

Intrarenal urothelial cancers confused as infiltrative renal masses: Report of 22 cases and literature review

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Abstract. Distinguishing infiltrative renal masses (IRMs) from intrarenal urothelial cancers (IUCs) is critically important, but may be challenging for any radiologist or urologist. The present study aimed to summarize the clinical, imaging and pathological characteristics of IRM, which were postoperatively confirmed as IUC. The analysis was performed using the records of 22 patients who were preoperatively diagnosed with IRM but the results of percutaneous biopsies or postoperative pathological analyses led to diagnoses of urothelial cancers (UCs) from January 2011 to December 2017. The demographic data, computed tomography (CT) imaging features and pathological characteristics were evaluated. The present study also reviewed the literature concerning the IRM and IUC. The mean age of patients was 62 years and 86.4% of them were >55 years. The sex and tumor side distributions were equal. Hematuria and/or flank pain were observed in 86.4% of patients. All patients exhibited endophytic solid renal masses with unclear tumor boundaries on CT images. The kidneys of 81.8% of patients maintained their normal shape while mild alternations were observed in 18.2% of cases. A total of 81.8% of patients maintained the reniform shape and 18.2% exhibited mild contour change. Of all patients, all tumors exhibited less or equal attenuation on unenhanced CT images and they were mildly improved on enhanced CT. A total of 6 cases were confirmed by biopsy, when patients underwent laparoscopic nephroureterectomy instead of radical nephrectomy. The remaining 16 patients underwent laparoscopic nephrectomy but the postoperative pathological diagnoses revealed the presence of UCs. All postoperatively confirmed cancers were stages T3 and T4 (62.5 and 37.5%, respectively). UCs should be suspected in middle aged or elderly middle-elderly patients presenting renal masses with endophytic solid unclear tumor boundary on unenhanced and slightly enhanced CT images,

accompanied with hematuria and/or flank pain. Preoperative biopsy is preferred for complicated cases.

Introduction

The most common type of malignant kidney cancer is renal cell carcinoma (RCC), which accounts for 85-90% of cases (1). Primary urothelial cancer (UC) of the upper tract is only diagnosed in about 7-10% of all patients with renal tumors (2,3). Macroscopic hematuria, flank pain and palpable flank mass are three main clinical presentation of RCC but such typical tumors are rare at present due to increasing use of imaging (4). Microscopic or macroscopic hematuria is the most common symptom of UC and symptomatic hydronephrosis occurs if the tumor locates at the ureteropelvic junction (5). Both RCC and UC are more common in men vs. women. RCC originates from proximal convoluted tubule including clear cell renal carcinoma, papillary RCC, chromophobe RCC, collecting duct RCC, renal medullary carcinoma and sarcomatoid RCC (6). While UC arises from the transitional epithelium, including papillary and non-papillary transitional cell carcinomas. Nephron sparing surgery (NSS) or radical nephrectomy are the main procedures for RCC, and radical nephroureterectomy (RNU) with en bloc excision of the periureteric bladder cuff is the standard surgical treatment for UCs (7,8). Computed tomography (CT) is mostly used to preoperative diagnosis of RCC and UC. Typically, the tumors of RCC are soft tissue attenuation and sometimes accompanied with necrosis and calcification, which have stronger or irregular enhancement during the corticomedullary phase. In contrast, for UC, filling defect or distortion of calyces are shown on CT scan and the tumors have mild enhancement during contrast CT (9,10). However, unusual infiltrative renal masses (IRMs) are similar to intrarenal UCs (IUCs) on imaging, which frequently results in misdiagnosis and mistreatment. The present study retrospectively evaluated the patients who were preoperatively diagnosed with IRM, but the subsequent pathological results confirmed UCs in First Hospital of Jilin University. A comprehensive review of the literature was also performed.

