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Special pathological type of upper urinary tract malignancy—squamous cell carcinoma of the renal pelvis: A case report and literature review

Xiaodong Zhu [a,*], Zhengfei Guo [a], Fang Wu [b], An Zheng [a], Zhengmin Guo [b], Jing Li [a]

[a] Department of Urology, Electric Power Teaching Hospital of Capital Medical University, Beijing, 100073, China
[b] Department of Pathology, Electric Power Teaching Hospital of Capital Medical University, Beijing, 100073, China

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ABSTRACT

Objective: To investigate the clinnical features for squamous cell carcinoma (SCC) of the renal pelvis.
Methods: We analyzed the medical records of a patient diagnosed with SCC of the renal pelvis and performed a literature review.
Results: SCC of the renal pelvis is a rare pathological type of upper urinary tract malignancy with nonspecific clinical features. Its diagnosis relies on postoperative pathology and immunohistochemistry. Radical resection is the gold standard for treatment.
Conclusion: Patients with long-term urothelial irritation should be regularly screened, pathogenic factors should be proactively addressed, and vigilance should be maintained to prevent the development of SCC.

1. Introduction

Primary tumors of the renal collecting duct system are very rare, accounting for 4–5% [1] of all urothelial tumors, and are mostly transitional epithelial tumors. Primary squamous cell carcinoma (SCC) of the renal pelvis is even rarer, accounting for 0.5–0.8 %[2,3] of all renal malignancies. The literature consists mainly of case reports, and thus the best treatment option for this disease remains unclear. In this work, we report on a patient with SCC of the renal pelvis, summarize the patient's clinical data, and discuss diagnostic methods and treatment options for this rare tumor in combination with a review of the relevant literature.

2. Case report

A 65-year-old male patient was admitted to the hospital following two weeks of painless gross hematuria but no other associated symptoms. He had a long history of renal stones and had undergone percutaneous nephrolithotomy for stone removal. No abnormalities were found on physical examination. Laboratory testing showed the following routine blood results: red blood cell count 3.82 × 10^{12}/L, hemoglobin 11.5 g/dl, hematocrit 33.9 %, blood calcium 2.86 mmol/L, uric acid 474 μmol/L, albumin 36.1 g/L, total protein 62.3 g/L, and high-sensitivity C-reactive protein 5.47 mg/L. The results of routine urine tests were normal, and no tumor cells were found via urinary cytology. Renal dynamic imaging revealed a parabolic shape in the left kidney and a low-signal elongated linear shape in the right kidney. The glomerular filtration rate (GFR) was 36.31 mL/min in the left kidney and 2.57 mL/min in the right kidney. An enhanced CT scan (Figs. 1 and 2) suggested an enlarged right kidney and significant hydronephrosis and multiple high-density shadows in the dilated renal pelvis, the largest measuring 14 × 19 mm. The enhanced scan showed hypoenhancement of the renal parenchyma, significant dilation, closing, and thickening of the ureter above the upper edge of the L4 vertebra, a soft tissue density shadow in the lumen, and blurring and enhancement of the surrounding fat spaces. These findings suggested a diagnosis of a malignant mass in the upper right ureter with right hydronephrosis, a high possibility of ureteral carcinoma, multiple stones in the right kidney, and reduced function of the right renal parenchyma. Positron emission tomography (PET)-CT was not performed. Radical nephroureterectomy with bladder cuff resection was performed; the gross specimen is shown in Fig. 3. Pathology revealed a morphology of the ureter in the right kidney that, combined with the immunohistochemical results, was consistent with SCC of the renal pelvis, showing poor-to-moderate differentiation with large areas of necrosis and calcification. The cancer tissue had infiltrated the full thickness of the renal pelvis and reached the surrounding adipose tissue, demonstrating involvement of the proximal ureter, renal parenchyma, renal capsule, and perirenal adipose tissues. Furthermore, tumor invasion of the nerves was observed, but no cancer was found in

* Corresponding author.
E-mail addresses: atlanda@163.com, 78465818@qq.com (X. Zhu).

