Case Report

A case of ipsilateral three simultaneous renal cell carcinomas with different histologic types

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Abbreviations & Acronyms
CKD = chronic kidney disease
CT = computed tomography
eGFR = estimated glomerular filtration rate
ESRD = end-stage renal disease
H&E = hematoxylin and eosin
IHC = immunohistochemistry
MRI = magnetic resonance imaging
PN = partial nephrectomy
RCC = renal cell carcinoma
RN = radical nephrectomy

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Introduction: Few reports have presented sporadic multifocal renal cell carcinomas of different histologic types occurring simultaneously in a single kidney. Here, we present a case of three ipsilateral renal cell carcinomas with three histologic types.

Case presentation: A 44-year-old man with end-stage renal disease due to nephrosclerosis was referred to our hospital for an incidental renal tumor. Following the introduction of hemodialysis, enhanced computed tomography revealed a renal tumor suggestive of clear-cell renal cell carcinoma with a cystic component. With a preoperative diagnosis of one renal tumor, he underwent laparoscopic radical nephrectomy. However, pathological examination revealed three renal cell carcinomas with three histological diagnoses: clear-cell, papillary, and clear-cell papillary renal cell carcinomas.

Conclusion: Preoperative imaging may not detect all synchronous ipsilateral multifocal renal cell carcinomas. Patients with severe renal function impairment may have synchronous multifocal renal cell carcinomas.

Key words: ipsilateral multifocal renal cell carcinoma, partial nephrectomy, radical nephrectomy.

Keynote message

Urologists must be aware of the possibility of small multifocal renal cell carcinomas when choosing operative methods, particularly for patients with severely impaired renal function. The surgical approach should carefully be considered depending on the tumor size, stage, location, renal function, and comorbidities.

Introduction

Concurrent multifocal RCCs are clinically rare, and most of them occur in hereditary diseases such as Von Hippel–Lindau disease or Birt–Hogg–Dube syndrome.[1,2] A study of a relatively large cohort indicated the incidence of bilateral simultaneous RCCs[3]; however, few reports have shown sporadic ipsilateral simultaneous multifocal RCCs with different histologic types. Herein, we report a case of ipsilateral simultaneous multifocal RCCs with three histologic types.

Case presentation

A 44-year-old man was incidentally found to have a renal tumor on a preoperative screening for peritoneal dialysis because of nephrosclerosis. His eGFR was 3.7 mL/min/1.73 m^2 at the time of first visit, and CKD stage was 5.[4] Ultrasound showed low-echoic cyst with mass inside at the upper pole. CT showed a cystic mass of 43 mm in diameter at the upper pole of the left kidney, with a 20-mm parenchymal component inside the cyst. Because malignancy could not be ruled out, hemodialysis was subsequently introduced 1 month after the first visit instead of peritoneal dialysis. Following the introduction of dialysis, enhanced CT was

performed, which showed a strong contrast effect on the tumor at the early phase, with the disappearance of this effect at the late phase, suggestive of clear-cell RCC with a cystic component (Fig. 1a–c). With MRI, the tumor showed intensity of T1-low and T2-high image (Fig. 1d,e). No evidence of metastatic lesions was found in other organs or lymph nodes.

With a preoperative diagnosis of cT1aN0M0 RCC, a laparoscopic left nephrectomy was performed. Although preoperative assessment showed a single renal tumor in the left kidney, pathological examination revealed three RCCs: one was a CT-detected tumor measuring 38 × 30 mm, and the other two were completely endophytic RCCs measuring 8 × 6 mm and 12 × 8 mm. Histologically, these three RCCs showed different types of RCCs: clear-cell RCC, G1 > G2, pT1a; papillary RCC, G2, pT1a; and clear-cell papillary RCC, G2 > G1, pT1a, according to the H&E staining, and IHC (Fig. 2a–d). Physical examination and medical interviews revealed no features or characteristics that would meet the diagnostic criteria for hereditary disease. A retrospective analysis of preoperative enhanced CT or MRI did not detect endophytic RCCs (Fig. 3a–e). The patient has been followed up with periodic imaging, blood tests, and physical examinations, and no evidence of disease recurrence or metastasis was observed to date (3 years after nephrectomy).