Case report

The study protocol was approved by the Institutional Review Board of the First Hospital of Jilin University (Jilin, China). A total of 22 IRM patients with pathologically confirmed IUCs

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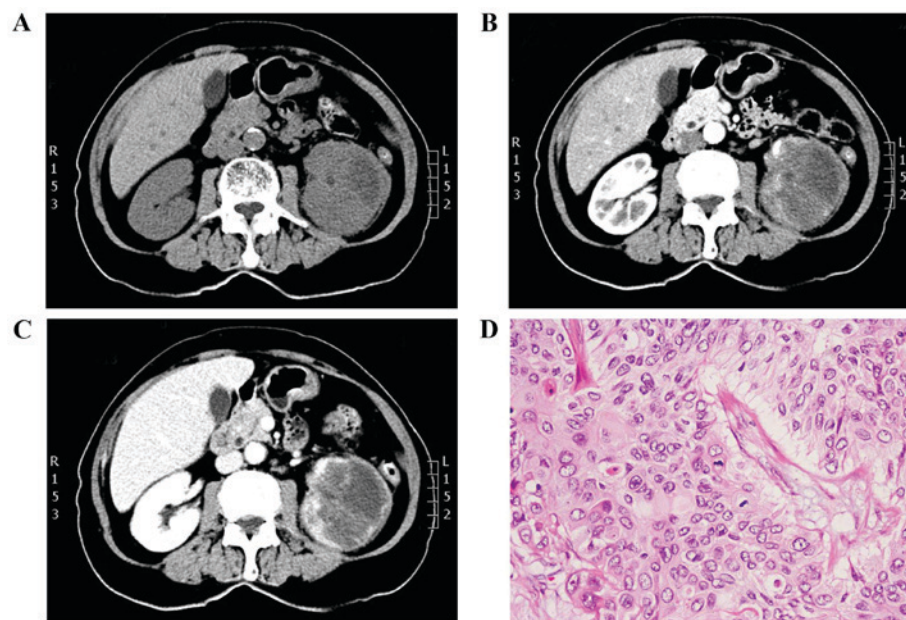


Figure 1. A 74-year-old female with a left renal mass. (A) A poorly defined isodense mass was shown on the axial unenhanced CT scan. Mild enhancement occurred on the (B) cortical and (C) nephrographic phases, showing an infiltrative, solid and unclear boundary. (D) Microscopic analysis demonstrated an infiltrative growth of tumor tissues, highly heterogeneous cells with irregular contours, abundant eosinophilic cytoplasm and vacuolar nuclei (hematoxylin and eosin staining, magnification, x400). CT, computed tomography.

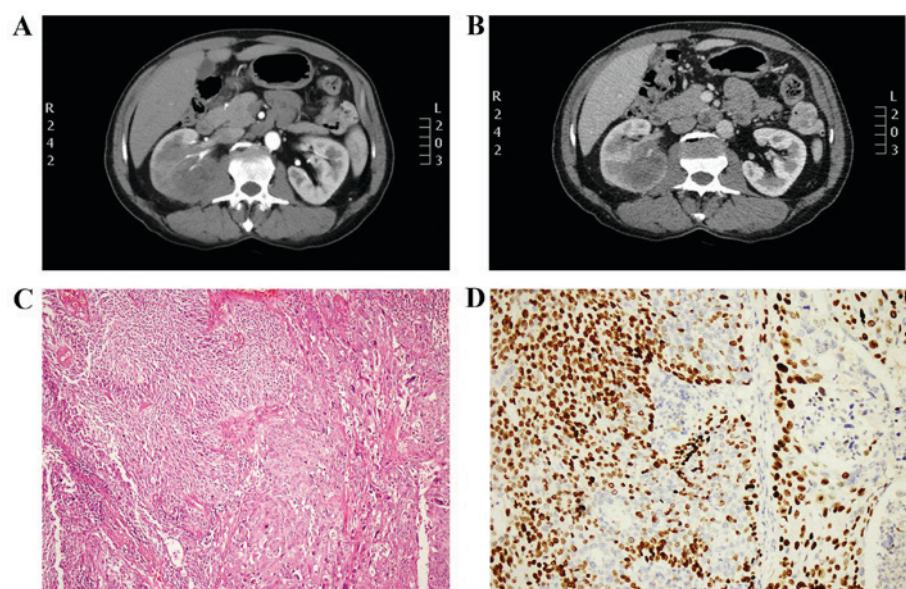


Figure 2. A 59-year-old male with a right renal mass. The contrast-enhanced CT imaging illustrated a mild enhancement on the (A) cortical and (B) nephrographic phases, exhibiting an endophytic, solid, preserved contour and an unclear boundary. (C) Microscopic analysis indicated papillary infiltrative growth pattern of tissue. Left was the typical UC and the right was squamous differentiation (hematoxylin and eosin staining, magnification, x100). (D) Positive expression of P63 in tumor cells (immunohistochemical staining, magnification, x200). CT, computed tomography; UC, urothelial cancer.

