CASE REPORT

^{99m}Tc-Sestamibi scintigraphy to differentiate benign and malignant renal masses: A case report

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SUMMARY

The increasing use of cross-sectional imaging has led to a rise in the incidental detection of small renal masses. However, anatomical imaging techniques often lack the ability to effectively distinguish benign from malignant renal lesions. Renal biopsy has inherent limitations, including a high non-diagnostic rate, poor negative predictive value, and associated procedural risks and costs. As a result, many benign renal tumours undergo unnecessary surgical resection due to the presumed malignancy. Technetium-99m (^{99m}Tc) sestamibi single photon emission computed tomography/computed tomography (SPECT/CT) is a molecular imaging modality that differentiates benign oncocytomas and hybrid oncocytic/chromophobe tumours from malignant renal cell carcinomas (RCCs). This differentiation is based on variations in mitochondrial density and multidrug resistance pump expression. We present a case of a 61-year-old male who underwent ^{99m}Tc-sestamibi SPECT/CT for renal mass evaluation, demonstrating its usefulness in differentiating benign from malignant renal lesions. The lesion showed absent sestamibi uptake, raising strong suspicion for malignant RCC and prompting further diagnostic assessment. A targeted renal biopsy was subsequently performed, revealing a papillary neoplasm with transitional and glandular (mucin-producing) differentiation.

INTRODUCTION

The widespread use of abdominal cross-sectional imaging has led to an increasing detection rate of renal masses. However, distinguishing benign from malignant renal tumours remains a clinical challenge. Conventional modalities such as contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) often yield indeterminate lesions.[1]

Among benign renal tumours, oncocytoma is the most frequently diagnosed, accounting for approximately 10% of all solid renal masses.[2] In contrast, RCC is significantly more common, with clear cell RCC alone comprising approximately 70–75% of malignant renal tumours.[3] This striking difference in prevalence highlights a key clinical dilemma: while accurate non-invasive identification of oncocytoma is important to prevent unnecessary surgery, the probability that a solid renal mass represents RCC remains much higher, reinforcing the need for cautious interpretation of imaging findings and, when necessary, histopathological confirmation.

Renal biopsy is an established diagnostic tool, but has notable limitations, including a non-diagnostic rate of 8–14%[4] and less effective for small renal masses.[5]

Non-invasive imaging modalities such as ^{99m}Tc-sestamibi SPECT/CT have gained prominence as promising tools and has been proposed as an alternative to renal mass biopsy for distinguishing renal oncocytomas from RCCs.[6] This technique exploits differences in mitochondrial content and multidrug resistance pump expression between benign and malignant renal tumors.[7]

CASE PRESENTATION

A 61-year-old male presented to Hospital Raja Perempuan Zainab II, Malaysia, in 2022 with lower urinary tract symptoms, fatigue, and persistent vomiting over three months. Clinical examination was unremarkable.

Imaging with ultrasound of the kidney, urinary and bladder revealed bilateral gross hydronephrosis, bilateral renal calculi, and a right lower pole lesion. CT Urography confirmed the presence of an isodense lesion at the right lower pole with calcifications (1.6 × 3.3 × 3.4 cm), suggestive of a residual renal cortex with parenchymal calcification or renal lesion. A renal MAG3 scan demonstrated mildly reduced right renal function with evidence of urinary outflow obstruction and moderate-to-severe left renal dysfunction. A CT renal 4-phase scan identified a rounded, hypodense lesion in the right lower pole (2.2 × 2.9 × 3.2 cm), with progressive enhancement in the corticomedullary and nephrogenic phases, followed by washout in the excretory phase (Figure 1).

Due to the uncertain nature of the lesion, ^{99m}Tc-sestamibi renal SPECT/CT was performed. The scan showed absence of

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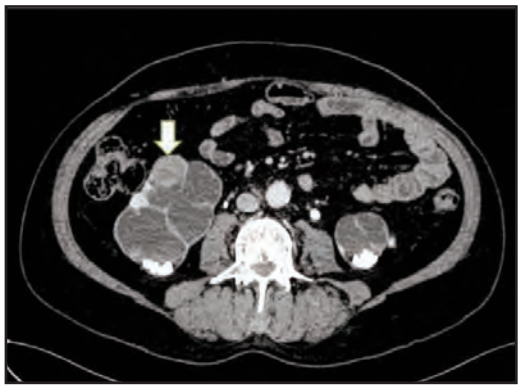

Fig. 1: Axial CT renal 4-phase scan showing a rounded, hypodense soft tissue lesion at right lower pole (arrow)

