

Metastatic Penile Cancer Presenting as Hypercalcemia and Pathological Fracture of the Humerus: A Rare Event

C C K Ho, MD*, J Nazri, MS*, M Z Zulkifli, MS*, S Sritharan, FRCS*, A R Hayati, DCP**

*Division of Urology, Department of Surgery, **Department of Pathology, Hospital Universiti Kebangsaan Malaysia, Jalan Yaakob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur

Summary

Distant haematogenous metastasis in penile cancer is rare. A patient who had total penectomy and bilateral inguinal lymphadenectomy for penile cancer but later presented with hypercalcemia of malignancy and pathological fracture of the humerus is reported.

Key Words: Carcinoma of penis, Hypercalcaemia, Pathological fracture, Long bone metastasis

Introduction

Carcinoma of the penis is rare. It usually spreads by direct invasion to the inguinal lymph nodes. Haematogenous distant metastasis is unusual and occurs late. This is the first reported case of penile cancer metastasizing to the long bone, that presented with hypercalcemia and pathological fracture.

Case Report

A 55-year-old Chinese man presented with a fungating mass involving the glans penis and prepuce. Inguinal lymph nodes were not palpable at the time of presentation. A biopsy of the lesion revealed squamous cell carcinoma. A total penectomy with perineal ureterostomy was performed. Histopathological examination (HPE) showed well-differentiated, keratinising squamous cell carcinoma invading the corpus spongiosum, corpus cavernosa and distal urethra. Perineural and vascular invasion were present.

One month after the operation, it was noted that the inguinal lymph nodes were palpable bilaterally. Right radical inguinal lymphadenectomy was performed followed by the left, one month later. HPE revealed involvement of the superficial and deep inguinal lymph nodes bilaterally. The deep lymph nodes of Cloquet were not involved. A computerised tomography (CT) scan of the abdomen and pelvis done three months later did not show any recurrence.

However, after six months, he complained of lethargy, loss of appetite and weight, with vague pain over the chest and scapula. He had raised serum calcium, with a corrected calcium level of 4.64 mmol/L (normal value 2.2-2.6 mmol/L). A deformity of the right arm was noted but he denied any history of trauma. An x-ray of the right arm showed pathological fracture of the humerus

(Figure 1). The serum parathyroid hormone level was normal and urine for Bence-Jones protein was negative.

This article was accepted: 15 August 2006

Corresponding Author: Christopher Ho Chee Keong, Department of Surgery, Hospital Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur

CASE REPORT

Hydration with eight pints of normal saline and diuresis with furosemide were immediately commenced. He was also given 4mg of zoledronic acid through intravenous infusion. His corrected calcium level eventually reduced to 3.36 mmol/l, with a further drop to a level of 2.06 mmol/l the following day. A bone scan revealed multiple osteoblastic and osteolytic lesions involving the right humerus, both femurs, sternum, right sacroiliac joint, and the right 5th, 6th and 10th ribs. Ultrasound of the abdomen and CT scan of the brain were normal.

Internal fixation by interlocking nail was performed for the fracture of the humerus. A histopathological examination of the biopsy taken from the lesion of the humerus showed metastatic, well-differentiated, keratinising squamous cell carcinoma. The malignant cells contained abundant eosinophilic cytoplasm with nuclear pleomorphism (Figure 2).

Discussion

Penile carcinoma is uncommon. The incidence is higher in the developing as compared to developed countries. In Malaysia, the incidence is 0.3 per 100,000¹. It tends to occur in the elderly, most

commonly on the glans (48%) and prepuce (25%). Ninety-five percent are squamous cell carcinomas.

Penile carcinoma is mainly a localised disease (39%), with carcinoma-in-situ making up 37% and regional disease 13%. Distant metastasis from haematogenous spread is rare (2.3%) and the mean life span of those with distant metastasis is 7.4 months². Cases reported in the literature were of metastasis to the kidney, adrenal gland, retroperitoneal lymph nodes, lung, brain and dorsal spine^{3,4} but not to the long bones.

Our patient presented with hypercalcemia secondary to bone metastasis with pathological fracture. Hypercalcemia has been reported in penile cancer without bone metastasis and this was attributed to the elaboration of parathyroid hormone related protein resulting in paraneoplastic syndrome⁵.

