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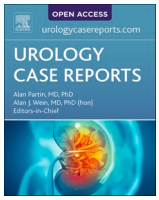

Oncology

# Renal cell carcinoma metastasis without a primary: A case report

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ABSTRACT

In Australia, approximately 3 % of all cancers diagnosed each year are renal cancers. Renal Cell Carcinoma (RCC) represents 90 % of all primary renal malignancies. RCC are slow growing and often asymptomatic, thus are often found incidentally.

Here we present the case of a 76-year-old male who was found to have a metastatic RCC in a para-aortic lymph node with no primary lesion. He underwent a retroperitoneal lymphadenectomy and 15 months after the surgery, has had no signs of primary tumours or metastasis.

This case reports on a rare instance of metastatic RCC without an identified primary renal malignancy.

## 1. Background

Kidney cancers compromise 3 % of all annual cancer diagnoses in Australia.[1] Renal Cell Carcinomas (RCC) is the most common sub-type of kidney cancers RCC's commonly metastasise to lung, lymph nodes, bone, liver and brain 2. They are twice as more common in males and most commonly occurs at 60–80 years. With the increasing availability and advances in imaging technology a higher number of RCCs and their sequelae are being detected earlier with many likely as an incidental finding. The presence of biopsy confirmed RCC without a primary renal lesion is an unusual presentation.

## 2. Case presentation

A 78-year-old gentleman with known hepatocellular carcinoma underwent regular annual surveillance with ultrasound. In March 2022 an abdominal ultrasound demonstrated a new 8mm hypoechoic liver lesion in segment 5. A subsequent computed tomography (CT) abdomen and pelvis with contrast, did not identify the liver lesion in question, however a secondary finding of a prominent 25 × 29mm left para-aortic lymph node mass was identified which was not seen in a CT scan conducted 2 years prior (Fig. 1A). A whole body FDG Positron Emission Tomography (PET) demonstrated avid uptake (5.8 SUV) isolated to the retroperitoneal mass (Fig. 1B), with no suggestion of site of either a primary or other metastatic disease elsewhere in the body, in particular the genitourinary tract.

His past medical history includes hypertension, type 2 diabetes, ischaemic heart disease, atrial fibrillation. He has had previous low grade transitional cell carcinoma of his bladder 20 years prior for which he underwent 10 years of surveillance with no recurrence. He is an ex-smoker, quitting over 20 years prior to the current diagnosis.

A core biopsy of the retroperitoneal mass was suggestive of a metastatic carcinoma, with an immunohistochemistry profile, in particular demonstrating positive staining for paired box gene 8 (PAX8), raising the suspicion of a renal origin. Following a multi-disciplinary meeting, the patient underwent flexible cystoscopy and laparoscopic retroperitoneal lymphadenectomy. Flexible cystoscopy showed no concerns of urothelial malignancy and the nodal mass with removed with identification of some desmoplastic reaction surrounding the mass.

Pathology of the resected specimen confirmed a clear cell RCC. The excised gross specimen was 46 × 31 × 20 mm and weighed 11g. It contained a single large lymph node, 32 × 17 × 27 mm within which was a centrally placed tumour, with clear margins. Microscopic examination revealed malignant cells, with large pleomorphic nuclei and clear cytoplasm (Fig. 2A). Immunohistochemical staining was positive for CK20, CD10, AMACR, PAX8, CAIX and Ck8/18, was consistent with RCC (Fig. 2B). Negative staining for GATA3, NKX3.1 and germ cell tumour markers excluded urinary, prostate and testicular primary. Negative staining for TTF-1 excluded thyroid carcinoma.

One month after the resection and pathology report, a repeat PSMA PET was undertaken which once again demonstrated no recurrence and no residual PSMA avid disease. He remains on close surveillance 3 monthly with no signs of recurrence at 15 months following his resection.

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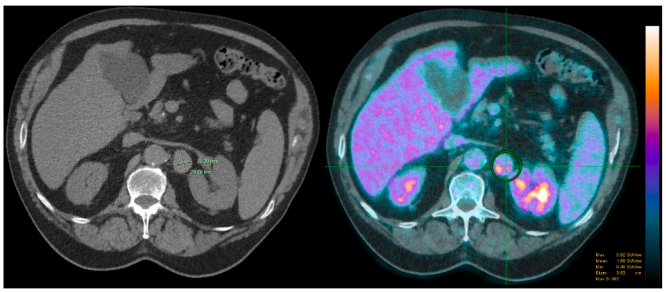

**Fig. 1.** Computed tomography (CT) abdomen and pelvis demonstrating a 25 × 19mm left para-aortic lymph node (A). FDG Positron Emission Tomography (PET) highlighting a 5.8 SUV max para-aortic lymph node.

