



## Accurate lesion localisation facilitates nephron sparing surgery in reninoma patients: case report and discussion

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### ABSTRACT

A 21-year-old female was referred with a suspected juxtaglomerular cell tumour (reninoma) in the superior pole of the left kidney. She underwent renal biopsy and renal vein sampling (RVS) to confirm the diagnosis. Following an uncomplicated laparoscopic partial nephrectomy, antihypertensive medications were ceased. Histopathology confirmed the diagnosis. Reninoma is a rare but reversible cause of secondary hypertension and should be considered along with primary hyperaldosteronism and pheochromocytoma when investigating hypertension in a young person. The subtle appearance of reninoma on imaging can necessitate other investigations to confirm the diagnosis. Definitive localisation is essential to prevent unnecessary loss of nephrons.

### 1. Introduction

Reninoma are slow-growing renal tumours with low metastatic and recurrent potential. Around 100 reninoma have been identified since the 1950s(1). Typically occurring in patients under 30 years, small lesions can secrete renin resulting in hypertension. Lesion size and rarity has frequently resulted in delayed diagnosis; reninoma are easily overlooked on imaging. Young patients may be managed for years with antihypertensives prior to discovery of the underlying diagnosis.<sup>1</sup> Renal vein sampling (RVS) and renal biopsy (RB) are useful diagnostic investigations.<sup>2</sup> Surgical resection is an effective cure for reninoma and accompanying consequences of renin hypersecretion.<sup>2,3</sup> Laparoscopic, nephron sparing surgery yields favourable outcomes for these young patients.

### 2. Case presentation

A 21-year-old female with no relevant family or medical history was referred to urological services for management of suspected juxtaglomerular tumour. Hypertension had been identified incidentally at age 15 during routine primary-care evaluation prior to commencing an oral contraceptive. She was asymptomatic and renal ultrasound showed no vascular abnormalities. Due to her age, the practitioner was reluctant to commence antihypertensives. However, ongoing asymptomatic

hypertension (165/110mmHg) prompted further investigation three years later. Elevated serum aldosterone and renin were noted, however MRI was unremarkable, so the patient was commenced on antihypertensives. Two years later, the patient advocated for further investigations after experiencing adverse antihypertensive effects including fainting and hypokalaemia (K<sup>+</sup> 2.5mmol/L). Contrast CT scan now showed a 13mm, well-circumscribed, partly exophytic, minimally enhancing cortical lesion in the left kidney's superior pole, also now evident on repeated MRI. Renal vein and subsegmental venous sampling confirmed increased renin secretion compared with mid- and lower poles and contralateral kidney. Referral was made to urological services. RB was consistent with reninoma. Patient and health system factors delayed definitive management; CT repeated preoperatively showed minimal interval growth (6mm in 3 years) with no evidence of metastatic disease. Pre-operatively, intermittent hypokalaemia and poorly controlled hypertension (systolic 190 mmHg) were managed with multimodal antihypertensive therapy and potassium replacement. Renal function was unaffected. Laparoscopic partial nephrectomy was performed ten years after hypertension recorded onset. Tumour margins were identified using intraoperative ultrasonography (IUS). 18 minutes of warm ischaemia time were recorded; bleeding was negligible. Recovery was uncomplicated. Antihypertensives were not required post-operatively; this has been maintained for over 12 months of follow-up.

*Abbreviations:* RVS- renal-vein sampling, MRI-magnetic resonance imaging.

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**Fig. 1.** Macroscopic partial nephrectomy specimen showing a circumscribed solid tumour.

