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A rare case report of femoral neck metastasis secondary from penile carcinoma and literature review

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ABSTRACT

Metastatic bone diseases are common in the advanced stage of numerous cancers, but rarely reported to be secondary from penile cancer. To date, there are only 9 cases of skeletal metastasis from penile cancer reported in literature worldwide. Herein, we report a rare case of the femoral neck metastasis secondary from penile carcinoma in a 35-year-old Chinese male. Based on the case study and more importantly, the literature review, we attempted to identify the clinical features of the metastatic bone diseases secondary from penile cancer.

Introduction

Skeletal metastasis could be secondary from numerous types of cancers. On the other hand, penile cancer is a fairly uncommon and localized malignancy. It usually spreads via lymphatic routes, and hematogenous dissemination seldom occurs even in the advanced stage due to the natural barrier functions of Buck's fascia.[1] Metastatic bone disease secondary from penile carcinoma is extremely rare, with only 9 cases reported in literature worldwide to date. Most of these publications consist of a single case report, while a summary is still unavailable.

Case description

A 32-year-old male was referred to with an ulcerated lesion over the dorsum of the penis for one-year duration. On admission, histological biopsy revealed squamous cell carcinoma (SCC). The patient underwent partial penectomy and bilateral inguinal lymphadenectomy. In the resected specimen, microscopically, the tumor cells showed infiltrative growth pattern, in nest and cord, and focally invaded corpora cavernosum. Metastasis was detected in 3 out of 9 resected right inguinal lymph nodes (Fig. 1a and b). According to the European Association of Urology (EAU) guidelines, he was diagnosed with penile carcinoma (pT3N2M0, stage II). Adjuvant TP chemotherapy regimen scheduled as 1 time per month after operation (paclitaxel 250mg continuous intravenous infusion 24 hours d1 and cisplatin 40mg d1-3, q3w).

Two months after surgeries, he complained about right thigh pain. Pelvic computed tomography (CT) showed a hypodense mass, measuring 1.8*2.9cm, located in the right femoral neck. A histological biopsy of the right femoral neck lesion was performed, and revealed SCC. The diagnosis of metastatic bone diseases secondary from penile cancer was considered firstly. Possible primary tumors of other sites were excluded by clinical examinations and standard radiologic workups, including negative abdominal and pulmonary CT scans. After a multidisciplinary team reviewed, his third chemotherapy was postponed, and a right total hip replacement arthroplasty was performed. The postoperative pathology results confirmed metastatic SCC in the femoral neck (Fig. 1c and d). Magnetic resonance imaging (MRI) revealed this mass had low T1 and long T2 signal, with bone destruction (Fig. 2a–d). According to the EAU guidelines, the final tumor classification was pT3N2M1 stage IV. The postoperative courses were uneventfully, and his chemotherapy cycles continued after operations. However, three years later, he complained about right thigh pain. Imaging examinations indicated tumor recurrence in the right hip joint. Our patient received oral capecitabine chemotherapy (500mg, bid) and local radiotherapy (300cGy per fraction, 10 fractions in all). He was still alive 5 years after the initial diagnosis.

Discussion

Fairly uncommon, penile cancer is a localized malignancy. The invasion pattern of penile cancer has been commonly described as lymphatic route spread, because the penis has a rich lymphatic network. We searched PubMed, Google Scholar and Web of Science for cases of osseous metastasis from penile cancer between 1987 and 2020. Only 9 cases are included. We briefly summarized their major clinical features, as shown in Table 1.

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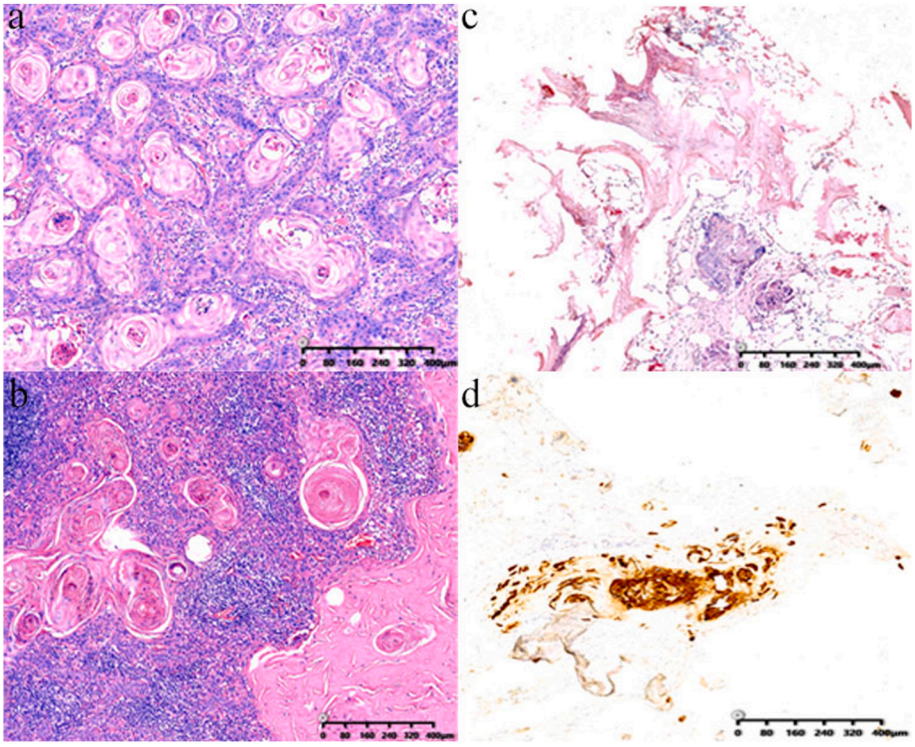

