Letter

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Renal oncocytoma mimicking chromophobe renal cell carcinoma: Management using proposed diagnostic algorithm with emphasis on 99mTc-sestamibi SPECT/CT

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SUMMARY: Renal oncocytomas are benign renal tumours characterized by a central stellate scar that are indistinguishable on CT/MR imaging from malignant chromophobe renal cell carcinomas (ChrRCCs). Renal oncocytomas and ChrRCCs can be separate entities but can also co-exist on a spectrum in hybrid oncocytic/chromophobe tumours. In the past, invasive biopsy and pathologic diagnosis has been relied on to differentiate these lesion and direct management. Early research demonstrates the effectiveness of technetium 99m sestamibi (99mTc-sestamibi) single-photon emission computed tomography (SPECT)/CT in differentiating benign versus malignant renal tumours. A new diagnostic algorithm has previously been proposed to reduce unnecessary biopsy and/or targeted therapy in managing enhancing 1-4 cm renal masses by incorporating 99mTc-sestamibi SPECT/CT in management. We present a case of suspected renal oncocytoma found incidentally on surveillance imaging post-treatment of uveal melanoma. We illustrate the incorporation of the proposed diagnostic algorithm using 99mTc-sestamibi SPECT/CT for enhancing 1-4 cm renal masses into the existing diagnostic algorithm for incidental renal masses and demonstrate its use in our case of suspected renal oncocytoma.

Keywords: renal oncocytoma, chromophobe renal cell carcinoma, hybrid oncocytic/chromophobe tumour, 99mTc-sestamibi SPECT/CT

A renal oncocytoma is a benign renal tumour, representing 3-7% of all renal tumours (*1*). Renal oncocytomas are classically described as having a distinctive central stellate scar which can be seen in 33–80% of cases (2). On MRI they exhibit low T1 signal and high T2 signal in addition to a classic central stellate scar. In over 50% of cases, patients are asymptomatic (*1*). When symptomatic, the most common symptoms include flank pain, gross hematuria, or palpable mass (*1,2*). Renal oncocytomas are benign but share a similar imaging appearance to malignant chromophobe renal cell carcinoma (ChrRCC), as both arise from intercalated cells in the kidney, and thus require further differentiation (*1-4*). ChrRCCs represent 5% of all renal cell carcinomas and are the third most common subtype of renal cell carcinoma behind clear cell and papillary (*5*).

Renal oncocytoma and ChrRCC can be differentiated on pathology using a combination of histopathology and immunohistochemistry. On histopathology, renal oncocytomas have a nested or tubular architectural pattern while ChrRCCs have a solid or trabecular architectural pattern (*6*). On immunohistochemistry, renal oncocytomas will have minimal cytokeratin 7 (CK7) staining and positive staining for cluster of differentiation 117 (CD117) while ChrRCCs will have positive CK7 and CD117 staining (*6*). Pathological differentiation is complicated by the existence of hybrid oncocytic/chromophobe tumours (HOCTs) that display both features of renal oncocytomas and ChrRCCs. There is no consensus on whether HOCTs are malignant or benign, and they can occur in 10-32% of cases (*2,3*). Due to challenges associated with imaging and pathological diagnosis, renal oncocytomas are frequently surgically resected, accounting for 73% of all surgically resected renal tumours (*2,3*). Resection of benign renal tumors should be avoided as it may be associated with post-surgical morbidity and can precipitate renal dysfunction in individuals with pre-existing borderline renal function.

A systematic review and meta-analysis by Wilson *et al*. (2020) suggests that technetium 99m sestamibi (99mTc-sestamibi) single-photon emission computed tomography (SPECT)/CT could differentiate renal oncocytomas versus malignant renal lesions with 86% (95% CI: 66–95%) sensitivity and 90% (95% CI: 80–95%) specificity when considering HOCTs malignant

(*4*). When considering HOCTs benign, 99mTc-sestamibi SPECT/CT identified renal oncocytomas and HOCTs vs malignant lesions with 88% sensitivity and 95% specificity (*4*). The ability to differentiate renal oncocytomas from other renal lesions on 99mTc-sestamibi SPECT/CT is attributed to the high density of mitochondria compared to other lesions and the tendency for lipophilic cations like sestamibi to accumulate in mitochondria due to their negatively charged inner membrane potential (*3*). Emerging research in CT radionomics also shows promise in differentiation of oncocytomas and ChrRCCs although more work will be needed prior to implementation in a clinical setting (*7*). Diffusion kurtosis tensor MR imaging has been shown to be able to differentiate different pathological types of renal cell carcinoma, but more work is needed to assess its ability to distinguish ChrRCCs from oncocytomas (*8*).

