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Is the presence of upper tract transitional cell carcinoma in a calyceal diverticulum a risk factor for early metastasis? A case report and review of the literature

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Abstract

Upper tract transitional cell carcinoma poses diagnostic challenges due to its prevalence and diverse clinical presentations. This case report describes the incidental discovery of high-grade transitional cell carcinoma during the management of a 48-year-old male with ischemic heart disease and an asymptomatic right renal stone. During flexible ureteroscopy for stone removal, papillary lesions were identified within a calyceal diverticulum and confirmed as high-grade transitional cell carcinoma. The unique anatomy of the calyceal diverticulum, characterized by its restricted wall thickness, may predispose the tumor to early metastasis. Additionally, there is a concern about potential iatrogenic dissemination of tumor cells to the bladder during the ureteroscopic procedure. This case highlights the diagnostic complexities associated with upper tract transitional cell carcinoma in rare anatomical locations and emphasizes the need for careful consideration of both procedural factors and anatomical features to manage the risk of metastasis and tumor dissemination effectively.

Keywords

Upper tract transitional cell carcinoma, calyceal diverticulum, tumor dissemination, metastasis, ureteroscopic procedure

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Introduction

Upper tract urothelial carcinoma (UTUC) constitutes fewer than 5% of urothelial cancers.[1] The precise etiology of upper urinary tract transitional cell carcinoma (TCC) remains elusive, although several discernible risk factors have been established. These include exposure to a spectrum of chemicals,[2] susceptibility to infections, pharmaceutical influences, genetic predispositions, dietary patterns,[3] and tobacco consumption.[4] Males have a higher incidence of developing this condition compared to females.[5] Upper urinary tract stones, often associated with recurrent urinary tract infections, pose a notable risk for upper tract cancers such as squamous cell carcinoma, TCC, and adenocarcinoma, and this risk is attributed to chronic inflammation leading to urothelial proliferation and malignant transformation.[5] UTUC arising within a calyceal diverticulum is an exceedingly uncommon pathological occurrence, with documented cases in the medical literature being exceptionally rare.[5–7] Herein, we present a case of UTUC that was uniquely discovered during flexible ureteroscopy for a symptomatic calyceal kidney stone.

Case presentation

A 48-year-old male patient with a history of ischemic heart disease and an asymptomatic right renal stone since childhood presented to our urology department with severe right flank pain accompanied by nausea. He reported experiencing mild episodes of right flank pain over the 2 months prior to his presentation but sought medical attention only after his last episode. He denied experiencing dysuria or hematuria.

