

Renal-type clear cell carcinoma of the prostate: A case report

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Abstract. Renal-type clear cell carcinoma of the prostate is a rare and novel tumor that has only been identified in recent years. The present study describes a lesion in the prostate of a 64-year-old male with a two-year history of urinary frequency, urgency and difficulty, who was admitted to the San Ai Tang Hospital for benign prostatic hyperplasia, and subsequently underwent transurethral resection of the prostate. In total, 12 g of tissue was resected, which demonstrated morphological and immunohistochemical similarities to clear cell carcinoma of the kidney. Ultrasound inspection and computed tomography revealed prostate enlargement. Although no renal-enclosed mass was identified, metastatic lesions were revealed in the lungs, sternum and clavicles. In addition, right pleural thickening and a small amount of effusion in the pleural cavity were detected. Clear cell carcinoma was identified throughout the prostate, with surrounding regions of ordinary-type prostatic adenocarcinoma (Gleason score, 4+4). The urinary bladder exhibited no dysplasia or neoplasia. It was therefore concluded that the tumor represented a primary renal-type clear cell carcinoma that had arisen in the prostate. To the best of our knowledge, this type of extra-renal tumor has only been reported in three other previous studies.

Introduction

Clear cell carcinomas that occur in the lower urinary tract are usually variants of more frequently diagnosed cancers, including prostatic adenocarcinoma and transitional cell carcinoma (1), however, they may also be a less common type of carcinoma, such as clear cell carcinoma, which is similar to Müllerian tumors and metastatic renal cell carcinomas (RCCs) (2). RCC is the most common subtype of clear cell carcinoma, which originates from renal tubular epithelial cells and accounts for 85% of all renal tumors (3). Patients

with RCC are usually asymptomatic in the early stages of the disease, however, as the tumor size increases patients most commonly present with a lump in the lower abdomen or back, lower back pain and hematuria (4). The most common sites of RCC metastases are the lungs, bone and liver (5,6). However, metastases affecting the lower urinary tract, namely the prostate and bladder, are extremely rare (7,8). In 2012, the worldwide age-standardized mortality rate for RCC was 1.8 deaths per 100,000 individuals (9). At present, treatment for RCC includes radical surgery, immunotherapy and chemotherapy (10). To the best of our knowledge, renal-type clear cell carcinoma occurring as a primary tumor in an extra-renal location has only been described in three other previous studies (11-13) which revealed that RCC of the prostate is a novel pathological entity, that exhibits histological and immunohistochemical features similar to those of RCC.

Case report

A 64-year-old male with a two-year history of urinary frequency, urgency and difficulty, that had undergone treatment with a detaining urethral catheter for eight days, was referred to the San Ai Tang Hospital (Lanzhou, China) due to lower urinary tract obstructive symptoms on January 3, 2009. A rectal examination revealed third-degree diffuse enlargement of the prostate, nodosity and disappearance of the central sulcus, with the absence of any tenderness. An ultrasound examination revealed prostate hyperplasia (Fig. 1). The serum prostate-specific antigen (PSA) value was 10.2 ng/ml, which was slightly higher than normal (normal range, <4 ng/ml). The cystourethroscopy findings were unremarkable. A computed tomography (CT) scan identified hyperplasia of the prostate. The suggested diagnosis was that of clear cell carcinoma, which had most likely originated from the kidneys. However, a review of the radiological imaging studies revealed the absence of a renal tumor. Furthermore, metastatic lesions were identified in the lungs, sternum and clavicles. In addition, right pleural thickening and a small amount of effusion in the pleural cavity were observed. The results of samples retrieved from random cystoscopic biopsies of the bladder and prostatic urethra, as well as bladder washings, were benign. The urinary bladder demonstrated no evidence of dysplasia or neoplasia. Subsequent to thorough counseling, the patient elected to undergo transurethral resection of the prostate in order to relieve the symptoms. In total, 12 g of tissue was resected. The

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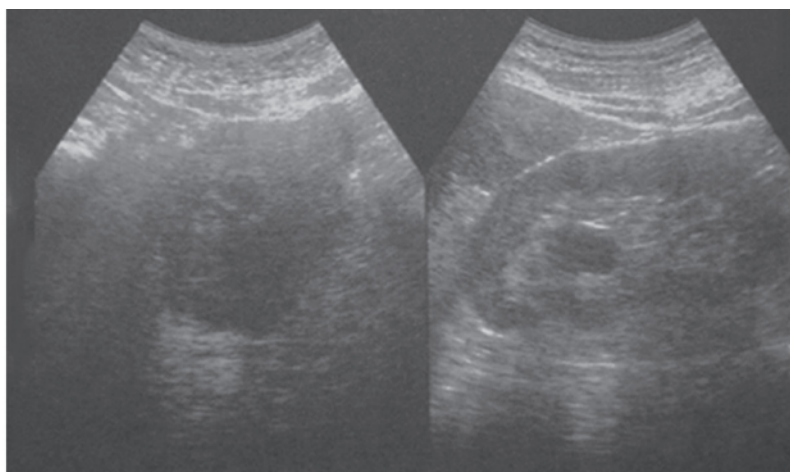


Figure 1. Ultrasound inspection of the prostate (left image) and kidney (right image). The prostate was enlarged, with a clear outline, a coarse prostatic capsule echo and an uneven substantive echo. The bilateral kidney was of normal size, with a clear outline and a uniform substantive echo.