Using the findings of the systematic review and meta-analysis by Wilson *et al*., a review article published in 2022 proposed using 99mTc-sestamibi SPECT/CT in a diagnostic algorithm in managing enhancing 1–4 cm renal masses (*3*). Benign lesions such as suspected renal oncocytomas measuring 1–4 cm with positive radiotracer uptake (tumor-to-renal parenchyma ratio ≥ 0.6) could be managed with active surveillance while those with negative radiotracer uptake could be directed toward biopsy for further characterization (*3*). The ≤ 4 cm threshold was chosen based on evidence showing increased detection of small renal masses with only slight reduction in mortality (*3,9*). The 1 cm lower bound was chosen based on already existing American College of Radiology (ACR) guidelines for addressing completely characterized incidental renal masses without fat that are < 1 cm. We demonstrate how the proposed diagnostic algorithm using 99mTc-sestamibi SPECT/CT can be incorporated into the existing ACR diagnostic algorithm for a completely characterized incidental solid renal mass without fat (Figure 1) (*3,10*). Detailed descriptions of the original individual diagnostic algorithms can be found in their respective articles (*3,10*).

An asymptomatic 80-year-old male presented for bi-annual surveillance imaging with MRI post-treatment for uveal melanoma. Initial MRI without and with contrast of the abdomen and pelvis (Figure 2) demonstrated an 8.3 × 8.2 × 6.5 cm well-circumscribed, exophytic mass arising from the upper pole of the left kidney. The mass was heterogeneously T1 hypointense and heterogeneously T2 hyperintense with early arterial enhancement that is prolonged on portal-venous and delayed phase. The central stellate scar was T1 hypointense and T2 hyperintense with no enhancement. The suspected diagnosis was a benign renal oncocytoma. Implementing the proposed diagnostic algorithm for management of a completely characterized solid renal mass without fat (Figure 1), a solid mass measuring 8.3 cm requires

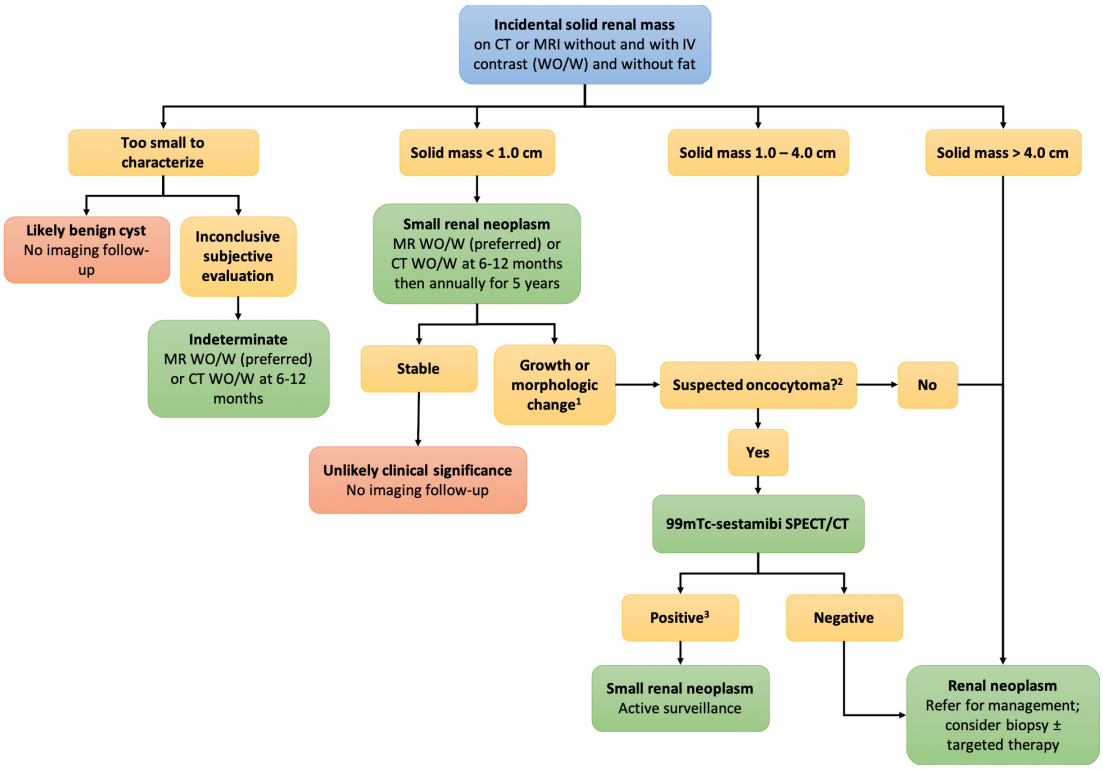

Figure 1. Proposed diagnostic algorithm for a solid renal mass without fat that is completely characterized on CT or MRI without and with IV contrast that combines ACR guidelines with propose use of 99mTc-sestamibi SPECT/CT. [1]Growth ≥ 4 mm per year or change in number of septa, contour, or attenuation; [2]Suspected renal oncocytoma based on classic imaging features such as a central stellate scar, low T1 signal, and high T2 signal; [3]A positive 99mTc-sestamibi SPECT/CT means a tumor-to-renal parenchymal ratio ≥ 0.6.