Discussion

Sporadic ipsilateral multifocal RCCs were found in 6.8% of RCC cases, except for patients with known hereditary or familial renal syndromes.[5] Multifocal RCCs often coexist with various pathologic types, with pathologic discordance between the primary tumor and satellite tumors of 6–30%.[3,6] In the present case, we observed three different histologies in one kidney: clear-cell RCC, papillary RCC, and clear-cell papillary RCC. Regarding histology, polycystic disease-associated RCCs are reported to be multifocal and bilateral.[7] In addition, a relatively higher rate of papillary RCC compared with clear-cell RCC for sporadic multifocal RCC was reported.[8] Considering the pathological discordance, even if a clear-cell RCC-like tumor is detected by preoperative imaging, there may be other hidden non-clear RCCs that are more difficult to detect by imaging. Furthermore, the detection rate by diagnostic imaging is even lower for tumors with small diameter.[9] In this case, RN was performed because the patient was undergoing hemodialysis. However, if he had had a better renal function, PN can be a treatment option with a preoperative diagnosis of one RCC in one kidney. For preoperatively known multifocal ipsilateral renal tumors, previous reports have shown that PN does not worsen cancer-specific survival compared with RN in multifocal ipsilateral renal tumors.[10–12] However, the effect on overall survival between RN and PN for preoperatively known multifocal renal tumors is unknown. The surgical approach should carefully be considered depending on the tumor size, stage, location, renal function, and comorbidities.

Patients with ESRD have a significantly higher risk of RCC, and patients with a longer duration of dialysis have a higher risk for RCC.[7,13] Clear-cell papillary RCC is a unique RCC but also occurs in patients without ESRD.[7] It is reported to be less aggressive than conventional RCCs. Oxidative stress in ESRD kidneys, upregulation of the hepatocyte