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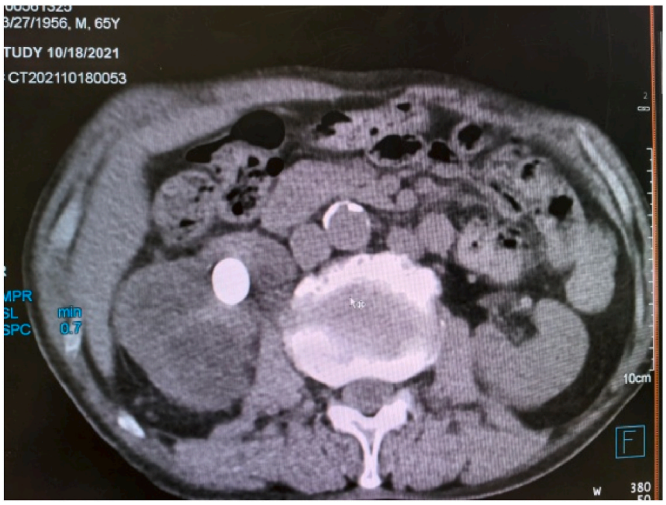

Fig. 1. Enhanced ct image.

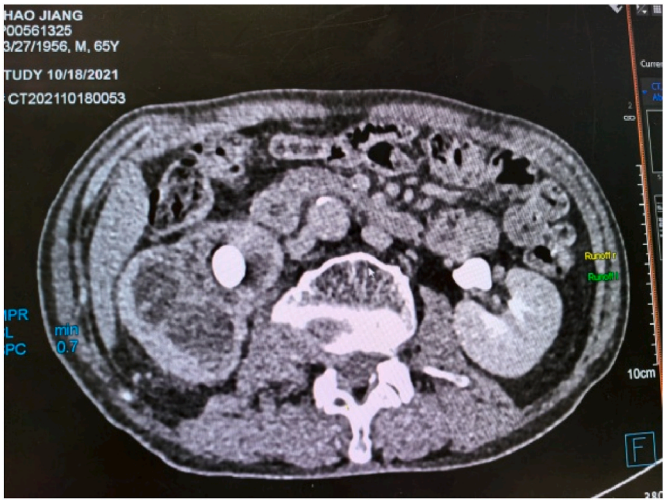

Fig. 2. Enhanced ct image.

the ureter stump, and no metastasis was evident in the hilar lymph nodes. The immunohistochemical results were as follows: GATA-3 (partial+), CK7 (partial+) (derived from epithelial cells, including glandular and transitional epithelia, tumor possible), P40 (+) (squamous epithelial marker), CK5/6 (+), and K1-67 (80 %+) (a high percentage, suggesting rapid cell proliferation and high malignancy). The microscopic findings are shown in Figs. 4 and 5. After surgery, the patient did not receive adjuvant chemotherapy, radiotherapy, or immunotherapy and did not undergo genetic testing. The patient died of lung metastasis after 11 months without treatment.

3. Discussion

Primary SCC of the upper urinary tract is very rare; most reports of SCC of the urinary tract involve the bladder and urethra. SCC of the renal pelvis is a rare solid tumor with an unclear pathogenesis. It is speculated that under long-term chronic stress, the epithelium of the renal pelvis undergoes the following pathological processes sequentially: the transitional epithelium develops squamous metaplasia, progressing to atypical hyperplasia and carcinoma,[4] and some cytokines are secreted during the inflammatory process to support tumor formation.[5] The factors that lead to chronic stress of the renal pelvis epithelium include stones, chronic infection, renal tuberculosis, long-term percutaneous nephrostomy, schistosomiasis, endogenous and exogenous chemical factors, radiotherapy, and vitamin A deficiency.[6] Among them, renal stones and chronic pyelonephritis are the most commonly reported epidemiological factors for SCC of the renal pelvis.[7] Notably, some cases have been reported in the literature without any apparent cause. Our patient had a 20-year history of renal stones and had undergone percutaneous nephrolithotomy for stone removal, both of which are epidemiological factors for developing SCC of the renal pelvis.