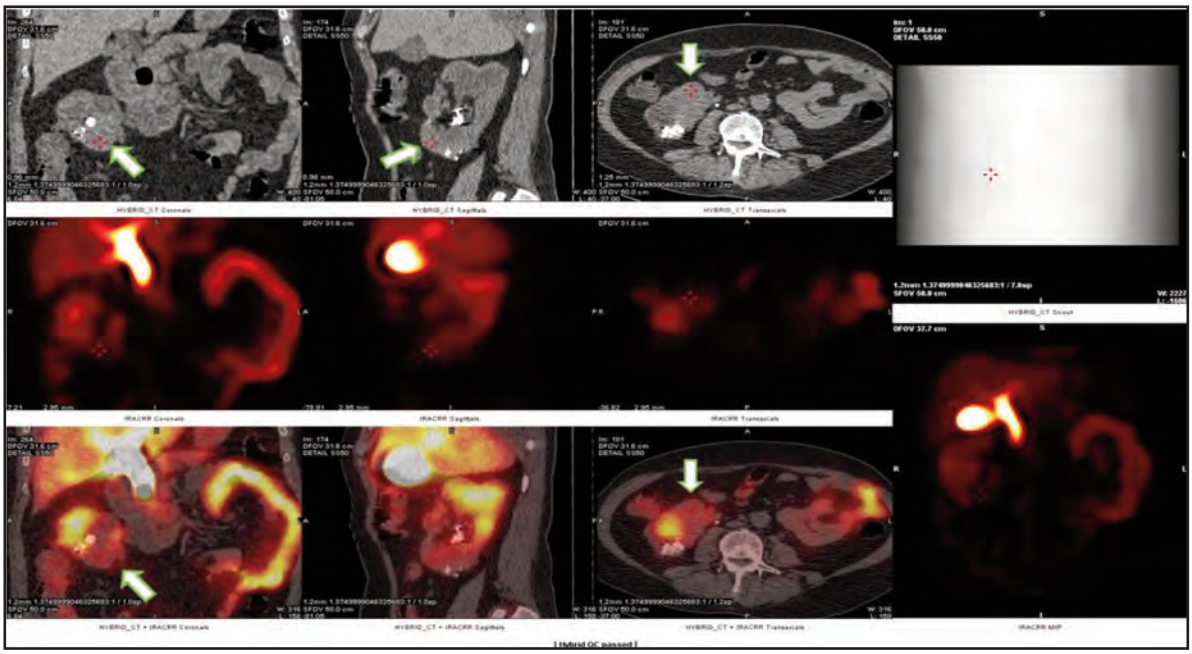

Fig. 2: First row: CT images; second row: SPECT images; third row: SPECT/CT fusion images. Absence of sestamibi tracer uptake is observed at the right lower pole corresponding to a soft tissue lesion

radiotracer uptake in the right lower pole, corresponding to the soft tissue lesion identified on CT, raising suspicion for RCC (Figure 2).

A repeat CT renal 4-phase scan in July 2024 demonstrated a slight increase in the size of the soft tissue lesion at the lower pole of the right kidney. Subsequently, a renal biopsy was performed in November 2024, revealing features consistent with a papillary neoplasm exhibiting transitional and glandular (mucin-producing) differentiation. However, the biopsy was superficial and inadequate for comprehensive assessment. The patient was advised to undergo surgery but declined the recommendation and default subsequent follow-up.

DISCUSSION

This case highlights the clinical utility of ^{99m}Tc-sestamibi SPECT/CT in renal mass characterization. Contrast-enhanced CT remains the first-line imaging modality for characterising renal masses; however, its ability to differentiate benign oncocytomas from malignant RCC is limited. Published studies report only modest performance, with sensitivity ranging from 60–70%, specificity from 55–75%, and overall diagnostic accuracy of approximately 63–70%.[8,9] Although MRI offers superior soft-tissue contrast compared to CT, conventional MRI sequences still perform suboptimal in distinguishing benign oncocytomas from RCC. Reported diagnostic metrics remain modest, with sensitivity ranging from 65–80%, specificity from 60–85%, and overall diagnostic accuracy of approximately 70–78%.[9,10] Similarly, FDG PET/CT demonstrates limited sensitivity for differentiating benign oncocytic tumours from malignant RCC because both can show low or variable uptake, resulting in modest overall accuracy.[11]

In contrast, ^{99m}Tc-sestamibi SPECT/CT has emerged as a promising adjunctive modality due to the differential uptake of sestamibi between oncocytomas and RCCs is attributed to variations in mitochondrial density and multidrug-resistant

(MDR) pump expression. Oncocytomas are composed of cells with abundant mitochondria, leading to high ^{99m}Tc-sestamibi retention. Conversely, RCCs exhibit reduced mitochondrial content and overexpression of MDR transporters, leading to low radiotracer uptake.[7] This phenomenon enables ^{99m}Tc-sestamibi SPECT/CT to differentiate benign from malignant renal masses, offering a non-invasive alternative to renal biopsy in selected cases.

Systematic review and meta-analyses by Wilson et al.[12,13] and Rowe et al.[13] report that ^{99m}Tc-sestamibi SPECT/CT offers high diagnostic performance, with sensitivity ranging from 92–95% and specificity from 88–91% in differentiating benign oncocytic tumors from malignant RCC. And study by Sistani et al.[14] suggested that this imaging technique could reduce unnecessary nephrectomies in patients with benign renal tumors.

While this approach holds promise, some limitations exist. False-positive uptake can be seen in chromophobe RCC and hybrid oncocytic/chromophobe tumors, which may share high mitochondrial density similar to oncocytomas.[15] Conversely, false-negative findings may arise in oncocytomas with central fibrosis or necrosis, small lesions affected by partial-volume effects or tumors with high multidrug-resistance expression which reduce sestamibi retention.[13] Technical factors such as motion artefacts and limited sensitivity for cystic or predominantly necrotic lesions can further compromise accuracy. Therefore, while sestamibi SPECT/CT is a valuable adjunct for renal mass characterization, results must be interpreted cautiously in the presence of these biological and technical pitfalls. Furthermore, the limited availability of ^{99m}Tc-sestamibi SPECT/CT in routine clinical practice remains a barrier.

Despite these challenges, ^{99m}Tc-sestamibi SPECT/CT represents a valuable diagnostic tool for risk stratification of renal masses, reducing the reliance on invasive biopsy procedures.

CONCLUSION

99mTc-sestamibi SPECT/CT has emerged as a valuable imaging tool for distinguishing benign oncocytomas from malignant RCC, helping to overcome the diagnostic limitations of conventional imaging and, in some cases, renal biopsy. This case highlights the potential of ^{99m}Tc-sestamibi SPECT/CT to enhance diagnostic confidence and support more informed clinical decision-making, thereby reducing the likelihood of unnecessary surgical intervention. Its use is particularly advantageous in the further evaluation of renal masses that remain indeterminate on CT or MRI.

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