

A Case Report: High-Grade Urothelial Carcinoma in the Renal Pelvis with Complete Kidney and Ureter Duplication Featuring Heterologous Differentiation

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Abstract: This report describes a considerably rare case of high-grade urothelial carcinoma of the renal pelvis and ureter, presenting with heterologous differentiation, in a patient with bilateral duplicated kidneys. A 73-year-old male experienced intermittent gross hematuria for 5 months, accompanied by lower back and abdominal pain. Ultrasound and computed tomography scans revealed bilateral renal and ureteral duplication with multiple tumors in the left renal pelvis. A total nephroterectomy and bladder cuff resection were performed on the left two nephrons. Multiple space-occupying lesions were identified in the left renal pelvis and ureter. Histopathological examination showed poorly differentiated and diverse tumor cells, manifesting as sarcomatoid carcinoma, papillary adenocarcinoma, and infiltrating high-grade urothelial carcinoma. The tumor infiltrated the subcutaneous fibrous connective tissue of the renal pelvis and the full thickness of the ureter. Given the rarity of recurrent renal urothelial carcinoma with heterogeneous differentiation, comprehensive imaging and pathological assessments are vital to delineate the nature of the lesion and the direction of tissue pathological heterologous differentiation. These evaluations guide early radical surgical interventions, improving survival rates.

Keywords: Duplicated renal malformation; Renal pelvis; High-grade urothelial carcinoma; Heterologous differentiation

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1. Introduction

Urothelial cancer of the renal pelvis and ureter, while relatively rare, contributes to approximately 5% of all urinary tract tumors^[1]. This subset of urothelial malignancies^[1] is mostly comprised of transitional cell carcinoma, which is recognized for its potential to exhibit multiple types of differentiation, particularly in their high-grade forms. While this feature of cellular heterogeneity has been well-documented in bladder tumors, it's relatively rare in pelvic tumors^[2].

Notably, high-grade transitional cell carcinoma in the renal pelvis and ureter can display an array of histopathological patterns due to such differentiation. These variations often mimic other types of carcinoma,

confounding the process of histopathological diagnosis and potentially impacting the selection of the most appropriate therapeutic approach.

2. Case presentation

A 73-year-old man, suffering from gross hematuria for the past 5 months, was admitted to the Affiliated Hospital of Hebei University. He was diagnosed with an enlarged left ureter over a decade ago. Apart from lower limb edema, the patient exhibited no other significant symptoms and hence had not undergone any treatment. He had a history of hypertension and was prescribed antihypertensive medications accordingly. Laboratory analyses of his blood samples showed no abnormalities. However, abdominal ultrasound and enhanced computed tomography identified a duplicated renal pelvis and ureter in the right kidney. Additionally, a large cystic mass along with ureteral dilation, was detected in the left kidney (**Figure 1**). As shown in **Figure 1A**, the coronal plane imaging displayed the duplicated set of pelvis and ureter in the right kidney and a significant mass with ureterectasis in the left kidney. In the cross-sectional view (**Figure 1B**), the right renal cortex and medulla showed no significant abnormal density. However, the left renal parenchyma is compressed, deformed, and thinned due to the large mass with dilation in the renal pelvis and ureter. No significant abnormalities were observed in the density of the right renal cortex and medulla.

The patient was diagnosed with bilateral renal and ureteral duplication and multiple masses in the left renal pelvis. Owing to the unclear display of the opening below the left urinary duct, the presence of multiple tumors in the left renal pelvis was suspected. Consequently, the clinicians performed a total nephroterectomy and bladder cuff resection on the left two nephrons. Upon surgery, a tumor with a pedicled root measuring $13 \times 7.5 \times 6$ cm was observed in the pelvis of the upper left nephron. Multiple scattered tumors, ranging in diameter from 0.1 to 0.4 cm, were detected on the renal pelvis mucosa, and a rough area was observed in the corresponding dilated ureter. Histopathological examination revealed multiple malignant tumors with necrosis within the renal pelvis and ureter. Immunohistochemical staining-based pathological diagnosis indicated invasive cancer with heterogeneous differentiation, including sarcomatoid carcinoma, papillary adenocarcinoma, and high-grade urothelial carcinoma (**Figure 2**). Immunohistochemistry staining showed CK (+), CK20 (-), P63 (individual+), GATA-3 (partial+), Vimentin (-), S-100 (-), HMB-45 (-), Ki-67 (50%+), SMA (-), and Desmin (-). Despite the recommended postoperative radiotherapy and chemotherapy, the patient did not adhere to the medical advice and neglected regular follow-ups. However, a telephone follow-up conducted 14 months post-surgery reported the patient to be in a satisfactory condition, exhibiting good survival status.