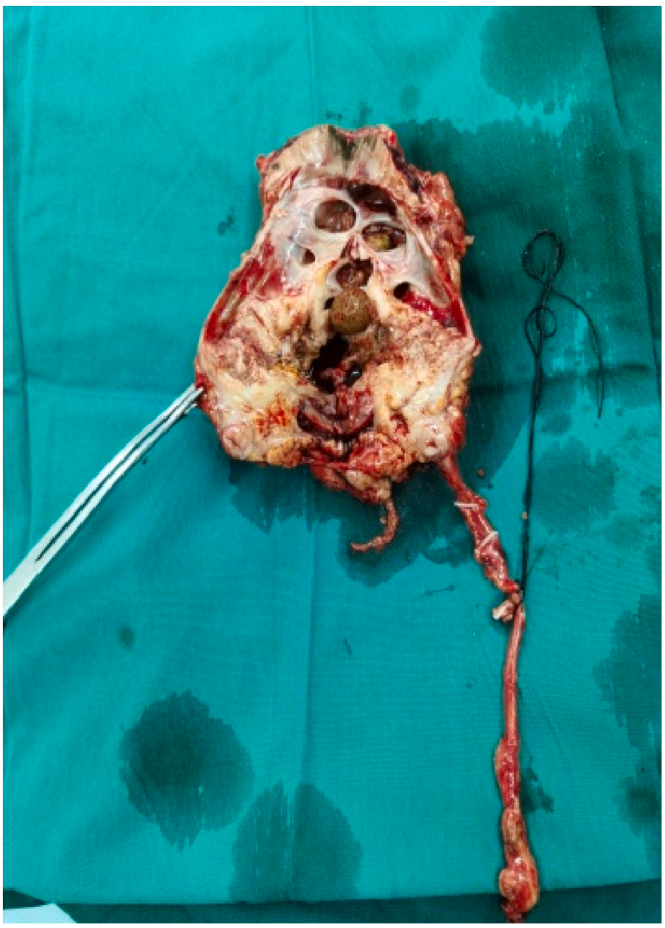

Fig. 3. Surgical specimen.