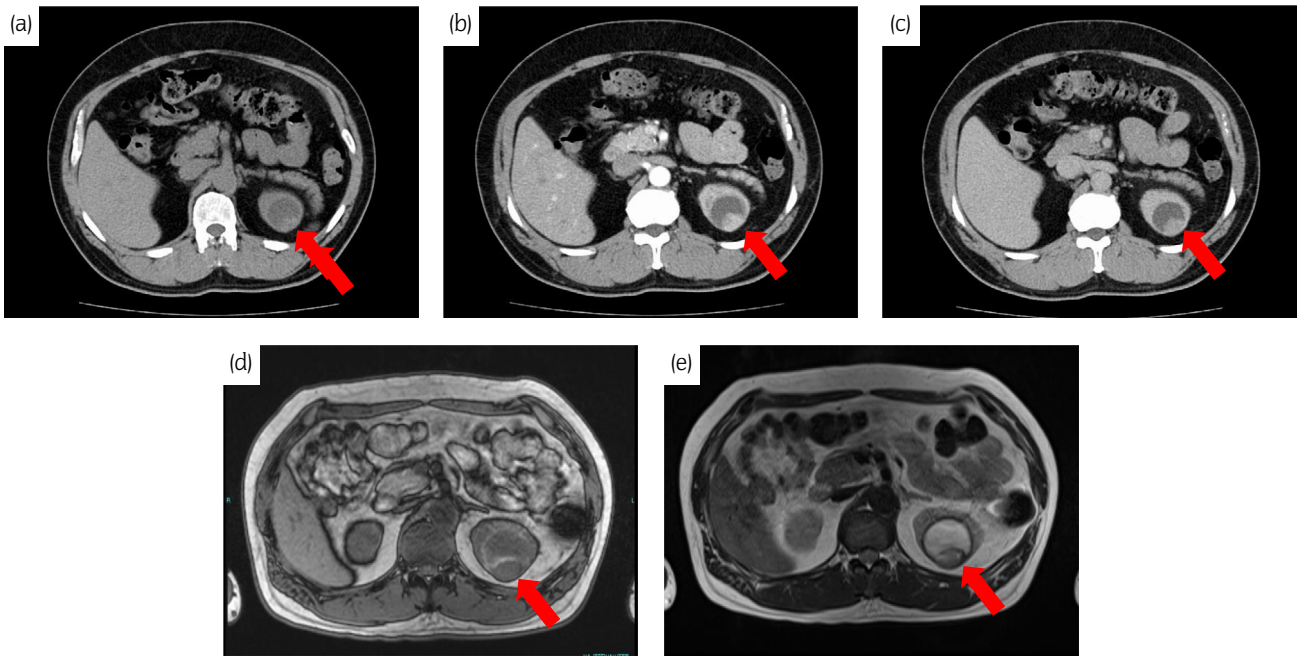

Fig. 1 Plain CT showed a cystic mass measuring 43 mm in diameter at the upper pole of the left kidney, with a 20-mm parenchymal component inside the cyst. Enhanced CT showed strong contrast effect on the tumor at the early phase, with disappearance of this effect at the late phase, suggestive of clear-cell RCC with a cystic component. With MRI, the tumor showed low intensity on the T1-weighted image and high intensity on the T2-weighted image. The red arrow indicates renal tumor. (a) Plain CT. (b) Early-phase enhanced CT. (c) Late-phase enhanced CT. (d) T1-weighted MRI. (e) T2-weighted MRI.

