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Contrast Enhanced Ultrasound Detects Recurrent Renal Cell Carcinoma in the Setting of Chronic Renal Insufficiency

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Keywords

Chronic kidney disease; Diagnostic imaging; Kidney cancer; Solitary kidney; Surveillance

Introduction

In managing patients with chronic renal impairment and a history of renal cell carcinoma (RCC), the question arises – when is a contrast cross-sectional study truly needed? Use of contrast computed tomography (CCT) poses not only additional radiation exposure but also a well-established risk of nephrotoxicity.¹ Although contrast magnetic resonance imaging (CMRI) with gadolinium is an alternative, it is expensive, uncomfortable for patients, and imparts the potential risk of nephrogenic systemic fibrosis.² Especially for patients with renal insufficiency, contrast-enhanced ultrasound (CEUS) represents a low cost, zero-radiation alternative that can help to determine when it is necessary to perform traditional cross-sectional contrast imaging.

Case Report

The patient is an 80-year-old man with a history of a congenital solitary left kidney who, at the age of 74 years, developed gross hematuria and was found to have an 11 cm left lower pole renal mass. He received 2 courses of neoadjuvant sunitinib that resulted in a significant decrease in the size of the mass. An open left partial nephrectomy was performed, and pathology demonstrated a pT2b Fuhrman grade 2 clear cell RCC with negative margins. Post-operatively, the patient had multiple surveillance imaging tests performed (noncontrast CT and grey-scale renal ultrasounds) showing no evidence of recurrent disease. The patient's baseline postoperative creatinine plateaued at 2 mg/dL (estimated creatinine clearance, 25 mL/min). Six years later, he developed new onset gross hematuria. For evaluation, a

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noncontrast CT and 2 MRI scans without contrast were initially performed, none of which showed any evidence of recurrent tumor (Figure 1). The patient continued to have gross hematuria and was advised to undergo a CEUS.

For the CEUS procedure, a GE LOGIQ E9 system with a C1-6 curved array transducer (GE Healthcare) was used, and 2 mL intravenous sulfur hexafluoride lipid-type A microspheres (Lumason; Bracco Diagnostics; Monroe Township, NJ) were injected. The normal and contrast-enhanced mode images can be seen in Figure 2. These demonstrated a 3.5 cm renal mass in the mid-kidney with enhancement. Given this finding, the patient was advised to undergo CCT to further evaluate the extent of the tumor. As seen in Figure 1, this abdominal CT demonstrated a 3.7 cm left upper pole renal mass as well as multiple areas of metastatic disease. Subsequent staging chest CT confirmed distant metastases. The patient was counseled on treatment options and elected to undergo systemic immunotherapy.

Discussion

Although CCT or CMRI remain the standard in surveillance imaging for patients with a history of RCC, providers are often faced with the difficult decision of whether and when to order these studies in patients with chronic renal impairment. For these patients, there is understandable reluctance to proceed straight to CCT given the potential nephrotoxic effects and frequency of surveillance imaging. Per American Urological Association (AUA) Guidelines,³ patients with moderate- to high-risk RCC (pT2-4N0 Nx or any stage N+) should undergo a baseline chest and abdominal scan within 3 to 6 months after surgery followed by continued imaging (ultrasound, chest x-ray, CT, or MRI) every 6 months for at least 3 years and annually thereafter to year 5. In this patient's case, he presented with gross hematuria outside of the 5-year follow-up range. The AUA guidelines address this scenario as follows: "patients may undergo further scanning (CT or MRI) beyond 5 years based on individual patient risk factors."