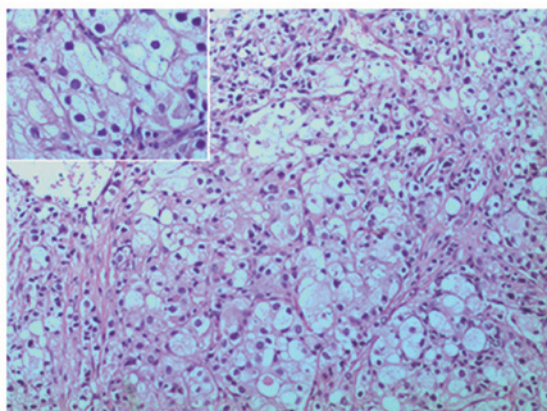


Figure 2. Hematoxylin and eosin staining of clear cell carcinoma (magnification, large image, x100 and inset image, x200).

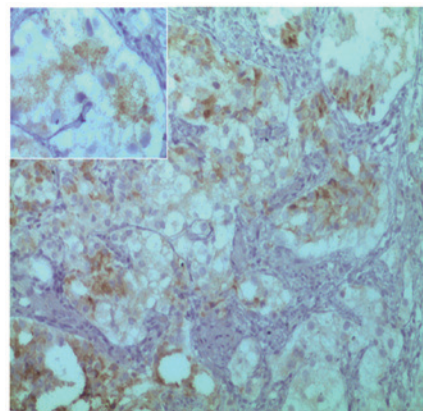


Figure 4. Positive immunostaining for α -methylacyl-CoA racemase (magnification, large image, x100 and inset image, x200).

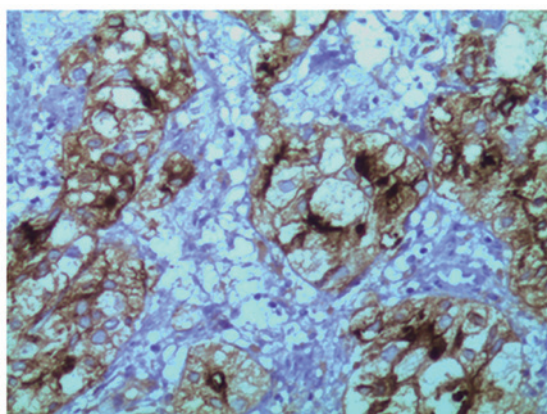


Figure 3. Positive immunostaining for cluster of differentiation 10 (magnification, x200).

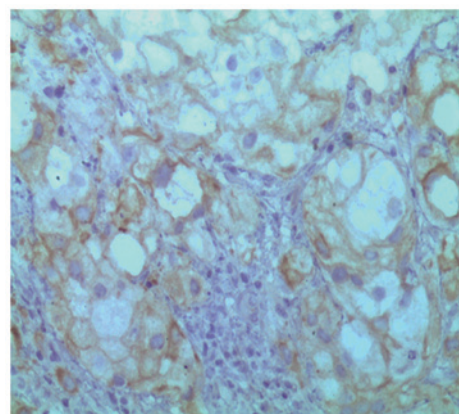


Figure 5. Positive immunostaining for low molecular weight cytokeratin (magnification, x200).

first 10 blocks of tissue submitted for microscopic analysis were primarily malignant, and exhibited morphological and immunohistochemical characteristics similar to those of clear cell carcinomas of the kidney. Clear cell carcinoma was subsequently identified throughout, with surrounding regions of ordinary-type prostatic adenocarcinoma [Gleason

score (14), 4+4]. In addition, confluent nests and/or tubules, composed of epithelium with uniformly clear cytoplasm and atypical, enlarged nuclei with prominent nucleoli, were observed (Fig. 2). An interstitial lymphocytic inflammatory infiltrate and an extensive, thin-walled vascular network were associated with the tumor cells. No evidence of significant

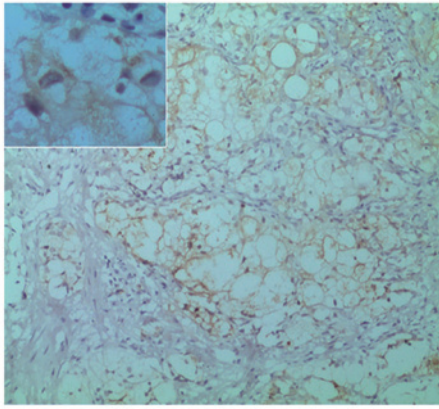


Figure 6. Positive immunostaining for prostate-specific acid phosphatase (magnification, large image, x100 and inset image, x200).