Fig. 1. (a,b) H and E staining of the resected specimen (× 100) (a) Histologic images showed neoplastic cells are well-differentiated and arranged in nest pattern. (b) Lymph nodes metastasis is observed, with significant keratinization. (c,d)The histopathological study of resected specimen of the femoral neck lesions. (c) the presence of tumor cells in the bone marrow tissue (H and E, × 100). (d) immunohistochemistry revealed the tumor cells were positive for cytokeratin (Immunohistochemical staining, × 100).

Penile cancer usually occurs in the sixth decades of life, with SCC representing the most common pathological type. For 9 patients of osseous metastasis from penile cancer, the mean age was 60 years (range 35–80 years), and the pathological types are all SCC. The metastatic sites were commonly spine (4/9 patients), followed by the femur (3/9 patients), humerus (1/9 patients) and tibia (1/9 patients). Symptoms caused by metastatic lesions were commonly pain (7/9 patients), paraplegia (2/9 patients), deformity (1/9 patients), swelling (1/9 patients) and fracture (1/9 patients); these discomforts were present at a mean time of 23 months (range 6–108months) after the diagnosis of penile carcinoma. And of the 9 cases, three cases were reported in which osseous metastasis preceded inguinal lymph nodes involvement.

For the diagnosis of metastatic bone disease, serological examinations are usually of low efficiency. Although hypercalcemia is often presumed to be associated with bone metastasis because of osteolysis, it may be a hallmark of paraneoplastic syndrome but not of skeletal metastasis in penile cancer.[2] In most of these cases, the diagnosis was made through imaging and histopathological examinations. Of the 10 cases, histological biopsy of the metastatic foci was performed in 5 cases, including the present case. The results of biopsy are mostly well-differentiated SCC, and consistent with final pathological results.

The management experience of skeletal metastasis from penile cancer is greatly limited due to its rarity. We believe its treatment should be individualized with purposes of palliating symptoms and maintaining functions. In these reported cases, spinal disseminated lesions were generally treated with palliative radiotherapies, with the aim of preventing cord compression. However, for metastatic lesions in the long bones, operations were often required to minimize discomforts and restore functions. Regarding the femoral metastasis from penile cancer, overall three cases were previously reported in literature. Two cases located in the femoral diaphysis, and both were treated with internal fixation. The remaining one was located in the subtrochanteric region, which was treated with total femur reconstruction after reconstruction nail fixation failed. Compared to endoprosthetic reconstructions, internal fixation is known to show a much lower life expectancy, due to its disability to prevent tumor progression.[3] In the present case of nodal involvement and femoral neck metastasis, adjuvant chemotherapy was employed after lymphadenectomy as postoperative chemotherapy is recommended for patients of penile cancer with two or more lymph node metastases according to the EAU guidelines, and a total hip replacement arthroplasty was performed to prevent impending pathological fracture.

A Surveillance Epidemiology and End Results (SEER) study, enrolling 1605 patients of penile cancer, has showed the mean life span was only 7.4 months for those with distant metastasis.[4] Given this context, the survival of patients with osseous metastasis from penile cancer would be dismal. And the survival of the present case would be significantly prolonged, which may be attributed to comprehensive management we employed.

Conclusion

The onset of bone metastatic symptoms mostly occurs within two years after the diagnosis of penile carcinoma. Radiologic imaging and histopathological examinations are valuable tools for the diagnosis of this rare entity. With aims of palliation, surgery is the preferred option of the treatments, especially for metastatic foci in the long bones.

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CRediT authorship contribution statement

Junjie Sun: Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization, Funding acquisition, Design, Definition of intellectual content. **Xiaoyi Chen:** Writing – review & editing, Formal analysis, Conceptualization. **Zhijie Xu:** Writing – review & editing, Writing – original draft, Funding acquisition. **Junjie Tian:** Formal analysis, Design, Writing – review & editing. **Baiye Jin:** Writing – review & editing, Writing – original draft, Conceptualization.