3. Discussion

Abnormalities of the kidney and urinary system encompass a wide range of disorders. Various classification methods have been proposed by researchers to categorize the different types of urinary dual systems ^[3,4]. In the present case, we observed bilateral duplication of both the kidneys and ureters. Around 40% of patients with duplicate kidneys present with pathological manifestations ^[5], usually discovered during routine physical examination or accompanied by other urinary tract diseases due to the absence of significant clinical symptoms. Common symptoms associated with this condition include pain, hematuria, dysuria, or abnormal urination frequency ^[5,6]. The patient in our report had a complete duplication of the kidneys and, more than ten years ago, was diagnosed with a megaureter at a local hospital (no official report was available). Recently, gross hematuria led to the observation of bilateral renal duplication accompanied by a renal pelvic mass. When patients present with chronic urinary tract disease or related organ disorders originating from the urinary system, the possibility of anatomical variation should be considered. This is because recurrent infections may be caused by the reverse

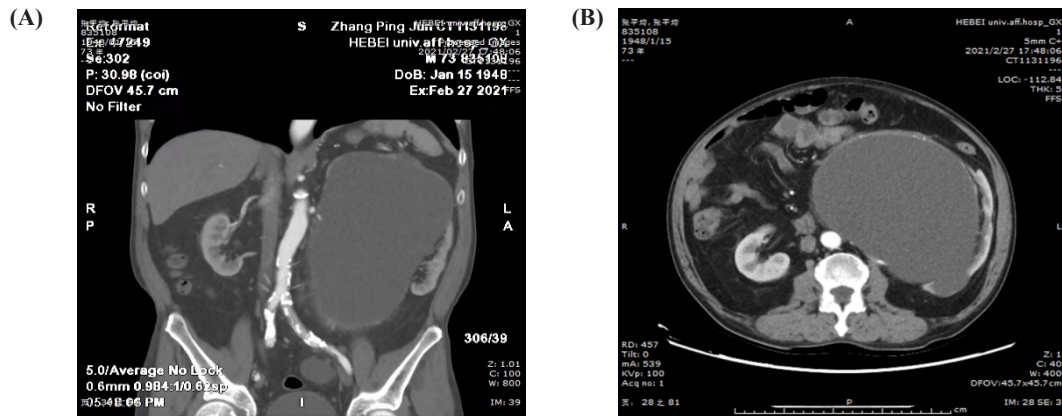


Figure 1. Computed tomography (CT) imaging in (A) the coronal plane, and (B) the cross-sectional plane

