Case Report

Upper tract transitional cell carcinoma clinically mimicking inflammatory renal pathology: A report of three cases

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ABSTRACT

Upper tract urothelial carcinoma (UTUC) of the renal pelvis and the ureter is incidentally detected in a small proportion of cases. However, the majority of UTUC cases present with hematuria, flank pain, and clot colic. Typical imaging features include hydronephrosis of the kidney (s) due to obstruction by the mass with a soft-tissue lesion that typically shows low-grade enhancement with or without a filling defect. Rarely, such a tumor may present with signs and symptoms mimicking an inflammatory or infective pathology of the kidney and is diagnosed only on biopsy or on nephrectomy. We present three such patients and cite another similar case we have published earlier. All three of these patients presented with signs and symptoms of an obstructed infected kidney with long-standing renal calculi and a forgotten DJ stent in one instance. Nephrectomy for the presumed infected kidney in all three cases revealed high-grade UTUC. In patients presenting with equivocal findings on cross-sectional imaging with a history of renal calculi or foreign bodies, we should have a high index of suspicion for malignancy.

INTRODUCTION

Upper tract urothelial carcinoma (UTUC) usually presents with hematuria, loin pain, clot colic, flank mass, constitutional symptoms, or sometimes is incidentally diagnosed on radiology. In this report, we present a series of three cases, where imaging and clinical findings were of nonfunctioning kidney due to inflammatory pathology, with histopathology of the final nephrectomy specimen showing high-grade UTUC.

CASE DETAILS

Case 1

A 66-year-old male, non-smoker, with no medical comorbidities, presented with right flank pain and intermittent low-grade fever of 1-year duration and also had decreased appetite and weight loss. General examination revealed pallor. On abdominal examination, there was a hard, nonmobile lump in the right lumbar region. Contrast-enhanced computed tomography (CECT) scan of the abdomen showed right hydronephrotic kidney with hyperdense material in the calyces and a large staghorn calculus in the pelvis [Figure 1a]. There was a heterogeneously enhancing area in the posterior cortex extending beyond the capsule with loss of fat planes with the psoas and muscles of the parietal abdominal wall [Figure 1b]. Renal functional scan showed a nonvisualized kidney on the right side. Based on the clinical picture of fever with leukocytosis and hydronephrotic right kidney with staghorn stone and hyperdense calyceal contents, a diagnosis of right-sided xanthogranulomatous pyelonephritis (XGPN) was made.

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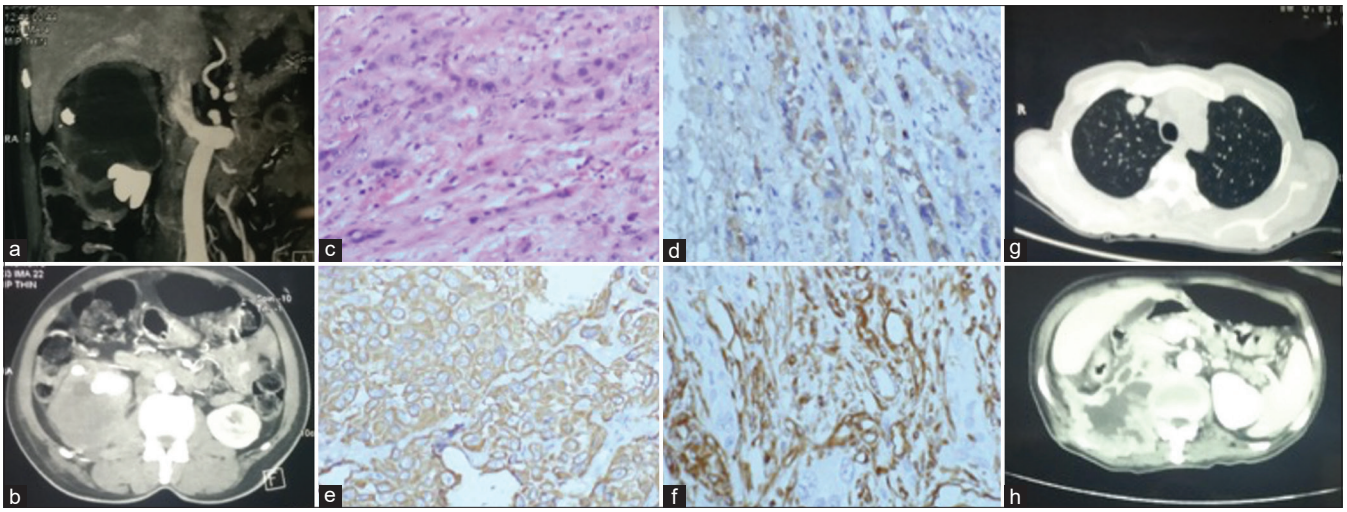