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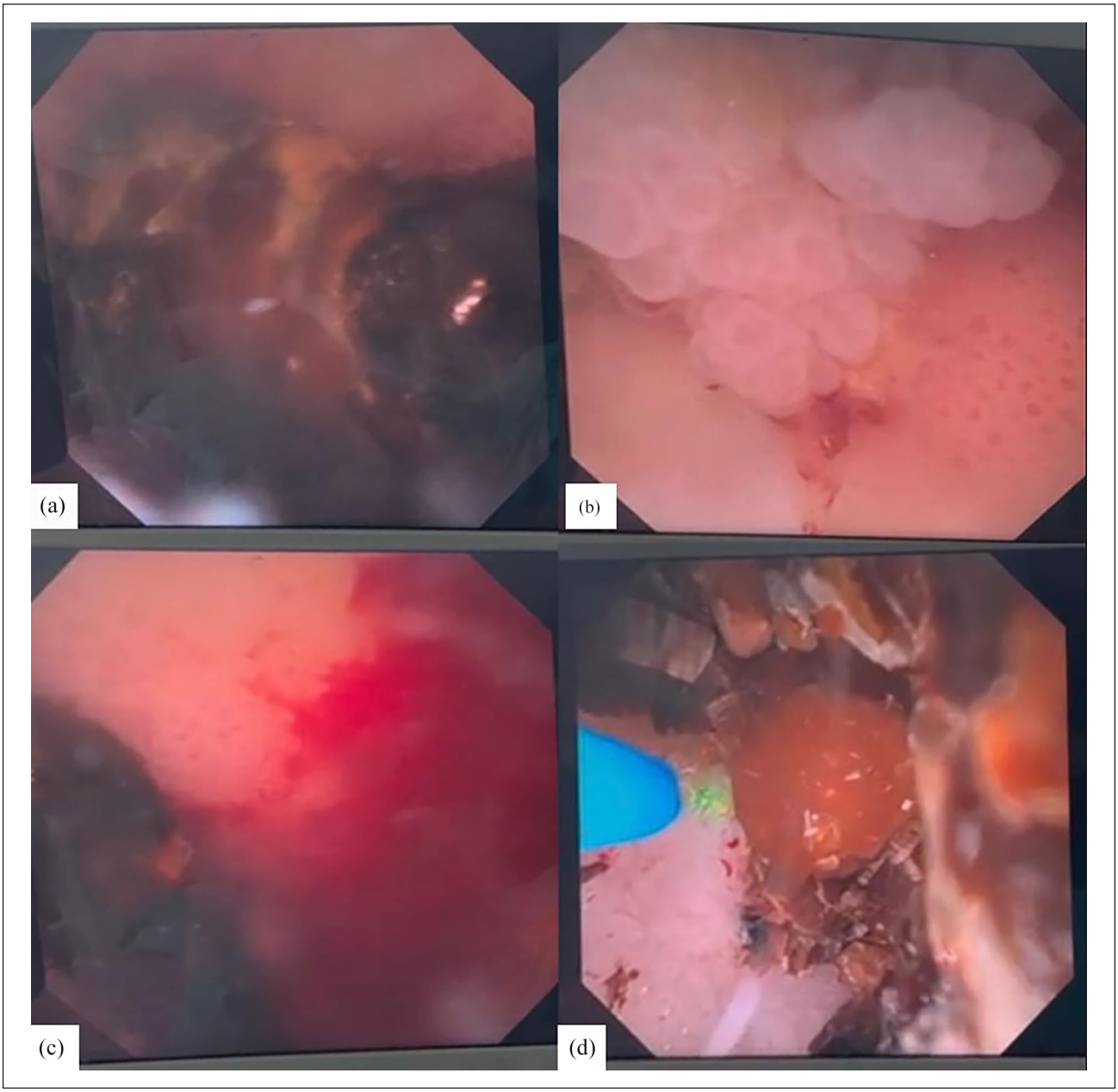

Figure 1. Images obtained during flexible ureteroscopy of the right kidney. (a) Right kidney stone, (b) papillary lesions protruding into the lumen of the diverticulum, (c) image showing the stone before fragmentation and the papillary lesions, (d) the stone after fragmentation with the surrounding papillary lesions.

A renal computed tomography (CT) scan without intravenous (IV) contrast revealed several findings: a horseshoe kidney, a 2-cm renal calculus on the right side, and a large renal cyst measuring 7 cm × 6 cm, with no significant hydronephrosis. Microscopic hematuria was detected in the lab results. Consequently, the patient underwent right retrograde ureteral stenting due to difficult access caused by a tight right ureteric orifice. After 1 month, he underwent laser lithotripsy of his right kidney stone using flexible ureteroscopy and replacement of the ureteral stent. During the procedure, while fragmenting the stone (Figure 1(a)), which was located in a calyceal diverticulum abutting the middle calyx and had a narrow opening that needed to be dilated to gain access, several papillary lesions were incidentally discovered (Figure 1(b)–(d)). Cytology was obtained and sent for histopathological analysis, revealing high-grade TCC, category VI according to Paris reporting system.[8]

Further staging was conducted through a CT-scan of the chest, abdomen, and pelvis with IV contrast, which revealed additional abnormalities including a relatively well-defined

