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Pathological staging of renal cell carcinoma: a review of 300 consecutive cases with emphasis on retrograde venous invasion

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Aims

- Pathological staging of renal cell carcinoma (RCC) can be challenging compared to other cancer types, as invasion often manifests as finger-like protrusions into vascular spaces or renal sinus tissue.
- Although prior studies have shown larger tumour size to be correlated highly with renal sinus invasion, prospective data on evaluating pathological stage are limited. We evaluated a large series reported by one urological pathologist.

Methods :

- Three hundred consecutive specimens were reviewed. Tumors larger than 5 cm were routinely sampled extensively or grossly re-reviewed when no extrarenal extension was identified on initial examination.
- Apparent multifocal disease was assessed critically for intravascular spread.

- Retrograde venous invasion was defined as ‘rounded or elongated nodules of tumour separated from the primary tumour by uninvolved renal parenchyma, in locations that conforms to the normal venous outflow of the kidney’, as described by Bonsib.
- As this includes, by definition, involvement of at least segmental vein branches, all such tumors were at least pT3a. The presence of retrograde venous invasion was confirmed by a second genitourinary pathologist

Results

- Retrograde venous invasion was reported in 15 of 300 (5%) cases, 13 of 15 of which were clear cell RCC. Of a total of 163 specimens with clear cell histology, only five of 34 (15%) tumors 7 cm or larger were reported as pT2, all of which had an explanatory comment indicating the absence of definitive extrarenal spread. In contrast, 15 of 20 (75%) pT2 tumors were non-clear cell histology (papillary, chromophobe and translocation-associated).
- Comparing pT3a or higher tumors, the median tumour size in cases with retrograde venous invasion was 8.0 cm, compared to 6.2 cm in cases without retrograde venous invasion ($P = 0.005$).