CEUS has previously been shown to have excellent sensitivity for detecting solid tumors. Compared with CT, it displays strong concordance while providing reduced cost and radiation exposure for patients⁴. Moreover, specific to the detection of cystic renal masses, CEUS has the ability to upgrade Bosniak grading, given its higher sensitivity for detecting septal enhancement compared with CCT.⁵ A recent meta-analysis has shown that CEUS has a sensitivity of 88% and specificity of 80% in differentiating RCC from benign renal masses.⁶

With regard to CEUS after treatment for RCC, most of the existing literature has centered on patients undergoing ablative therapy, where CEUS compares favorably with both CT and MRI. Barwari et al⁷ prospectively showed that CEUS was successful in demonstrating the absence of a renal mass treated with laparoscopic cryoablation in 45 patients. At 3 and 12 months follow-up, there was strong concordance compared with CT. In this study, CEUS demonstrated a specificity of 90% and a negative predictive value of 100% for detecting tumor recurrence after ablation, findings corroborated by others.⁸ Meloni et al⁹ performed a retrospective study comparing CEUS versus CT or MRI in 29 patients who underwent

radiofrequency ablation. During the mean follow-up of 24.6 months, they reported concordance between CEUS and both CT and MRI in 27 of 28 (96.4%) patients.

Multiple aspects of our patient's case are important to consider. First, this patient had a solitary kidney and underwent a partial nephrectomy, creating significant concern for the potential of nephrotoxicity, given his poor renal function. This limited the types of surveillance and diagnostic imaging available for the patient. Second, he underwent both CT and MRI studies that were unable to detect the recurrent mass, likely owing to the lack of contrast. An MRI without contrast is unable to generate subtraction images, thereby making it more difficult to differentiate tumor from other entities, including postsurgical scarring, motion artifact, and normal renal contours.¹⁰ Third, our patient's date of recurrence was beyond the 5-year timeframe mentioned in the AUA guidelines, highlighting the fact that currently there is no consensus on the preferred imaging modality in patients like him who present with such a delayed recurrence. This likely reflects the balance between an overall decreased risk of recurrence for these patients weighed against the possible harms of contrast-enhanced CT and MRI.

Conclusion

CEUS is a safe and effective surveillance modality in patients with chronic renal insufficiency that might otherwise not receive contrast imaging and thereby may have a recurrent RCC overlooked. Although this is only one case, it suggests that CEUS could be the preferred initial imaging modality compared with a noncontrast CT or MRI scan and help direct further imaging evaluation. Although CEUS does not have the resolution or detail of CCT or MRI, it may help patients decide when it is necessary to accept the risks of intravenous contrast and when this may be safely avoided. Further studies are needed to confirm this.

CEUS can provide improved lesion detection and characterization over noncontrast CT and MRI. It represents a safe and useful alternative imaging modality to help diagnose recurrence in patients with renal insufficiency and a history of RCC.

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Clinical Practice Points

- In patients with a history of renal cell carcinoma and chronic renal insufficiency, whether to perform contrast axial imaging can be a difficult decision for the practicing urologist.
- There are concerns for nephrotoxicity with iodinated contrast computed tomography (CT), and nephrogenic systemic fibrosis with gadolinium contrast magnetic resonance imaging (MRI).
- Noncontrast CT and MRI can be limited in their diagnostic ability of renal cell masses.
- Contrast-enhanced ultrasound provides a relatively low cost, zero radiation alternative that has been shown to have high sensitivity for detecting renal masses.
- We present the case of a patient with a solitary left kidney status post previous partial nephrectomy, who ultimately was diagnosed with a recurrent left renal mass after noncontrast CT and MRI failed to identify the lesion.
- Our case demonstrates the role for contrast-enhanced ultrasound as an alternative imaging modality in the workup of a suspected renal masses, especially for those patients with chronic renal insufficiency.

Figure 1.

Initial Surveillance Noncontrast Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) Compared With Contrast CT. (A) Axial Noncontrast T2-weighted MRI Image Demonstrates No Discrete Evidence of Renal Mass Within the Left Kidney. (B) Axial Noncontrast CT Fails to Show Left Renal Mass Recurrence. (C) Administration of Iodinated Contrast Confirms the Enhancing Mass in the Anterior Mid-polar Region Abutting a Dilated Renal Pelvis (Black Arrow)

Figure 2.

Dual Screen Gray Scale and Contrast Enhanced Ultrasound. On the Left, the Gray-scale Image Demonstrates a Vague Area of Soft Tissue Fullness That Is Incompletely Characterized (White Arrow). The Corresponding Contrast-enhanced Ultrasound Image on the Right Confirms a Discrete Mass With Marked Hypervascularity (White Arrow) Compared With Adjacent Renal Parenchyma