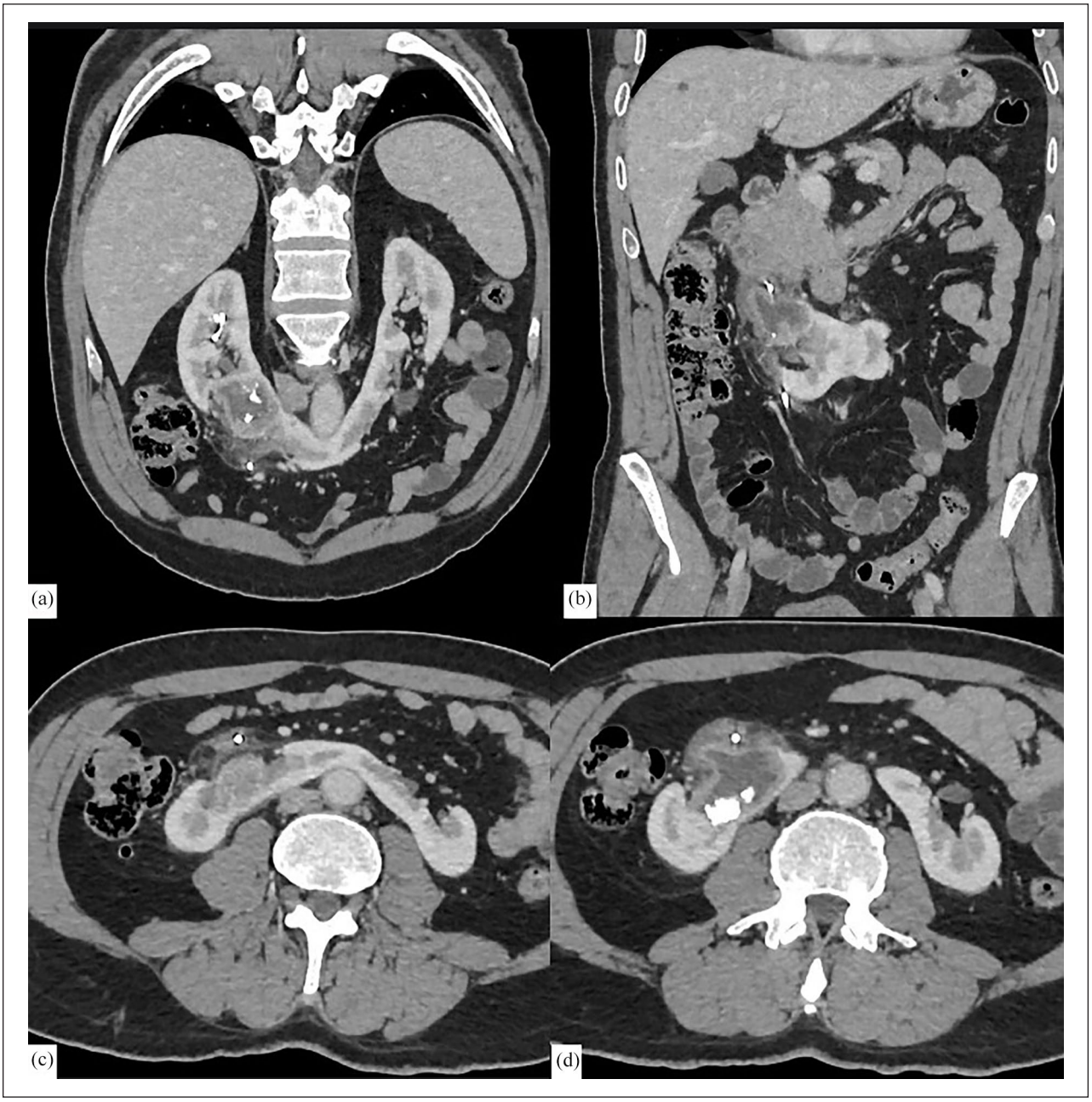

Figure 2. CT scan with IV contrast, the venous phase is showed. (a) and (b) Coronal views. (c) and (d) axial views showing: horseshoe kidneys with duplex calyceal system, a relatively well-defined cystic structure with thick wall seen in the mid portion of right kidney measures about 4.5 cm with multiple adjacent stones/calcifications. The right kidney presents urothelial thickening and surrounding fat stranding. The DJ-stent seen in the right upper calyceal group.