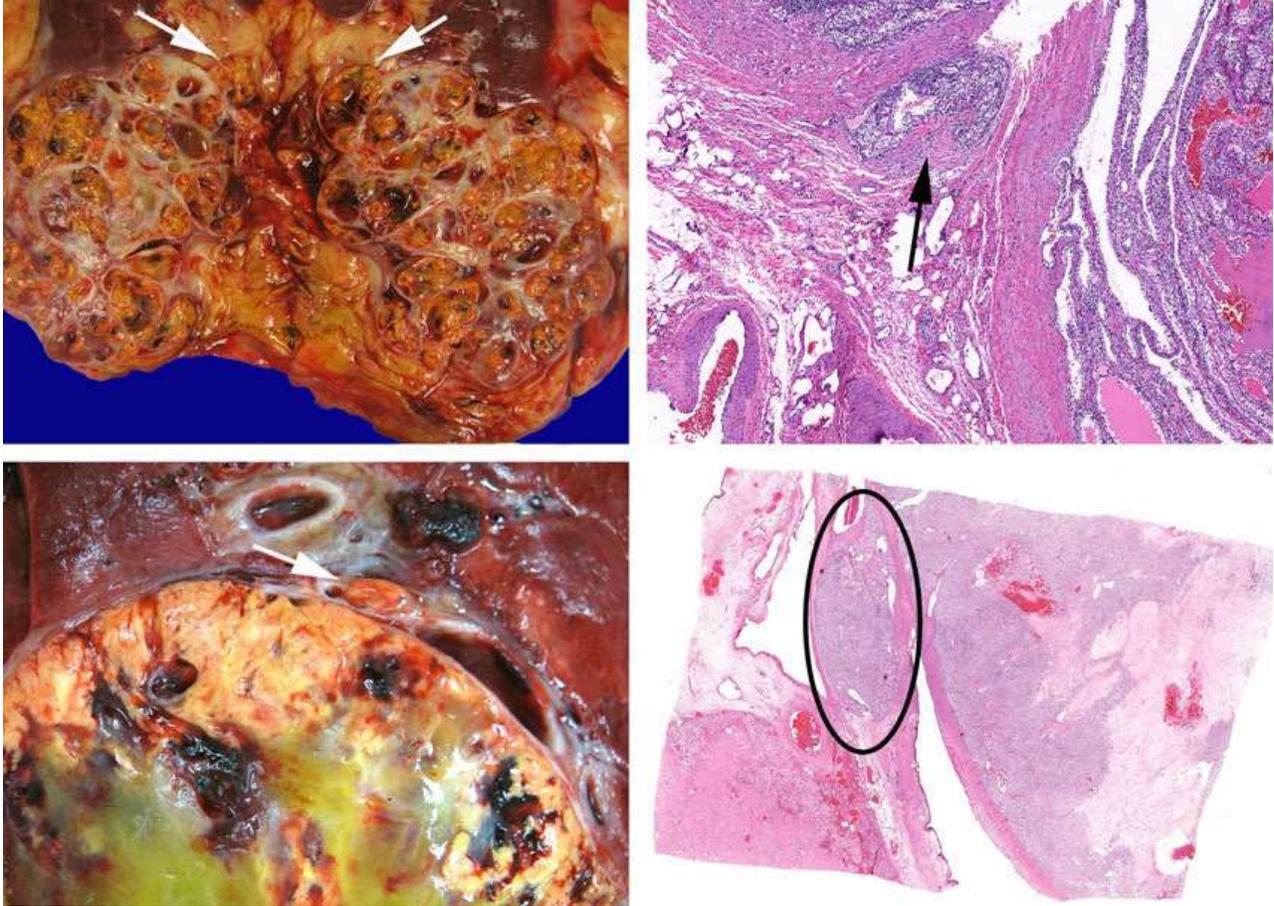


Figure 1. Staging scenarios in renal cell carcinoma. A, This clear cell renal cell carcinoma tumour is very large and multinodular, with multiple outpouchings that bulge into the renal sinus (arrows). B, Histological confirmation of renal sinus invasion was difficult, but interpreted as focally present due to tumour extending beyond a fibromuscular pseudocapsule into the loose fibrovascular tissue of the renal sinus. C, This clear cell renal cell carcinoma demonstrates a gross outpouching that deviates from the spherical shape of the rest of the tumour, which was confirmed to be early segmental vein branch invasion histologically (B).