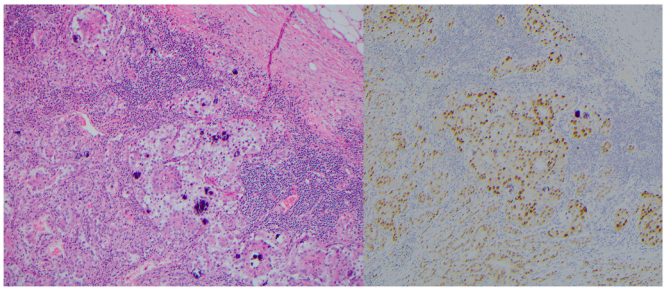

**Fig. 2.** Immunohistochemical staining of the resected left para-aortic lymph node. (A) Haematoxylin & eosin staining demonstrating malignant tumour cell invasion with large pleomorphic nuclei, prominent nucleoli and moderate amount of eosinophilic to clear cytoplasm. (B) Resected sample demonstrating positive PAX8 staining.

## 3. Discussion

Metastatic RCC without any evidence of a primary lesion is exceedingly rare with only a handful of case reports and series. Approximately 25 % of patients are diagnosed with metastatic RCC at presentation, with the most common sites being lung, lymph nodes bone liver, adrenal and brain [2,3]. Incidental cancer findings are becoming increasingly common with rapid technological advances in imaging modalities and easier patient access to imaging. A cross-sectional study in England, found an incidental detection rate of 4 % for all cancers and 13 % for renal cancers.[4] Similar to the case presented here, the patients in their study were asymptomatic of the cancer, undergoing imaging for monitoring of a pre-existing condition or as part pre-elective surgery workup for unrelated indication.

The literature only reports 8 patients with metastatic RCC without a primary (see Table 1). 3 patients had cutaneous metastases,[5–7] 3 patients to bone,[8,9] 1 patient to a supraclavicular lymph node.[10] Similar to the case presented here, only 1 previous patient had metastases to their retroperitoneum,[11] however they were symptomatic with abdominal pain. 7 of these 8 patients are alive and remain free of a primary kidney lesion at 6–20 months. One patient unfortunately developed bilateral lung nodules and succumbed 8 months after initial diagnosis.[8] The patients were either managed with surgical excision or a combination of radiation and chemotherapy.

Retroperitoneal masses have a wide range of differentials, other than a secondary metastatic process. Primary retroperitoneal masses can be neoplastic such as lymphoma, lymphangioma, mesothelioma, leiomyosarcoma; or non-neoplastic conditions such as retroperitoneal fibrosis or benign cysts.[12,13] In the case presented here, a biopsy of the retroperitoneal mass was organised by the patient's gastroenterologist given his history of previous HCC and FDG avidity. Immunohistochemical (IHC) staining is then crucial in determining a primary source and histological sub-type to guide choice of further therapy. Previously reported cases of metastases, similar to this case report, also commonly stained positively for CD10, Vimentin, cytokeratin (AE1/AE3) and PAX-8, whilst staining negatively for TTF-1, CK7. These IHC staining patterns are consistent with a diagnosis of metastatic RCC. CK20 positivity distinguishes RCC from oncocytoma, whilst CK7, CAIX and AMACR help to further classify the subtype of RCC..[14–18]

Metastatic RCC without primary presents a therapeutic dilemma for urologists, with only a few case reports and series in the literature. Diagnosis is hinged on obtaining tissue and IHC staining of the metastases. A number of theories have been postulated to explain the development of metastatic disease in the absence of a primary tumour. One possible theory is that the primary renal tumour is too small in size and/or volume to be detected. However, in this case this would be highly unlikely as there was no PET avid renal lesion. A rare phenomenon is

**Table 1**
Summary of renal cell carcinoma metastasis without primary. M: Male; F: Female; NR: not reported; HCC: hepatocellular carcinoma.