cystic structure with thick wall seen in the mid portion of right kidney measuring about 4.5 cm with multiple adjacent stones/calcifications. The right kidney presented urothelial thickening and surrounding fat stranding (Figure 2). Subsequently, the patient underwent a right radical nephroureterectomy with bladder cuff excision and insertion of a left ureteral stent. The procedure started with cystoscopy that showed small bladder lesions on the left lateral wall and doom, which were not resected or biopsied as these lesions were not typical of papillary growth and were considered as a reactionary lesion caused by the DJ stent. Histopathological examination confirmed a unifocal, invasive papillary urothelial carcinoma, high-grade, pT1, located in the lower pole of the right kidney, measuring 3.5 cm × 3.5 cm. The tumor showed no necrosis or invasion, and the ureteric and vascular margins were free of tumor (Figure 3).

Postoperatively, the patient remained stable with no significant decline in hemoglobin levels or serum creatinine and

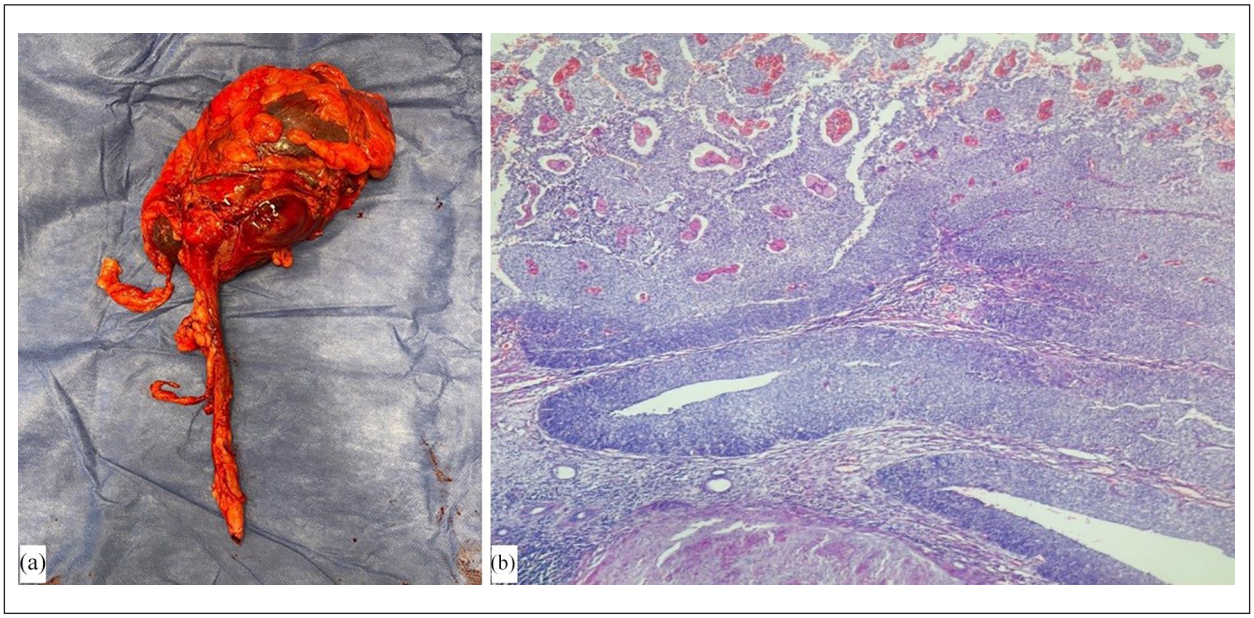

Figure 3. (a) Gross picture of resected right kidney, right ureter, and bladder cuff. (b) histopathologic examination showed papillary urothelial carcinoma, high-grade, with invasion into the subepithelial tissue (pT1).