at our institution from January 2011 to December 2017 were included in the present study. Representative cases are shown in Figs. 1 and 2. Detailed clinical and pathological data was available for all patients and the CT images were all performed in First Hospital of Jilin University (Jilin, China).

Lists of demographic and pathological data of the study cohort are shown in Table I. There were 14 males and 8 females with a median age of 62 years. A total of 11 patients were between 56-65 years (50%) and 8 patients were >65 years old (36.4%). There was no difference between the frequency

of occurrence of tumors on the left or right side (11 vs. 10 cases, respectively). Hematuria and/or flank pain were the main symptoms which accounted for 86.4% of patients. One patient was diagnosed during a routine physical examination and another two were initially admitted due to emaciation. Two patients exhibited symptoms of lung metastasis. A total of six patients (27.3%) who underwent laparoscopic nephroureterectomy were diagnosed by percutaneous biopsy. The remaining 16 patients underwent laparoscopic radical nephrectomy but the postoperative pathology led to diagnosis of UCs, among

Table I. Demographic and pathological data on 22 patients.

Parameters	No. of patients (%)
Age, years ^a	
45-55	3 (13.6)
56-65	11 (50)
>65	8 (36.4)
Sex	
Male	14 (63.6)
Female	8 (36.4)
Side	
Left	11 (50)
Right	10 (45.5)
Both	1 (4.5)
Symptoms	
No	1 (4.5)
Hematuria	6 (27.3)
Flank pain	6 (27.3)
Hematuria and flank pain	7 (31.8)
Emaciation	2 (9)
Suspected lung metastasis	2 (9)
Biopsy	6 (27.3)
Tumor stage	
pT1	0 (0)
pT2	0 (0)
pT3	10 (62.5)
pT4	6 (37.5)
Positive lymph node	2 (9)

^aThe median age was 62 years (range, 45-80 years).

Table II. CT imaging features of tumor.

Parameters	No. of patients (%)
Mean maximus diameter, cm (range)	4.8 3.6-6.5
Location	
Endophytic	22 (100)
Exophytic	0 (0)
Reniform shape	
No	18 (81.8)
Mild	4 (18.2)
Moderate	0 (0)
Severe	0 (0)
Tumor boundary	
Clear	0 (0)
Unclear	22 (100)
Component	
Cystic	0 (0)
Necrosis	0 (0)
Solid	22 (100)
Unenhanced CT density	
High attenuation	0 (0)
Isoattenuation/hypoattenuation	22 (100)
Degree of enhancement on CT	
Mild	22 (100)
Moderate	0 (0)
Severe	0 (0)
Lymph node enlargement	2 (9)

The mean maximus diameter was 4.8 cm (range, 3.6-6.5 cm). CT, computed tomography.

which, 10 (62.5%) were stage T3 and 6 (37.5%) were stage T4. A total of two patients were confirmed positive lymph node.

All tumor features identified in the CT images were shown in Table II. The mean maximum diameter was 4.8 cm. All tumors were endophytic and solid. All tumor boundaries were unclear. The reniform contours of the operated kidneys were completely preserved or mildly altered (81.8 and 18.2%, respectively). In unenhanced CT images, all tumors exhibited isoattenuation or hypoattenuation which were mildly enhanced on enhanced CT images. A total of 2 patients demonstrated lymph node enlargement.

Discussion

The surgical treatment and postoperative management of kidney cancers and renal pelvis cancers are significantly different. Therefore, distinguishing IRMs from IUCs is critically important but sometimes challenging (11). UC of the renal pelvis may display an infiltrative growth pattern, which results in a close radiological mimic of IRM.