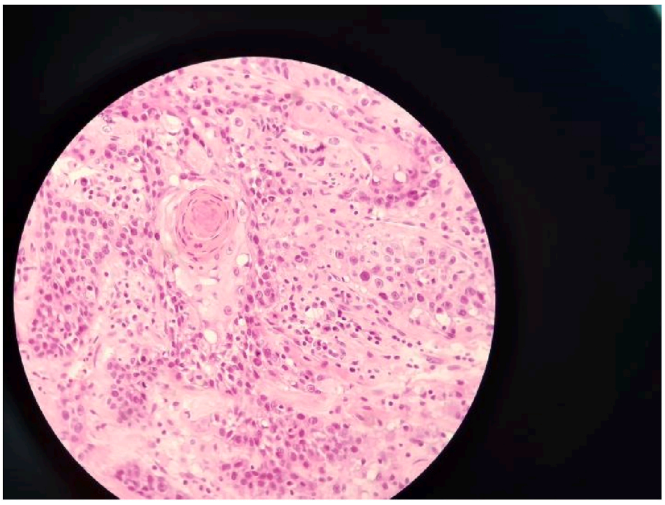

Fig. 4. Cancer nests with cellular keratinization, HE staining 40X

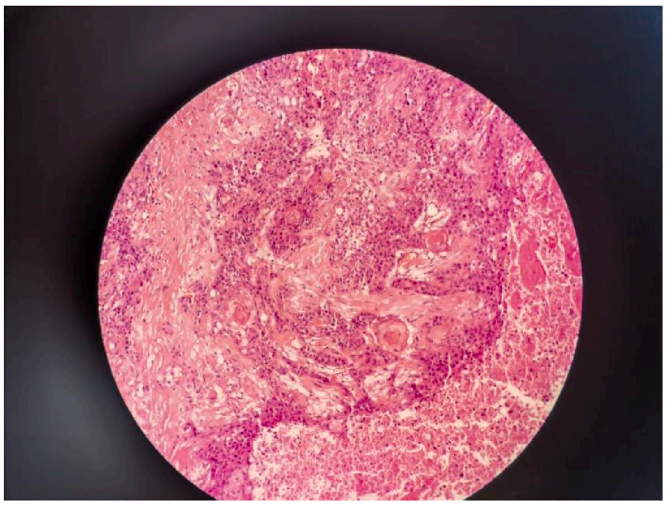

Fig. 5. Cellular keratinization with extensive cellular necrosis, HE staining 20X

SCC of the renal pelvis commonly occurs in people aged 50–70 years, with a median age of 56 years, and the incidence is similar in men and women.[8] Primary SCC of the upper urinary tract can be divided into central and peripheral types according to the tumor location; SCC of the renal pelvis is a central type. Due to the anatomical characteristics of the renal pelvis, tumors often show local invasion and a high rate of lymph node metastasis. However, symptoms can be masked by infections or stones, leading to late-stage diagnosis and poor patient outcomes, with a five-year survival rate of less than 10 %.[8] Most patients die within a year after surgery; the patient in the present study died 11 months after surgery.

SCC of the renal pelvis is histopathologically similar to SCC of other locations, presenting with pleomorphic cells with intercellular bridges microscopically, as well as characteristic keratinizing pearl formation and keratinized cellular debris,[7] but only those tumors that manifest mainly with keratin formation can be diagnosed as SCC.

The clinical manifestations of SCC of the renal pelvis include abdominal pain, hematuria, fever, anorexia, and weight loss, as well as paraneoplastic syndromes such as hypercalcemia, leukocytosis, and thrombocytosis.[9] Some reports of SCC of the renal pelvis have also describe an initial presentation with sinus tracts between the kidney and lumbar skin10. These symptoms are not unique to patients with SCC and can thus lead to delays in diagnosis. The patient in our study presented with hematuria, anemia, hypoalbuminemia, and elevated blood calcium.

There are no specific methods for imaging SCC of the renal pelvis. Ultrasound, CT, and MRI are commonly used. The imaging manifestation is usually hydronephrosis caused by stones and obstruction, and soft tissue shadows in the renal pelvis can be seen in some cases. High-resolution CT images can be used to effectively evaluate the malignancy and stage of the tumor. The MRI findings of SCC are nonspecific but rarely mentioned in the literature.[11] Few studies have investigated the application of PET-CT in diagnosing SCC of the renal pelvis; this imaging modality can reveal increased fluorodeoxyglucose (FDG) tracer uptake in tumors, but this is not a diagnostic feature.[12,13] Its advantage lies in the increased detection of cases of lymph node metastasis and distant metastasis. The utility of urinary cytology examinations is controversial; they are quite sensitive for high-grade tumors but often yield negative results for low-grade tumors.[14] Moreover, urinary cytology may reveal malignant cells, but only 70 % of the positive results are consistent with the actual pathology. The European Urology Guidelines recommend regular urinary cytology examinations for patients with transitional cell carcinoma of the ureter and renal pelvis.[15] In our case, the urinary cytology examination was negative.

