* 2005;90:65-70. [crossref](#)