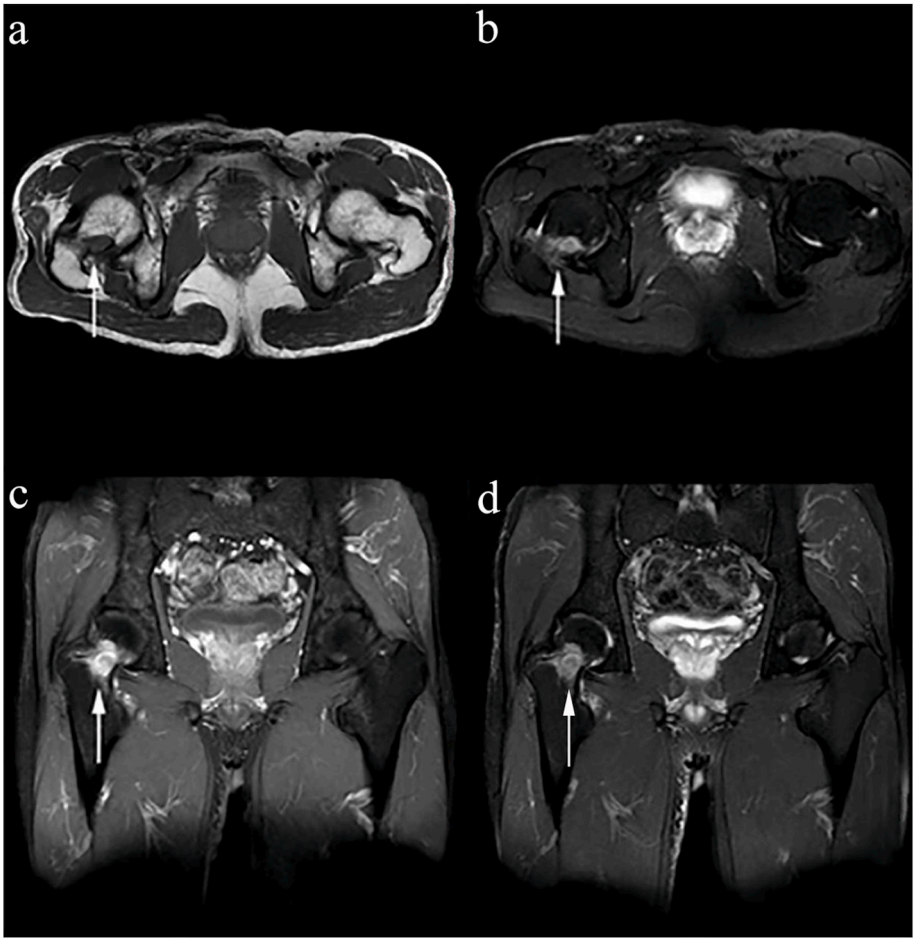

Fig. 2. The presence of the femoral neck bone destruction in the MRI after partial penectomy with right inguinal lymphadenectomy. (a) The lesion of femoral neck (white arrow) was low signal in T1-weighted MRI. (b) The lesion (white arrow) has slightly high signal T2-weighted MRI. (c,d) The metastatic lesion (white arrow) was located in femoral neck and showed significant enhancement both in coronal T1-weighted imaging(c) and coronal T2-weighted imaging(d).

Table 1
Summary of reported cases of skeletal metastasis secondary from penile cancer.

Year	Author	Country	Age	TI	LNI	Hypercalcemia	Presentation	Location	Treatment
1995	Jacob	India	51	7 m	Yes	NM	Paraplegia	Spine	Radiotherapy
1999	Punita	India	80	8 m	No	NM	Pain	Spine	Radiotherapy
2000	Nunez	Spanish	67	12 m	NM	NM	Pain + Paraplegia	Spine	Surgery
2006	Ho	Malaysia	55	6 m	Yes	Yes	Hypercalcemia + deformity	Humerus	Surgery
2013	Ramachandran	India	45	0 m	Yes	NM	Pain + swelling	Tibia	NM
2016	Shabbir	India	35	18 m	Yes	No	Pain	Femur	Surgery
2016	Sarah	UK	57	10 m	NM	NM	Chest pain	Spine	Surgery
2016	Laura	Sweden	71	18 m	No	NM	PF	Femur	Surgery
			76	108 m	NM	No	Pain	Femur	Surgery

TI refers time interval between the diagnosis of penile carcinoma and the onset of bone metastatic symptoms, *LNI* lymph nodes involvement, *m* month(s) *NM* not mentioned *PF* pathological fracture.

Declaration of competing interest

We have read and understood Urology Case Report's policy on disclosing conflicts of interest and declare that we have none.

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