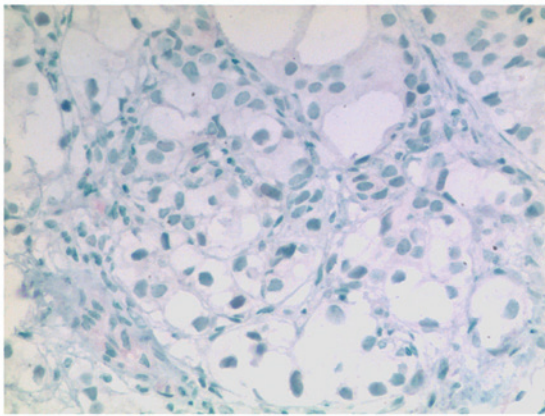


Figure 7. Negative immunostaining for paired box 8 (magnification, x200).

mitotic activity was observed. The clear cell lesion appeared to have originated from the prostate, but exhibited no desmoplastic stromal response. Standard immunohistochemical procedures using paraffin sections revealed that the lesion demonstrated positive immunoreactivity for vimentin (VIM), epithelial membrane antigen, membrane metalloendopeptidase (MME; also known as cluster of differentiation 10) (Fig. 3), α -methylacyl-CoA racemase (P504S; Fig. 4), low molecular weight cytokeratin (Fig. 5) and prostate-specific acid phosphatase (PSAP; Fig. 6). By contrast, no immunoreactivity was noted for PSA, broad-spectrum cytokeratin, high molecular weight cytokeratin, paired box 8 (PAX8; Fig. 7) or carcino-embryonic antigen (CEA). With the exception of PAX8, the results of the immunostaining analysis were almost identical to those obtained from clear cell carcinomas of the kidney.

The patient succumbed to the disease six months after surgery due to multi-organ system failure. Prior to mortality, the follow-up CT examination again failed to identify a second renal mass. Written informed consent for the publication of this case report and accompanying images was obtained from the patient's family.

Discussion

RCC is associated with a number of specific cytological features, including atypical, enlarged and prominent nuclei,

with classic structural features, such as tubules, solid nests or sheets in a richly vascularized stroma, with an interstitial inflammatory infiltrate (15,16). Metastatic RCC of the prostate is an extremely rare disease. Although prostate carcinomas may exhibit clear cell morphologies, the confluent nests of clear cells differ in that they usually lack marked vascularity and inflammatory cells, stain positive for broad-spectrum cytokeratin and PSAP, and do not generally co-express VIM (17). The clear cell lesion identified in the present study demonstrated an immunohistochemical profile almost identical to that of RCC, with positive expression of VIM, low molecular weight cytokeratin, epithelial membrane antigen, MME, PSAP and P504S, and a negative result for high molecular weight cytokeratin, CEA, broad-spectrum cytokeratin and PAX8. The expression of PAX8 is particularly noteworthy, as it is a marker of primary malignant tumors of the prostate (16). In addition, the lesion consisted entirely of clear cells, which exhibited large, prominent nucleoli. By contrast, nephrogenic adenomas contain cells in which the nucleoli are generally inconspicuous. The differential diagnosis was therefore suggestive of metastatic RCC, or a disease entity that has not yet been described; renal-type clear cell carcinoma arising in the prostate (18).

In the present study, an ultrasound inspection and CT scan of the abdomen did not identify the presence of a renal lesion. Therefore, it was concluded that the lesion represented a primary renal-type clear cell carcinoma that had arisen from the periurethral region of the prostate, and thus was treated appropriately with a radical cystoprostatectomy. To the best of our knowledge, no previous studies have described RCC presenting with metastases to the prostate at the time of initial diagnosis, but three cases of metachronous prostate involvement by primary RCCs have been reported (7,8). At diagnosis, these renal tumors were notably large, and following metastasis to the prostate, additional sites, including the lung and bone, were also affected. These previous cases indicate that RCC tumor dissemination occurs via hematogenous mechanisms (7,8). In the present study, the immunohistochemical staining results and the absence of detectable continuity between the two tumors supported the diagnosis of a pre-malignant role of nephrogenic carcinoma. It was concluded that the tumor represented a primary renal-type clear cell carcinoma that had arisen in the prostate. To the best of our knowledge, this type of extra-renal lesion has only been described in three previous studies. The mechanisms that underlie the development and biological course of renal-type clear cell carcinomas in the prostate are yet to elucidated.

In summary, the present study described a case of renal-type clear cell carcinoma of the prostate. This particular lesion is a novel pathological entity, with histological and immunohistochemical features that are extremely similar to those of renal clear cell carcinomas. However, whether or not its biological course is comparable to that of a renal clear cell carcinoma is yet to be investigated, as does the tissue origin of this novel type of tumor.

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