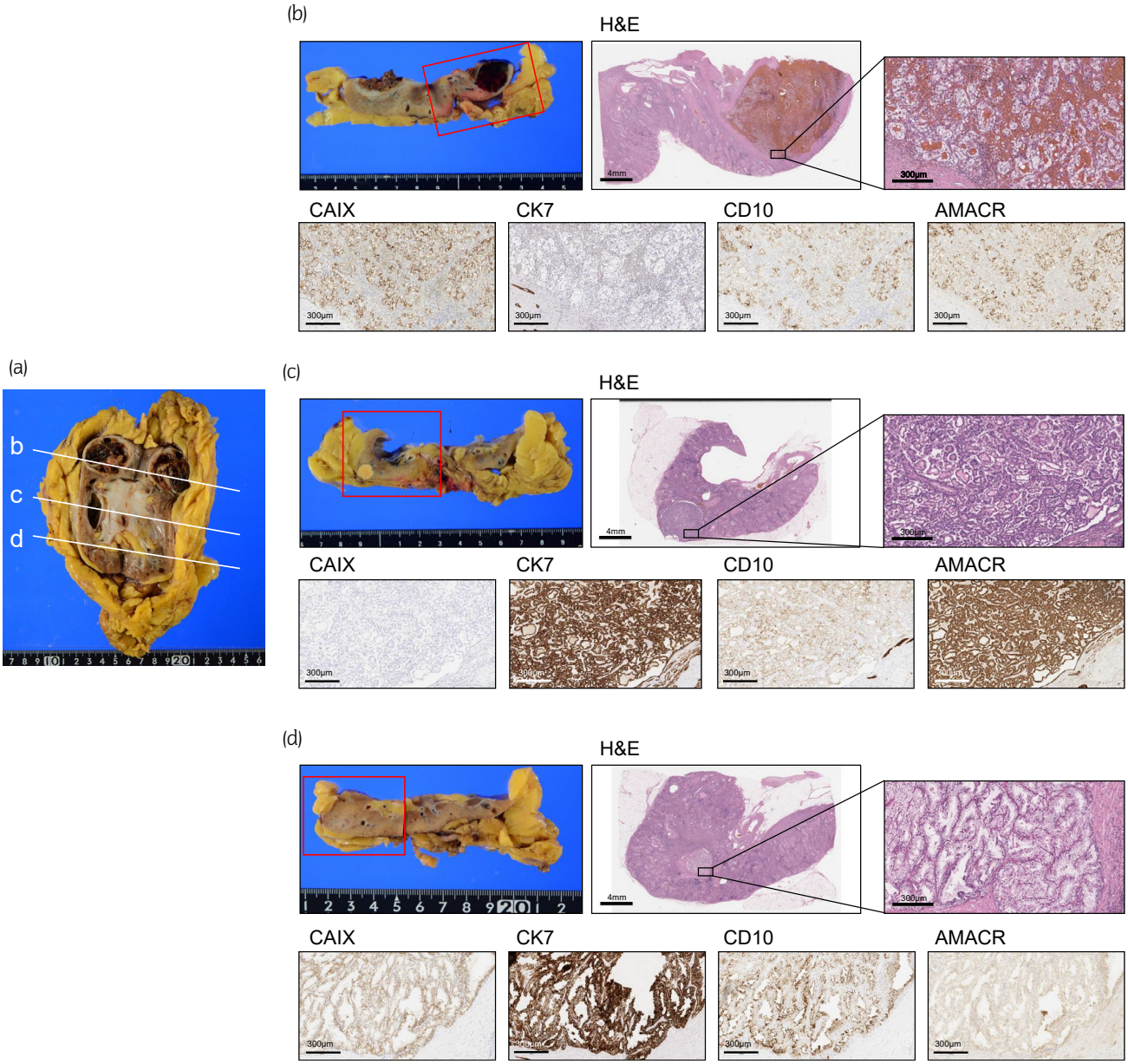

Fig. 2 (a) Macroscopic image of the kidney. (b) A 38 × 30-mm well-defined mass was detected at the upper pole of the kidney. The tumor was encapsulated, and cystic change with hemorrhaging and a yellow color area was observed inside the tumor. H&E staining showed nested growth pattern, composed of cells with clear cytoplasm, and IHC showed diffuse positive results for CAIX and negative results for CK7, consistent with clear-cell RCC. (c) A yellow enhancing mass (8 × 6 mm) without capsular formation was observed ventral to the mid-pole of the kidney. H&E staining showed papillary structures, and IHC showed negative results for CAIX and positive results for CK7, consistent with papillary RCC. (d) A 12 ×8-mm beige well-circumscribed mass is observed on the ventral side of the lower pole of the kidney. H&E staining showed nested and papillary pattern, and IHC showed diffuse cup-shaped positive results for CAIX and positive results for CK7, consistent with clear-cell papillary RCC. Macroscopically, no continuity was found between the three lesions.

growth factor, and mutations in mitochondrial DNA could induce the pathogenesis of tumors in ESRD kidneys.[13] Also, the risk of RCC was more than doubled in those with CKD stage 4/5 compared with those with CKD stage 2.[14] In the present case, hemodialysis was not initiated when the patient was found to have a renal tumor; however, he might be at risk for developing multiple RCCs, considering his severely impaired renal function.

Performing PN or RN to patients with impaired renal function, especially for patients with CKD stage 4, is controversial. PN for patients with CKD stage 4 delayed the requirement for postoperative dialysis[15]; on the contrary, PN for these patients resulted in unfavorable perioperative outcomes with high 90-day mortality, postoperative complications, or positive surgical margin, and rapid progression to ESRD.[16] As regards diagnosis, patients with severe CKD are not suitable for enhanced CT, and preoperative accurate diagnosis including multifocal RCC should be difficult. Although the histology of RCC in the ESRD kidney is relatively favorable, there might be hidden multifocal RCC when performing