Figure 1: (a) Contrast-enhanced computed tomography shows hydronephrotic right kidney with staghorn calculus with minimal contrast uptake. (b) Solid nonenhancing area posteriorly showing loss of fat planes with psoas muscle. (c-f) Hematoxylin and eosin staining shows high-grade infiltrating tumor with desmoplastic stroma, cells with high N: C ratio, prominent nucleoli, and a small amount of eosinophilic cytoplasm (a; ×400). On IHC, tumor cells are positive for CK 20 (b; ×200), CK7 (c; ×400) and positive for vimentin (d; ×400). (g and h) Contrast-enhanced computed tomography of the thorax shows lung nodule. Abdominal scans show an infiltrative mass in the right renal fossa

A percutaneous nephrostomy was placed that drained 200 ml of pus every day. Cultures grew *Escherichia coli* and intravenous (IV) antibiotics were given. Despite this, the patient continued to have a low-grade fever and persistent leukocytosis. He underwent a right open subcapsular nephrectomy. Histopathology revealed high-grade UTUC and coexisting XGPN. Immunohistochemistry was positive for CK7, CK20 (patchy), vimentin (focal), CD10, 34-beta-E12, p63, and negative for CD117 [Figure 1c-f]. The patient was started on gemcitabine and cisplatin chemotherapy. A restaging CECT of the chest and abdomen after 1 month showed lung and liver metastases with a recurrent mass in the right renal fossa [Figure 1g and h]. The patient subsequently passed away due to progressive disease.

Case 2

A 47-year-old female, with no prior tobacco use, and a history of left-sided ureteroscopic lithotripsy (URSL) 12 years prior, and a forgotten DJ stent *in situ*, presented with persistent low-grade fever and pain in the left flank for the past year. There was a pus discharging sinus on the left flank with surrounding erythema, pitting edema, and induration. CECT scan showed hypoenhancing mass replacing the left kidney with loss of fat planes with the descending colon and abdominal wall [Figure 2a]. Multiloculated collections with hyperdense contents were present in the kidney and perinephric region. The upper part of the broken DJ stent was seen *in situ* [Figure 2b]. There was an irregular sinus tract with a loculated collection extending into the posterolateral abdominal wall. Multiple enlarged para-aortic lymph nodes were also seen. On the basis of the clinical picture and radiological and laboratory findings, a presumed diagnosis of left-sided XGPN was made. Due to fever and raised TLC, a percutaneous drain was placed in the left kidney, which drained about 100 ml of purulent fluid daily. Culture from

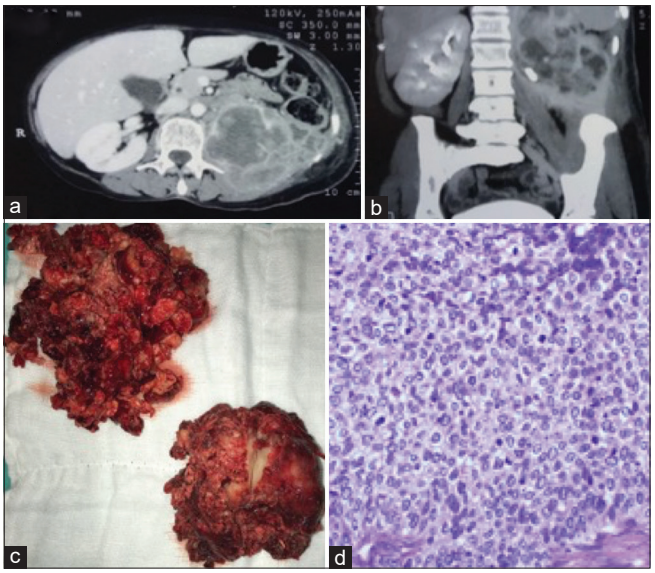

Figure 2: (a) Contrast-enhanced computed tomography shows nonenhancing phlegmon with the complete destruction of renal architecture and infiltrating posterior abdominal wall with overlying inflammatory fat stranding. (b) Tip of the broken DJ stent seen *in situ*. (c) Resected nephrectomy specimen. (d) Hematoxylin and eosin stained section from (H&E stain from what?) shows an infiltrative tumor disposed in sheets and fused nests. Tumor is composed of polygonal cells exhibiting moderate nuclear pleomorphism, clumped chromatin, prominent nucleoli, and pale eosinophilic cytoplasm (a; ×200). Foci of squamous differentiation are also seen (b; ×400)