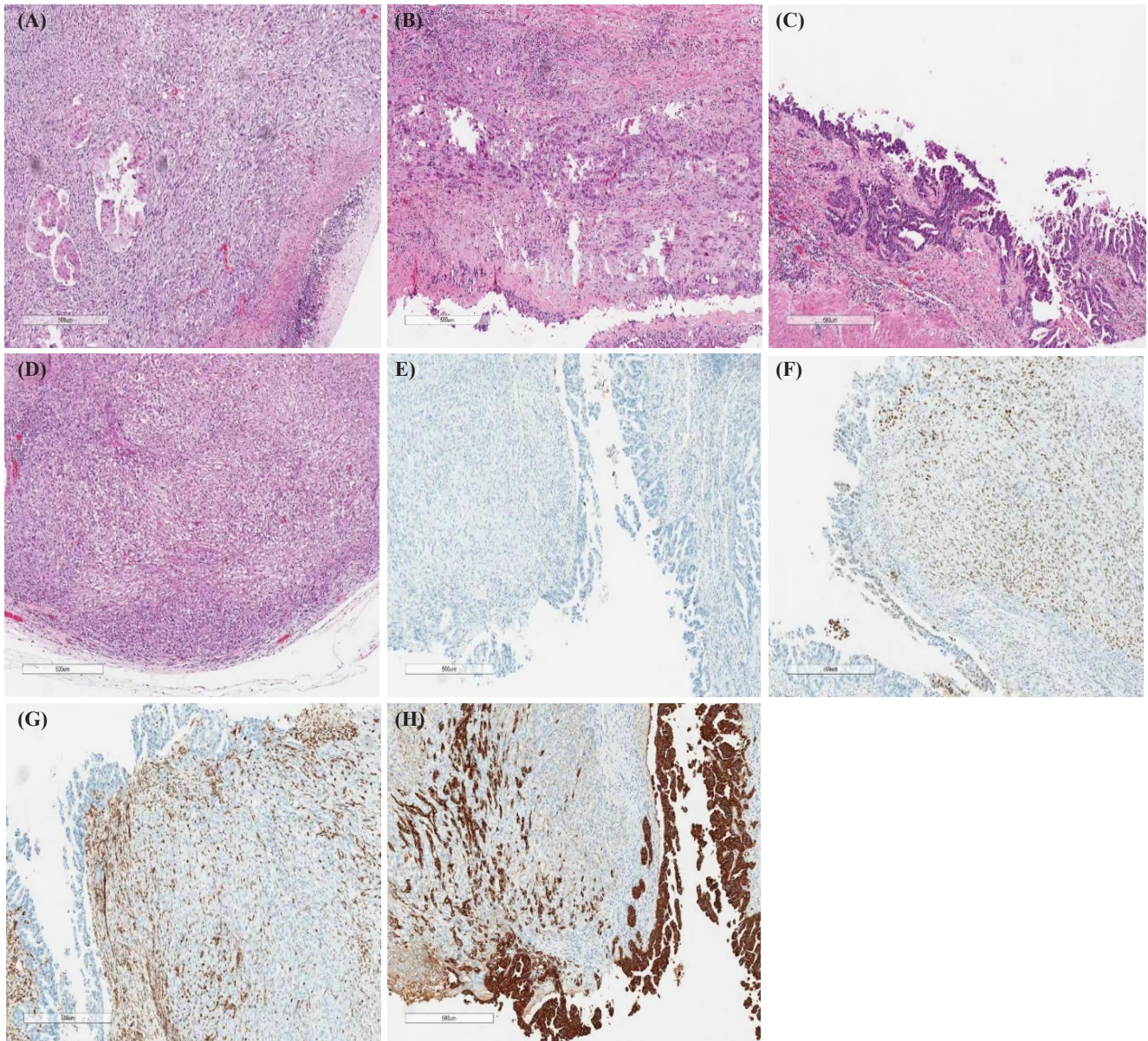


Figure 2. A: Tumor infiltration through the full thickness of the ureter. B: Adenoid differentiation is observable in the sarcoid-like component under high magnification. C: *In situ* urothelial carcinoma component and small foci of infiltration are apparent in the renal pelvis. D: The spindle cell component represents a region of sarcomatoid differentiation with notable cell atypia. E: Immunohistochemical staining of CK20 (-). F: Immunohistochemical staining of Ki-67 (50%+). G: Immunohistochemical staining of GATA-3 (partial +). H: Immunohistochemical staining of CK(+).

pressure on the collection system due to anatomical variation.

The incidence and prevalence of duplicated ureters in the general population are reported to range between 0.7%–4%, with a male-to-female ratio of 2:1 [6]. Furthermore, these patients carry an elevated risk of developing malignant tumors in the renal pelvis [7]. Although urothelial carcinoma of the renal pelvis is not rare, the emergence of this carcinoma from a duplicated renal pelvis, accompanied by multidirectional differentiation, is exceedingly rare. To the best of our knowledge, based on the available literature, there are no prior reports of such cases. Chen reported a case of hydronephrosis in the upper segment of the left kidney with sarcomatoid carcinoma of the renal pelvis [8]. Urothelial carcinoma exhibits the ability for multidirectional or heterologous differentiation taking on a variety of differentiation forms and variant subtypes. The resulting tumor is referred to as urothelial carcinoma with heterologous differentiation [9], and squamous cell carcinoma is the most common subtype of urothelial carcinoma [10]. In our patient, multiple space-occupying lesions were present in the renal pelvis and ureter. Renal pelvis carcinoma consists of glandular differentiation, distinguishing it from a micropapillary structure, which is highly susceptible to regional lymph node metastasis and distant metastasis. The sarcomatoid carcinoma in this case, a poorly differentiated epithelial malignant tumor, composed of non-specific spindle cells and cells of various forms, is often associated with lymph nodes and distant metastasis, resulting in a poor prognosis. The malignant tumor in this patient had infiltrated the subcutaneous fibrous connective tissue of the renal pelvis and the entire ureteral layer, accompanied by widespread atrophy of the renal parenchyma and smooth muscle hyperplasia. Moreover, the presence of high-grade invasive urothelial carcinoma with sarcomatoid differentiation indicated a poor prognosis. Despite the doctor's recommendations for postoperative radiotherapy and chemotherapy, the patient didn't adhere to these instructions and didn't undergo regular reexaminations. However, a satisfactory survival condition was reported in a one-year follow-up. The treatment of high-grade invasive urothelial carcinoma demands a personalized approach, taking into account multiple factors, including the patient's age, histological grade, and clinical stage. In patients with duplicate kidneys and high-grade invasive urothelial carcinoma, the entire renal bifunctional unit and bladder cuff should be completely excised because of the shared vascular communicating branches in the bifid renal system and the common origin of the two ureters. Postoperative pathology should ensure accurate classification and diagnosis, and consideration should be given to the impact of each type of differentiation on prognosis. Patients with a poor prognosis could benefit from postoperative radiotherapy and chemotherapy. In cases where there is a risk of recurrent kidney disease, regular monitoring of kidney function should be enforced to facilitate timely detection and complete removal of tumors. Subsequent treatment should be guided by a thorough postoperative evaluation.

Ethical statement

Written informed consent was obtained from the patient for the publication of this case report, inclusive of all accompanying images.

Disclosure statement

The authors declare no conflict of interest.

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