| Case | Age | Sex | Metastasis | Previous cancer history | Immunohistochemistry | Treatment | Recurrence |
|---|---|---|---|---|---|---|---|
| Bhatia et al.[6] | 63 | M | Nose | NR | Pos: CD10, vimentin<br>Neg: CK7 | Resection | None at 12 months. Alive. |
| Wayne et al.[7] | 61 | F | Forearm | NR | Pos: CD10, cytokeratin (AE1/AE3), PNRA, vimentin | Resection | Pancreas (9 months) and parotid gland (15 months). None since. Alive. |
| Choi et al.[11] | 69 | M | Supraclavicular lymph node | NR | Pos: pancytokeratin, vimentin, CD10<br>Neg: TTF-1, CK7, CK20, HSA | Radiotherapy and chemotherapy (sunitinib) | None at 20 months. Alive. |
| Kumar et al.[9] | 70 | M | Bone (scapula, ribs, pelvis) | NR | Pos: CAM5.2, vimentin, CD10 | Chemotherapy (sunitinib) | None at 18 months. Alive. |
| Kumar et al.[9] | 69 | F | Bone (knee) | NR | Pos: EMA, vimentin, CD10<br>Neg: CK7, CK20, calretinin, CD34, S100 and TTF-1 | Chemotherapy (sunitinib) – below knee amputation offered | Bilateral lung.<br>Succumbed in 8 months |
| Walton et al.[8] | 52 | M | Forearm | NR | Pos: CD10, PAX-8 | Resection | None at 27 months. Alive. |
| Petrinec et al.[12] | 50 | F | Retroperitoneum | None | Pos: cytokeratin (AE1/AE3), PAX-8, TFE3 | Resection and left nephrectomy | None at 6 months. Alive. |
| Hlaing et al.[10] | 70 | M | Bone (spine, ribs, pelvis) | None | Pos: cytokeratin (AE1/AE3), CD10, PAX-8<br>Neg: CK7, P40, TTF-1 | Radiation | NR |
| Razi et al. | 76 | M | Para-aortic lymph node | HCC, Bladder cancer | Pos: CK20, CD10, AMACR, PAX8, CAIX and Ck8/18<br>Neg: GATA3, NKX3.1, germ cell markers, TTF-1 | Laparoscopic Retroperitoneal lymphadenectomy | None at 7 months. Alive. |

Ectopic Immature Renal Tissue (EIRT) which is metanephric nephrogenic rests with a potential for malignant transformation.[19,20] A review of EIRT literature in 2012 reported that most cases were in the lumbar/sacral region, 11 % cases were reported to occur in the retroperitoneum and 77 % were under the age of 11.[20] It could be possible for the patient in this case have tumour in a nephrogenic rest which has now been removed.

## 4. Conclusions

In summary, this case adds to the current sparse literature of metastatic RCC without an identifiable primary. RCC's can metastasis to a wide range of local and distant sites, which can lay dormant for many years and most cases will be discovered incidentally. Due to this unpredictable nature and underlying histopathological RCC sub-type, the development of a robust standardised treatment and follow up plan is difficult. The literature currently reports treatment with excision and/or radiotherapy or chemotherapy. Patients with metastatic RCC without primary tumours should undergo prompt tissue diagnoses and a treatment and follow up plan determine with a multi-disciplinary team.

## Ethics approval and consent to participate

Ethics was not required for this case report.

## Informed consent

Written and informed consent was obtained from the patient for the publication.

## Consent for publication

Written informed consent was obtained by the patient for the publication of their clinical details and clinical images.

## Availability of data and material

All data generated or analysed during this study are included in this published article.

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## CRediT authorship contribution statement

**Basil Razi:** Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – original draft, Writing – review & editing, Visualization. **Dane Cole-Clark:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing, Validation, Visualization. **Duncan Self:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – review & editing, Validation, Visualization, Writing – original draft. **Raha Madadi Ghahan:** Data curation, Formal analysis, Investigation, Methodology, Resources, Writing – original draft, Writing – review & editing. **Edward Latif:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

## Declaration of competing interest

The authors declare no conflict of interest.

## Acknowledgements

Not applicable.

## Abbreviations

| | |
|---|---|
| CT | Computed Tomography |
| EIRT | Ectopic Immature Renal Tissue |
| PET | Positron Emission Tomography |
| RCC | Renal Cell Carcinoma |

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