the fluid grew *E. coli* and IV antibiotics were given as per sensitivity. The patient, however, remained febrile with persistent leukocytosis. A functional scan showed a nonfunctioning left kidney. The patient subsequently underwent a left open subcapsular nephrectomy. The necrosed perinephric fat was removed piecemeal [Figure 2c]. During mobilization of the kidney, the adherent descending colon was injured and a diverting end colostomy had to be made. Histopathology showed high-grade UTUC with foci

of squamous and sarcomatoid differentiation [Figure 2d]. The postoperative period was uneventful, and the patient recovered well. The patient was reviewed by a multidisciplinary team, and it was decided to start adjuvant chemotherapy 6 weeks postoperatively. At the time of submission of the article, this patient is undergoing gemcitabine and cisplatin combination chemotherapy, after a negative metastatic workup.

Case 3

A 57-year-old gentleman, smoker for 35 years, with a history of left-sided open pyelolithotomy done 20 years ago, presented with dull aching left-sided flank pain for the past 3 months. There was a healed left flank scar. An IV pyelogram revealed multiple left-sided renal calculi with mild-to-moderate hydronephrosis. There was no evidence of any filling defect or irregularity of the margins of the pelvicalyceal system [Figure 3a and b]. Left-sided mini percutaneous nephrolithotomy (PCNL) was done with the clearance of all calculi except a 10 mm lower calyceal nonobstructive calculus. DJ stent removal was done 6 weeks after surgery, and the patient was asymptomatic for the following 2 months. The patient then presented with complaints of continuous low-grade fever and left-sided aching pain in the left flank. On examination, a vague, hard, tender lump was palpable in the left flank with induration and erythema of the overlying skin. A CECT scan of the abdomen revealed enlarged, hypoenhancing left kidney with perinephric fat stranding and no excretion of contrast. The pelvicalyceal system (PCS) appeared dilated and filled with nonenhancing material [Figure 3c]. Differential function estimation by DTPA scan showed a nonfunctioning left kidney. Percutaneous drainage under ultrasound guidance was done by means of a pigtail catheter which drained 150 ml of thick pus. A preoperative diagnosis of pyonephrosis leading to nonfunctioning kidney was made, and the patient underwent subcapsular nephrectomy [Figure 3e and f]. On postoperative day 5, the patient had feculent discharge from the surgical wound. Repeat CECT showed colocutaneous fistula and collection with air fluid level in the left renal fossa [Figure 3d] which was managed conservatively as the patient did not exhibit any colonic symptoms and fistula output gradually decreased and stopped over the next 2 weeks. Histopathology of the nephrectomy specimen showed high-grade UTUC with squamous differentiation and involvement of the renal sinus fat. After 6 weeks of discharge, the patient was reviewed by a multidisciplinary team, and at present, this patient is undergoing adjuvant chemotherapy with gemcitabine and cisplatin, after a negative metastatic work up.

DISCUSSION

Urothelial tumors of the renal pelvis and ureters constitute up to 15% of the tumors of the kidneys.[1] UTUC is more common in the elderly and in males.[2] Majority of them are diagnosed due to hematuria, flank pain, palpable flank mass, and clot colic. About 15% of cases are asymptomatic and are detected incidentally.[3] All the three patients mentioned in this paper presented with complaints of flank pain. The first two cases had a history of continuous low-grade fever. The third patient had undergone PCNL for renal stones and