Patient with tumours of low metastatic potential (stages Tis, Ta, T1, grades 1-2 tumours) are candidates for organ preservation. Examples are Moh's surgery, limited-excision strategies, laser ablations or topical treatment like 5-fluorouracil or imiquimod, cream for Tis. Partial amputation is possible where a margin of 2cm is attainable. Otherwise, a total penectomy is necessary.

Approximately 50% of palpable inguinal nodes in penile carcinoma show reactive changes. Hence, antibiotic therapy is recommended and the nodes reassessed. In non-responsive cases, bilateral inguinal lymphadenectomy should be performed. However, up to 29% of clinically non-palpable inguinal nodes have

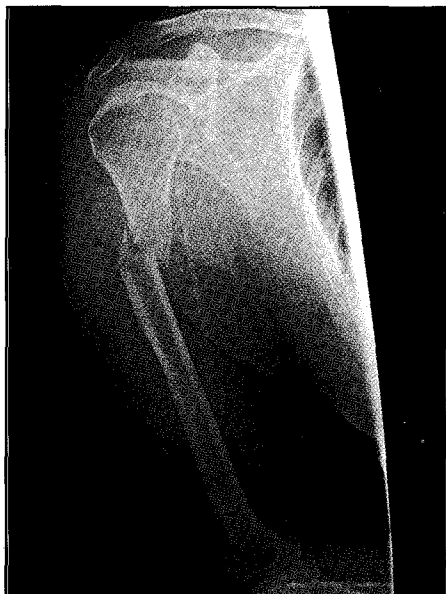


Fig 1: X-ray of the right humerus showing multiple osteolytic lesions and pathological fracture

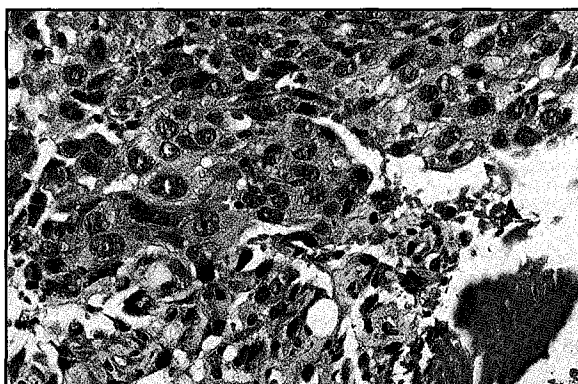


Fig 2: X-ray of the right humerus showing multiple osteolytic lesions and pathological fracture

micrometastases in the lymph nodes. The best indicators of inguinal node involvement are the stage and grade of the primary tumour and the presence of lymphatic or vascular invasion in the primary tumour. The use of sentinel lymph node biopsy has been advocated.

Metastatic penile cancer is moderately sensitive to chemotherapy. Partial responses are most common, occurring in approximately 64% of patients while complete responses occur in less than 15% of patients. Regimens that have been studied include methotrexate,

bleomycin and cisplatin (MBP), vinblastine, bleomycin and methotrexate (VBM), and cisplatin with 5-fluorouracil.

The prognosis for patients with distant haematogenous metastasis is poor and there is very limited experience in dealing with it. This challenging subset of patients are best managed with multimodal treatment employing palliative chemotherapy, radiotherapy and pharmacotherapy. However, our patient who was planned for radiotherapy to the humerus followed by palliative chemotherapy, defaulted follow-up.

References

1. Lim GCC, Halimah Y (eds). Second report of the National Cancer Registry. Cancer Incidence in Malaysia 2003. National Cancer Registry. Kuala Lumpur 2004.
2. Rippentrop JM, Joslyn SA, Konety BR. Squamous cell carcinoma of the penis: evaluation of data from the Surveillance, Epidemiology, and End Results program. *Cancer* 2004; 101: 1357-363.
3. Lutterbach J, Pagenstecher A, Weyerbrock A, Schultze-Seemann W, Waller CF. Early-stage penile carcinoma metastasizing to brain: case report and literature review. *Urology* 2005; 66(2): 432.
4. Lal P, Halder S, Datta NR. Carcinoma of the penis metastasizing to the dorsal spine. A case report. *Urol Int* 1999; 62(4): 249-51.
5. Dorfinger K, Maier U, Base W. Parathyroid hormone related protein and carcinoma of the penis: Paraneoplastic hypercalcemia. *J Urol* 1999; 161: 1570.