was discharged 3 days later. One month after his major operation, he underwent cystoscopy revealing multiple small papillary lesions throughout the urinary bladder, almost over all walls, with a noticeable location around the right ureteric orifice. Radical transurethral resection of the bladder tumor was done and histopathology showed non-invasive papillary urothelial carcinoma, WHO low grade, with no lamina propria, muscularis propria, or lymphovascular invasion seen. The patient received a 6-week induction course of intravesical Bacillus Calmette–Guérin (BCG), and a follow-up positron imaging tomography (PET-CT) revealed the presence of hypermetabolic nodule or a lymph node in the paraaortic region, inseparable from lower pole of the left kidney, measuring about 1.7 cm × 1 cm, suspicious for metastatic process. The multidisciplinary team agreed on proceeding for systematic chemotherapy, and to maintain the patient on regular cystoscopy follow-up, and commencing additional doses of intravesical BCG.

Discussion

The incidental finding of UTUC within a calyceal diverticulum during stone fragmentation is rare but clinically significant.[5] The shared embryological origin of the renal collecting system's urothelium explains the histological similarity and the potential for carcinoma development in these areas.[9] Several risk factors contribute to UTUC, including chemical exposure, infections, pharmaceuticals, genetics, dietary habits, and smoking.[2,3] Our patient, presenting at 48 years old, deviates from the typical epidemiological profile, highlighting the importance of considering malignancy across all age groups.[1,10]

The initial diagnostic workup did not reveal visible lesions, illustrating the challenges of diagnosing UTUC. However, positive urinary cytology prompted further investigation, revealing high-grade malignant cells, demonstrating the critical role of urinary cytology in UTUC diagnosis despite its limitations.[11–13] Radical nephroureterectomy is the standard treatment for UTUC, especially in cases with high-risk features such as multifocality and high-grade cytology. Our patient's case, complicated by a horseshoe kidney and multifocal lesions at the stone impaction site, required an open right nephroureterectomy, highlighting the surgical complexity in such scenarios.[14]

The occurrence of TCC in a calyceal diverticulum, as seen in this case, has been documented and is often associated with stone-containing diverticula due to chronic inflammation, infection, and irritation.[5–7,15–17] A review of these cases reveals no evidence that laser lithotripsy of the stone has led to tumor dissemination or implantation. Moreover, endoscopic techniques, including ureteroscopic and percutaneous approaches, have been utilized for managing UTUC through laser fulguration or biopsy,[18] and these have been associated with a higher risk of developing bladder recurrence.[19,20] Significant predictors of bladder recurrence after radical nephroureterectomy include patient-specific factors like male gender and a history of bladder cancer, tumor-specific factors such as high-grade and ureteral location, and treatment-specific factors like the laparoscopic approach and positive surgical margins.[21–23] Diagnostic ureteroscopy has been linked to an increased risk of recurrence.[19,20] A single dose of intravesical chemotherapy post-ureteroscopy for non-metastatic UTUC may reduce recurrence rates, based on low-level evidence.[21]

High-risk factors for metastasis in upper tract TCC include high-grade cytology, local invasion, tumor size greater than 2 cm, high-grade biopsy, histological subtype, multifocality, and hydronephrosis.[24] Our patient's multifocality and high-grade cytology indicated a high-risk disease. The presence of TCC in a calyceal diverticulum may contribute to early metastasis due to the lack of full-wall thickness in the diverticulum.

Our case challenges the diagnostic yield of routine approaches and prompts a reevaluation of biopsy strategies in cases of suspected UTUC, particularly in the absence of classic symptoms or prolonged symptomatic renal colic, with or without hematuria. This also raises questions about the utility of renal pelvis or calyx biopsy in cases with unremarkable stone characteristics, emphasizing the need for tailored diagnostic approaches based on individual patient presentations.[25]

Conclusion

The presented case emphasizes the complexity of diagnosing UTUC, particularly in atypical presentations, emphasizing the importance of considering malignancy in stone patients with multiple risk factors and the necessity for tailored diagnostic approaches to optimize patient outcomes.

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Author contributions

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Ethical approval

Our institution, Najah National University Hospital, does not require ethical approval for reporting individual cases or case series.

Informed Consent

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