Certain studies have attempted to differentiate IRM from IUC but the limitations were obvious. Raza *et al* (12) reviewed CT studies of 64 centrally located RCC and 34 IUC and found that the presence of a tumor centered within the collecting

system was the most valuable characteristic identified on the CT images. Bata *et al* (13), concluded that using multiple small ROIs was valuable for distinguishing IRM from IUC. However, based on one case and literature review, Li *et al* (14) reported that imaging results of hypovascular RCC were indistinguishable from IUC. Han *et al* (15), attempted to evaluate the potential systemic inflammatory markers to differentiate between infiltrative RCC and infiltrative UCs. Their analysis indicated that age and lymphocyte-monocyte ratio were significantly different between patients with IRM. To the best of our knowledge, the present study is the first to comprehensively evaluate clinical, imaging and pathological characteristics of IRMs that were postoperatively confirmed as IUCs.

In the present study, 63.6% of the patients were male and 36.4% were female. There was no obvious tendency about sex. Zhu *et al* (16) retrospectively assessed 29 patients with invasive renal parenchymal urothelial carcinoma (IRPUC) and found that IRPUC was more likely to occur in the right kidney (82.7%). However, in the present study, the ratio of malignancies in left and right kidneys was 11 vs. 10. Raza *et al* (12), also supported our results. It was observed that prevalence of the disease was increased among middle-elderly patients, over 56 years old (86.4%), which suggests that older age may be associated with the development of IRC.

The mean maximum diameter of tumors was between 3.6 and 6.5 cm. A previous study demonstrated that if such tumors were renal cancers, hematuria and flank pain were infrequent (17). However, in the present study, 27.3% of patients exhibited either a symptom of hematuria or flank pain and 31.8% exhibited both hematuria and flank pain, which indicated that hematuria and/or flank pain were the principal predictive symptoms.

The CT images revealed that all 22 tumors were endophytic and solid. All patients were free from cystic or necrotic alterations. The results were similar to those previously reported by Raza *et al* (12). RCC may be associated with a moderate or severe renal shape distortion, however, in the present study, a total of 18 patients (81.2%) retained the renal contour and 4 patients (18.2%) underwent mild alteration of shape. However, IRM does not necessarily alter the reniform contour in all patients and certain patients with IUC can sometimes exhibit a distorted renal shape (18,19). An unclear tumor boundary was identified in each case included in the present study, which was an important and valuable CT characteristic. Isoattenuation or hypoattenuation occurred in all patients and were visible in unenhanced CT images and all tumors exhibited poor homogeneous enhancing masses in contrast-enhanced CT images.

Although, several special CT features can help distinguish IRM from IRC, in the majority of cases, other similar neoplasms are present, including renal lymphoma, collecting duct carcinoma, metastasis, xanthogranulomatous pyelonephritis and medullary carcinoma (20,21). Biopsy is a necessary procedure in case of misdiagnosis and mistreatment. Guarnizo *et al* (22), assessed the diagnostic accuracy of ureteroscopic biopsy and found that ureteroscopic multi-biopsy can lead to an accurate diagnosis of urothelial carcinoma in 89% of cases and can predict the exact histopathological grade in 78% of cases. Furukawa *et al* (23), assessed a total of 40 patients and found that ureteroscopic biopsy could lead to determination of the pathological grade of nephroureterectomy specimens with an accuracy rate of 87.5%. Recently, Huang *et al* (24) reviewed 26 cases of upper tract lesions and found that percutaneous biopsy was also a safe and effective method.

In conclusion, it is challenging to thoroughly make a distinction between IRM and IUC preoperatively; however, the elder accompanied with hematuria and/or flank pain are more likely to indicate IRM, who with special CT features: endophytic, solid and unclear tumor boundary on unenhanced CT and slightly enhancement on contrast-enhanced CT. Pre-operative endoscopic or percutaneous biopsy, is a valuable tool for complex cases.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

XD, XM, YJ and HL and YW were all involved in this conception of this study and helped to draft the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Institutional Review Board of the First Hospital of Jilin University (Jilin, China). Verbal informed consent was obtained from the patients.

Consent for publication

Verbal informed consent was obtained from the patients.

Competing interests

The authors declare that they have no competing interests.

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