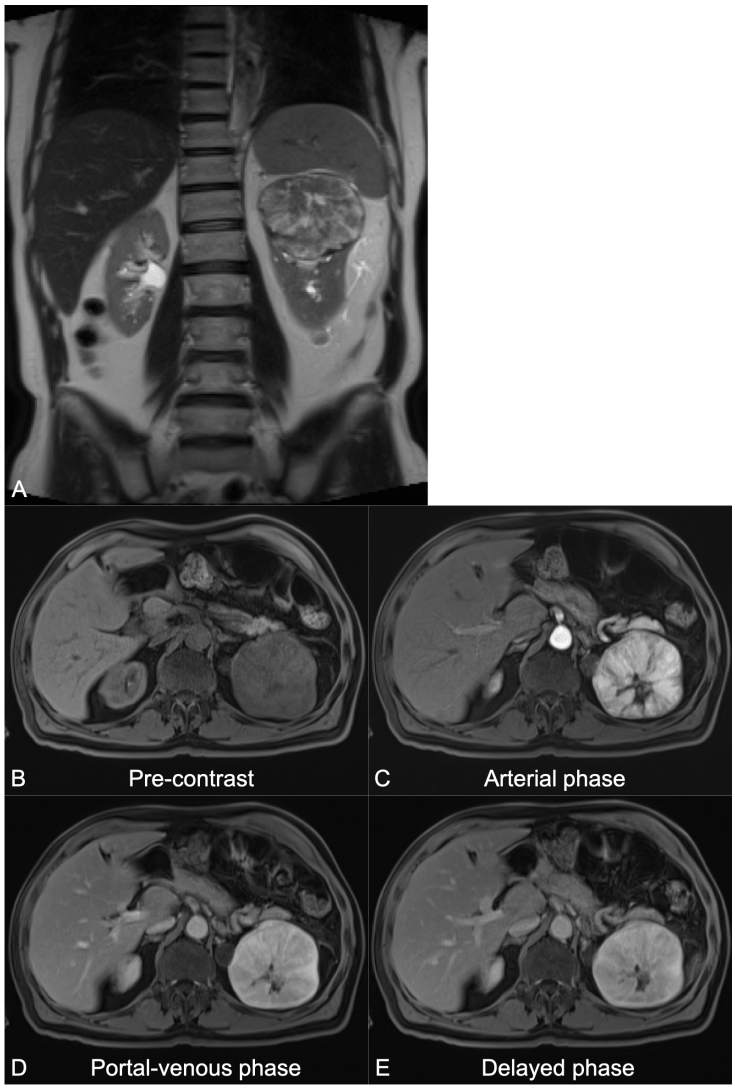

Figure 2. MRI with and without contrast of the abdomen and pelvis showing a suspected renal oncocytoma in the upper pole of the left kidney. (A) Coronal T2-weighted image; **(B)** Pre-contrast axial T1-weighted image; **(C)** Arterial phase (18 second post-contrast) axial T1-weighted image; **(D)** Portal-venous phase (2 minute post-contrast) axial T1-weighted image; **(E)** Delayed phase (5 minute post-contrast) axial T1-weighted image.

referral for management with consideration for biopsy. Urology was consulted and image-guided biopsy of the lesion for pathological diagnosis was recommended.

An ultrasound-guided left renal biopsy was performed and four kidney core samples were obtained and sent for pathologic diagnosis. On immunohistochemistry, the tumour showed negative CK7 staining and positive CD117 staining. The final diagnosis of the left kidney biopsy on the pathology report was an oncocytic renal neoplasm, favoring oncocytoma. The case was managed conservatively with reassessment of interval stability on his bi-annual MR surveillance for uveal melanoma.

We illustrated the previously proposed diagnostic algorithm using 99mTc-sestamibi SPECT/CT for differentiating benign versus malignant 1–4 cm renal masses in the context of the ACR guidelines for completely characterized solid renal masses without fat. It should be noted that this proposal is based on a single systematic review and meta-analysis consisting of 4 studies and 56 total patients. Validation of these results requires a larger sample size, and as a result, this has not been implemented in ACR guidelines. Hence, there is no current case managed using 99mTc-sestamibi SPECT/CT for active surveillance. However, we do present a case with classic features for a renal oncocytoma that when applied to the combined diagnostic algorithm, is appropriately directed toward referral with consideration for biopsy. If the proposed combined diagnostic algorithm is validated, a renal mass showing classic imaging features such as shown in our case but smaller and measuring 1-4 cm could be directed toward 99mTc-sestamibi SPECT/CT for further assessment. Early research (*3,4*) suggests that incorporating 99mTc-sestamibi SPECT/CT in assessing suspected renal oncocytomas could maintain high sensitivity and specificity in differentiating benign versus malignant renal lesions while reducing unnecessary invasive procedures.

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