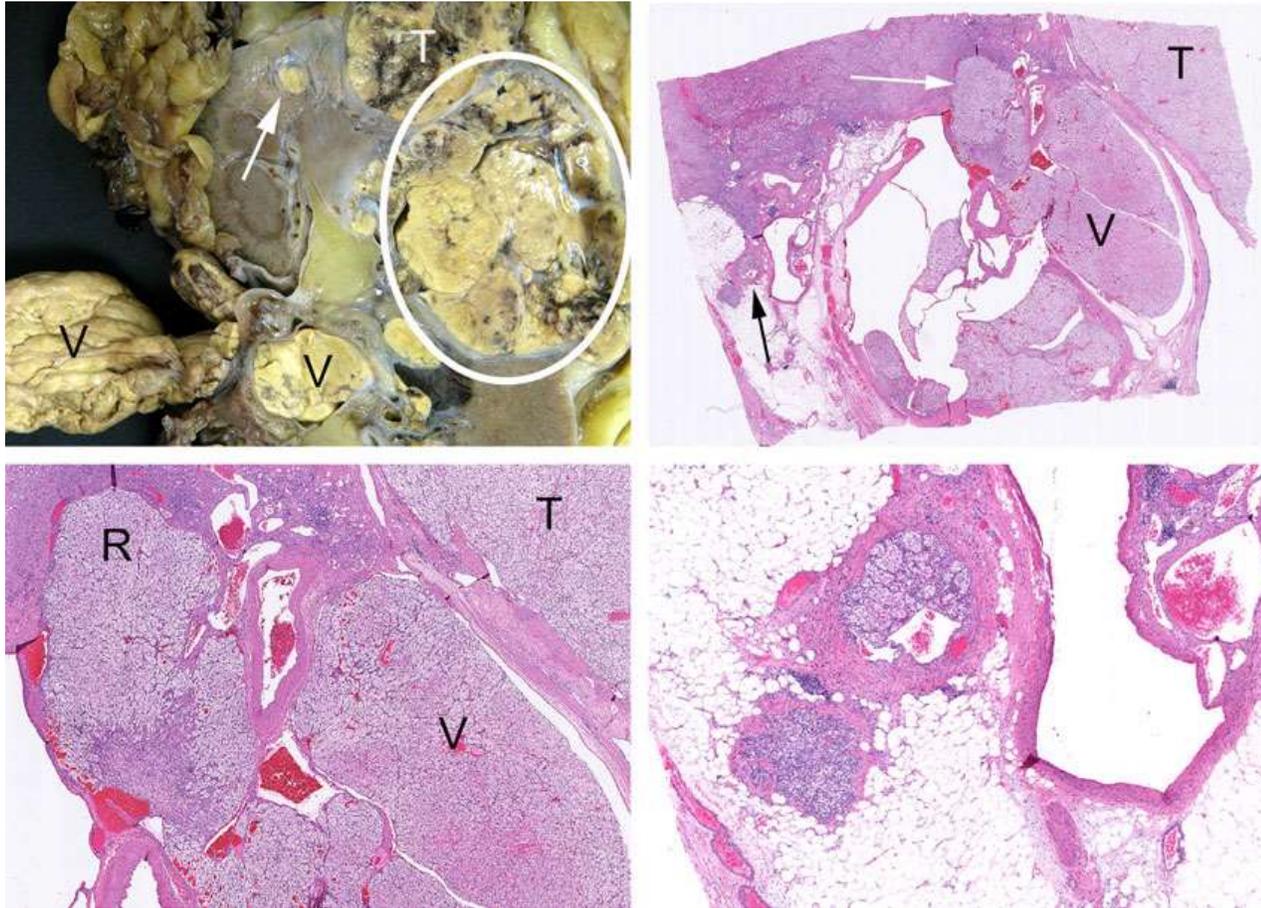


Figure 2. Retrograde venous invasion: A, This gross appearance demonstrates a primary tumour (T) with main renal vein invasion (V) and nodules of retrograde venous invasion that appear as 'satellite' lesions (arrow). A large confluent mass area in the mid-kidney (circled) is difficult to discern as confluent venous growth versus primary tumour. B, Histology of the same tumour demonstrates the primary tumour (T) with sinus vein invasion (V) and early retrograde extension backwards into the kidney (white arrow). Satellite nodules of intravascular spread are also present in the renal sinus (black arrow). C, Higher magnification of the same area from panel B shows the main tumour (T), vein involvement (V) and beginning of retrograde spread (R). D, Higher magnification of the renal sinus area from B shows the intravascular sinus involvement.

Table 3. Univariable analysis showing the clinicopathological variables associated with the presence of retrograde venous invasion

| Variable | Retrograde venous invasion absent (<i>n</i> = 285) | Retrograde venous invasion present (<i>n</i> = 15) | <i>P</i> -value |
|---|---|---|-----------------|
| Male gender, <i>n</i> (%) | 188 (66) | 9 (60) | 0.781 |
| Age, years, median (IQR) | 62 (54.5–70.0) | 70 (63.0–73.0) | 0.012 |
| Tumour size, cm, Median (IQR) | 3.8 (2.5–5.8) | 8.0 (6.4–10.0) | < 0.001 |
| Histology, <i>n</i> (%) | | | |
| Clear cell | 152 (53) | 13 (87) | 0.015 |
| Non-clear cell | 133 (47) | 2 (13) | |
| ISUP modified nuclear grade, <i>n</i> (%) | | | |
| Grade 1 | 7 (3) | 0 (0) | < 0.001 |
| Grade 2 | 122 (48) | 0 (0) | |
| Grade 3 | 104 (41) | 7 (50) | |
| Grade 4 | 19 (8) | 7 (50) | |
| Not applicable (chromophobe/other) | 33 (11) | 1 (< 1) | |

IQR, interquartile range.

Limitations

- Although this is one of the larger studies emphasizing pathological classification of renal cancer stage categories, a potential limitation is that all were reported by one pathologist, which may be a source of subjective bias.
- At the same time, this might also be considered a strength of the study, as the interpretation is subsequently more uniform than reports from multiple pathologists, who might have interpreted the same findings differently.
- This was also mitigated partly by second review by another genitourinary pathologist to confirm retrograde vein invasion

Conclusion

- Our findings support that retrograde venous invasion should be considered carefully before diagnosing multifocal clear cell RCC, which is rare in the sporadic setting.
- In the absence of vascular invasion, multifocal clear cell papillary RCC can be a mimic.
- pT2 occurs more frequently with non-clear cell histology (particularly papillary or chromophobe RCC).
- This study adds to the existing knowledge regarding pathological staging of renal cell carcinoma, highlighting that multiple tumors of clear cell histology are quite rare in the sporadic setting and this interpretation should be approached with caution, especially if any single tumour is large or multinodular, raising the possibility of intravenous spread.