The diagnosis of SCC of the renal pelvis is mainly based on histopathology, often of the specimens resected with radical surgery. Some researchers have indicated that fine-needle cytology of the renal pelvis is very helpful for the preoperative diagnosis of SCC. To date, two cases of SCC of the renal pelvis have been reported to be diagnosed through fine-needle cytology of the renal pelvis, yielding results consistent with those of post-radical surgery pathology.[16,17]

The most important differential diagnosis for SCC of the renal pelvis is xanthogranulomatous pyelonephritis, the causes of which include stones and stone-associated hydronephrosis, similar to SCC. Imaging typically shows a solid mass in the renal pelvis with hydronephrosis, stones, or invasive manifestations, with involvement of adjacent structures, and enhanced CT may show a “bear’s paw” sign, making differentiation challenging.[18] Some researchers have noted that SCC of the renal pelvis and xanthogranulomatous pyelonephritis rarely coexist.[6]

Currently, there are no standard guidelines or treatment options for primary SCC of the renal pelvis. We suggest that a treatment plan be established based on a comprehensive consideration of factors such as patient age, general health, tumor grade and stage, and compliance. For patients with tumors confined to the kidney, radical surgery (radical nephrectomy with or without ureterectomy) is the gold standard treatment.[19] Even for patients with metastasis, radical surgery is valuable, as it can effectively control symptoms and allow a pathological diagnosis.[8,19] Our patient underwent radical total nephroureterectomy.

In recent years, the application of platinum-based chemotherapy regimens (including the gemcitabine + cisplatin regimen) has achieved favorable results in patients with transitional cell carcinoma of the urethra. Researchers have also attempted to use these regimens for patients with postoperative SCC of the renal pelvis, but evidence shows limited efficacy and no survival benefits.[19] For patients with metastatic SCC of the renal pelvis, adjuvant chemotherapy and palliative radiotherapy are recommended to control symptoms, but there is no evidence of survival benefits.[2,3,6,19] However, evidence for immunotherapy is scarce, and its effectiveness in the literature is limited.[19] Genetic testing may provide suggestions for the selection of therapeutic drugs, but no studies have been published on this topic in the literature. Our patient refused radiotherapy, chemotherapy, and immunotherapy after radical surgery. There is currently no standard protocol for following up on patients with SCC of the renal pelvis, but regular physical examinations, laboratory tests, and chest and abdominal imaging examinations are recommended.

SCC of the renal pelvis is typically diagnosed at a late stage with a high tumor stage, so adjuvant therapy offers little benefit, resulting in a poor prognosis. It has been reported that the five-year survival rate of patients with SCC of the renal pelvis is less than 10 %, with an average survival time of 7 months.[2,3,6,8] Most patients die within a year after surgery; our patient died 11 months postoperatively.

It is difficult to make a definitive diagnosis of SCC of the renal pelvis via conventional means before surgery; currently, fine-needle cytology of the renal pelvis offers the only possible method for an early diagnosis. For patients with risk factors for developing SCC of the renal pelvis, especially those with long-term renal stones and chronic infection, it is crucial to consider the possibility of this disease. Since long-term kidney stones can cause infection, renal function impairment, and squamous metaplasia, leading to SCC, it is essential to proactively treat the stones.[16] Patient metabolic assessment and stone composition analysis and a urine output of more than 2.5 L per day can effectively reduce stone recurrence.

4. Conclusion

SCC of the renal pelvis is a rare pathological type of upper urothelial tumor. In most cases, diagnosis is delayed due to atypical clinical manifestations and imaging features, resulting in a high tumor stage at the time of diagnosis. A definitive diagnosis relies on postoperative histopathological analysis of the surgical specimen, but adjuvant therapies result in poor outcomes and offer minimal benefits. Early diagnosis

is the only way to improve the disease prognosis. For patients presenting with relevant pathogenic factors, the possibility of SCC should be considered. Regular screening may enable early detection. Proactive intervention targeting these risk factors should form the basis for preventing the occurrence of SCC of the renal pelvis.

CRediT authorship contribution statement

Xiaodong Zhu: Writing – original draft, Writing – review & editing. **Zhengfei Guo:** Writing – review & editing. **Fang Wu:** Visualization. **An Zheng:** Visualization. **Zhengmin Guo:** Visualization. **Jing Li:** Writing – review & editing.

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