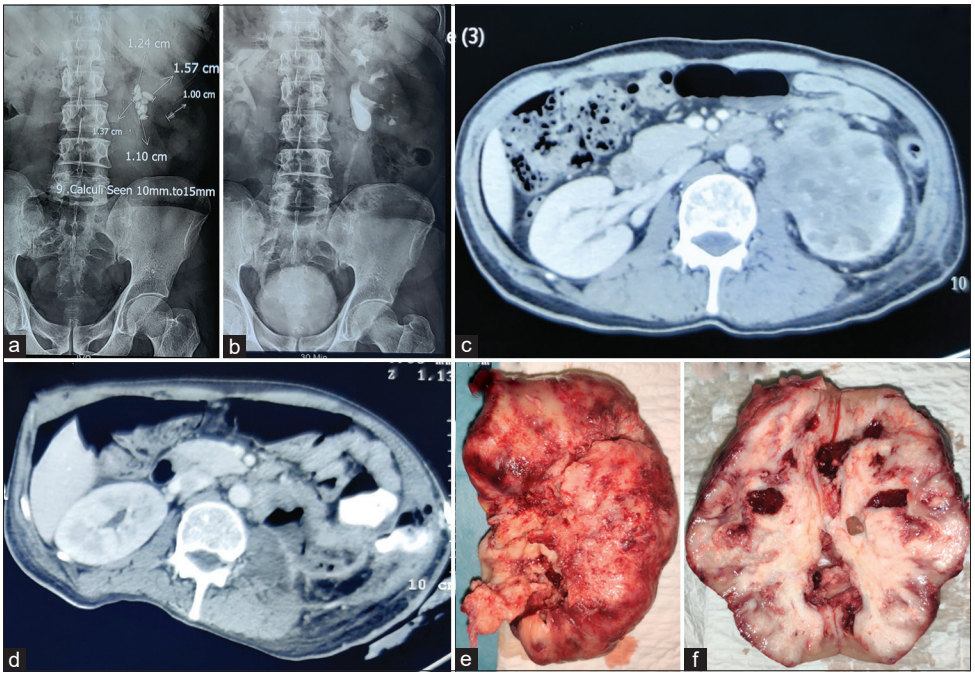

Figure 3: (a and b) Intravenous pyelogram showing left-sided multiple renal calculi with moderate hydronephrosis with normal uptake and excretion. (c) Contrast-enhanced computed tomography showing left hypoenhancing kidney with dilated Pelvicalyceal system with hypodense contents and multiple hypoenhancing areas suggestive of abscesses with perinephric fat stranding. (d) Contrast-enhanced computed tomography showing collection and inflammatory phlegmon in the left renal fossa with a colocutaneous fistula. (e and f) Specimen of the subcapsular nephrectomy showing near complete destruction of the renal parenchyma. No definite visible growth in the pelvicalyceal system

then presented with fever and flank tenderness. None of these patients ever had any hematuria. This combined with elevated leukocyte counts pointed toward an inflammatory pathology. Hence, clinically, the suspicion of UTUC was very low. The usual radiological signs of an upper tract neoplasm, a soft-tissue lesion with low-grade enhancement, collecting system filling defect, stipple sign, phantom calyx, etc.[4] were absent in both cases. Imaging features such as the presence of large staghorn calculus in the first case and the presence of a forgotten DJ stent in the second case along with hydronephrosis and hyperdense contents in the PCS led us to consider XGPN as the first diagnosis. XGPN has been described as an imitator of malignancy and has been reported to be associated with renal cell carcinoma. UTUC presenting as XGPN is even more uncommon, with a total of four cases reported in the literature, of which three cases were not associated with urolithiasis.[5-7] Chronic staghorn calculi may give rise to squamous cell carcinoma (SCC) due to squamous metaplasia, but the cause of transitional cell carcinoma (TCC) remains unclear.

The third patient had a history of recent mini PCNL. The history of percutaneous intervention along with fever, tender flank lump with inflammatory changes of the overlying abdominal wall combined with the CT scan, and sonographic findings of the hydronephrotic kidney with pus in the PCS suggested an obstructed kidney with infection pointing toward pyonephrosis. Moreover, during nephroscopy during the PCNL, the PCS was inspected, as is routinely done for any migrated stone fragments. In all the three cases above, our first diagnosis was an inflammatory pathology of the kidney probably secondary to infection of the obstructed system. We managed all patients with percutaneous drainage. In our cases, the drainage of thick pus through the percutaneous drains and the persistent leukocytosis all suggesred pyonephrosis. There was no suspicion of an underlying malignancy. Differential GFR of all the three patients showed a nonfunctioning kidney. The prevalence of carcinoma in stone disease with nonfunctioning kidneys remains unclear. Sporadic reports, such as the one by Yeh *et al.*, have suggested a high incidence of malignancy, in 24 of 47 (51%) renal calculi patients diagnosed with a nonfunctioning kidney.[8] This re-affirms the importance of pathological evaluation of specimens.

We have previously published another report of UTUC in a patient, whose initial presentation was that of a renoalimentary fistula.[9] CT-guided biopsy of the renal lesion had shown a high-grade UTUC, which was confirmed on immunohistochemistry. UTUC can develop coincidentally in the urothelium of a kidney with staghorn calculi. It may coexist with or take on the appearance of XGPN, and the loss of parenchymal integrity can theoretically predispose to the early extracapsular spread of malignancy leading to adjacent organ involvement before the patient presents with common signs and symptoms.[10]

CONCLUSION

Occasionally, UTUC may have an uncommon presentation with atypical imaging findings. Whenever such findings are encountered in setting on nonfunctional kidneys with long-standing stones, foreign bodies, or renoalimentary fistulae, a low threshold of suspicion for underlying malignancy with prior biopsy may help to plan treatment better.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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