### 3. Pathology

A well circumscribed 18mm soft, brown tumour was interrogated microscopically (Fig. 1). Epithelioid cells arranged in nests and islands were associated with prominent vasculature and thick-walled hyalinised vessels. Cell clusters were also seen around extracellular deposits of densely eosinophilic hyaline matrix. Cells had uniformly round or ovoid nuclei with fine chromatin, occasional nucleoli and moderate eosinophilic cytoplasm within indistinct cell borders. Focal papillary architecture lined by cuboidal epithelium was seen. Mitotic activity was not identified. Immunohistochemistry showed strong diffuse staining for CD34 and vimentin. Immunostaining for CKIT highlighted numerous mast cells but was negative in tumour cells. Immunostaining for synaptophysin showed weak para-nuclear dot-like staining of uncertain

significance and was negative for AE1/AE3 (Fig. 2). Staining for smooth muscle actin showed focal amounts in less than 10% of tumour cells. Tumour electron micrographs demonstrated characteristic rhomboid renin photogranules (Fig. 3).<sup>4</sup> Juxtaglomerular cell tumour was diagnosed from this characteristic pathology and clinical history.

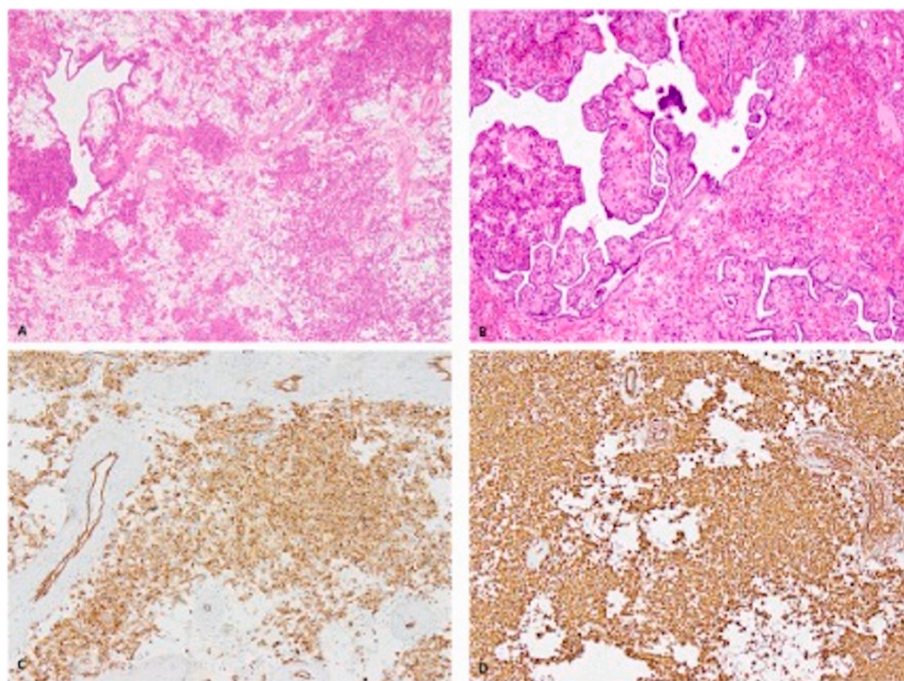
### 4. Discussion

Reninoma is a rare renal cortical tumour. Small lesions may be functionally significant; average tumour size is just 3cm (range 0.2–9cm).<sup>1</sup> High clinical suspicion is important as clinically significant lesions can be easily overlooked on imaging.<sup>1,3</sup> Treatment and diagnostic delays are common in the literature and relevant to this case. 86 patients had documented hypertension on average 47 months prior to reninoma diagnosis (range 0–23 years).<sup>1</sup>