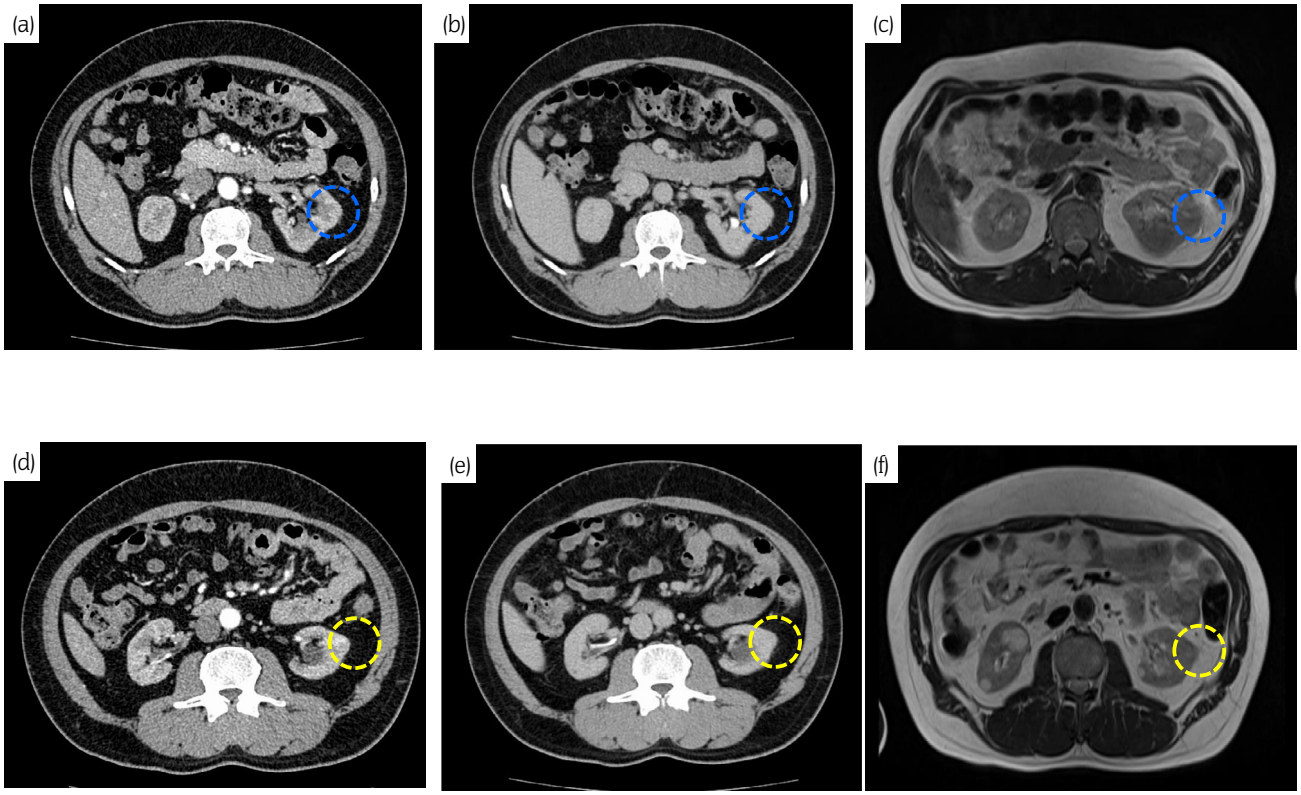

Fig. 3 Retrospective analysis of preoperative enhanced CT or MRI did not detect endophytic RCCs. The blue and yellow dot circles indicate the area of lesions that tumors could be detected. (a) Early-phase enhanced CT of the middle pole. (b) Late-phase enhanced CT of the middle pole. (c) MRI of the middle pole. (d) Early-phase enhanced CT of the lower pole. (e) Late-phase enhanced CT of the lower pole. (f) MRI of the lower pole.

PN for the ESRD kidney. Therefore, RN would be recommended for patients with ESRD (eGFR <15 mL/min/1.73 m^2). Close follow-up for the residual kidney is necessary to detect such tumors, even after the introduction of dialysis. Further studies are warranted to show the relationship of incidence of multiple RCC and CKD or ESRD.

Conclusion

Preoperative imaging may not detect all the synchronous ipsilateral multifocal RCCs. Patients with severely impaired renal function may have synchronous multifocal RCCs.

Author contributions

Satoki Tanaka: Data curation; investigation; writing – original draft. Yusuke Goto: Conceptualization; investigation; project administration; writing – original draft; writing – review and editing. Ayumi Fujimoto: Data curation; writing – original draft. Takayuki Arai: Data curation. Hiroaki Sato: Validation. Tomokazu Sazuka: Supervision; writing – review and editing. Yusuke Imamura: Supervision. Shinichi Sakamoto: Supervision. Jun-Ichiro Ikeda: Supervision. Tomohiko Ichikawa: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

This study was approved by our institutional ethical reviewer board with an approval number of 2554.

Informed consent

Informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

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