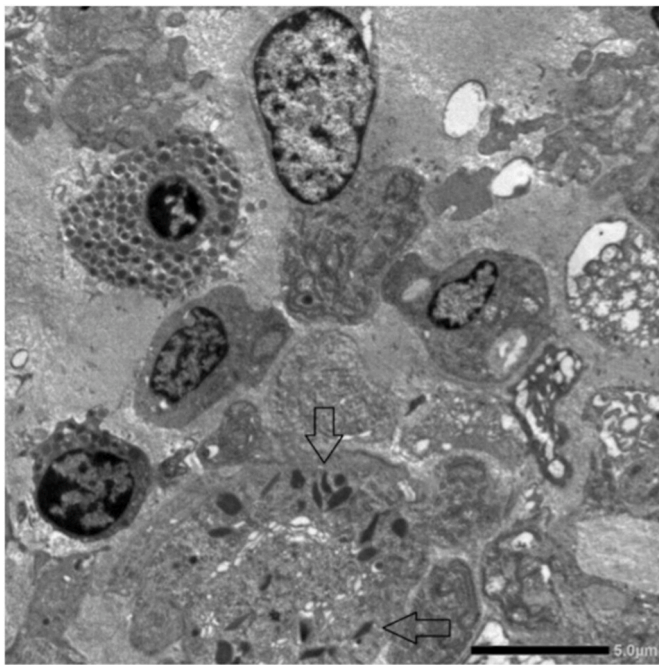
Importantly, delayed treatment has not been associated with impaired blood pressure regulation post-operatively, recurrence or malignant potential, although the latter has been reported in a small number of patients with large tumours (>9cm).<sup>5</sup> Benefits of timely diagnosis and management are clear in pregnant patients and for long-term cardiovascular health.

In our experience, both RVS and RB contributed to preoperative planning, diagnosis and tumour localisation. RVS can reliably localise functional reninoma when lesions are too small to confidently identify on imaging.<sup>3</sup> However, low perceived diagnostic value of RVS has been cited as a barrier to performing the procedure, which can be affected by antihypertensives, recumbency and dietary factors(3). Protocols are infrequently reported in the literature, making the true diagnostic value difficult to assess. RB was also uncommonly conducted. Despite the frequent cortical location of reninoma, non-diagnostic results can occur following image-guided biopsies due to small lesion size.

Diagnosis based on clinical history, imaging and RVS performed to a high standard can negate the need for biopsy. However, RB is readily available, while RVS is best performed at experienced centres and requires meticulous planning and patient compliance to achieve diagnostic results. One or both can be utilised depending on patient factors,



**Fig. 2.** A-D The tumour demonstrated the classical histological features of a juxtaglomerular cell tumour. A [H&E x40] Tumour cells arranged in nests and islands with surrounding stromal oedema and hyalinised vasculature; B [H&E, x100] Focal papillary architecture; C [x 100] CD34 immunostaining shows diffuse positivity in the lesional cells; D [x100] Vimentin immunostaining showing diffuse positivity in the lesional cells.



**Fig. 3.** Electron micrograph [x1500 magnification] demonstrating a tumour cell containing rhomboid shaped renin photogranules (arrows).

resources and clinician experience.

Accurate diagnosis and localisation of reninoma is extremely important to facilitate nephron-sparing surgery. Reninoma are frequently amenable to this treatment due to their small size and cortical location. Despite this, 45% of patients in a series of 89 cases were managed with radical nephrectomy. 40% (n = 36) of patients had partial nephrectomy; just one was performed laparoscopically.<sup>1</sup> Nephron sparing surgery is ideal for young patients and can be increasingly performed as laparoscopic techniques and access to robotics improve. Operative time, blood-loss and ischaemia times in the literature were comparable to our case. We used IUS to confirm excision margins due to small lesion size. Nephron sparing surgery is most beneficial in young

patients for whom a radical nephrectomy may carry long term consequences.

## 5. Conclusion

Functional reninoma can be subtle on imaging. Young patients benefit from careful lesion localisation; one or both of RVS and RB should be considered based on patient, lesion and health system factors. Preventable loss of nephrons resulting from poor surgical planning is likely to have long term implications. Delaying surgery to facilitate nephron-sparing surgery is not associated with complications if the effects of renin hypersecretion are appropriately managed. Reninoma can be successfully treated with nephron-sparing minimally invasive surgery.

## Consent

Written consent was obtained from the patient.

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## Declaration of competing interest

The authors have none to declare.

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