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Retrograde venous invasion in renal cell carcinoma: a gross diagnosis

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Abstract

Renal cell carcinoma, notably clear cell renal cell carcinoma in particular, show remarkable predisposition for intravenous growth. Retrograde venous invasion results in intravascular emboli in renal sinus and intrarenal veins, and nodules in renal parenchyma (after extravascular spread). In our experience, we observed this phenomenon in five cases out of 204 renal cell tumors: four in clear cell renal cell carcinomas (4/166 or 2.4%) and 12.5% of those clear cell carcinomas with major renal vein invasion (4/34 or 12.5%). Since it is a recently described phenomenon, easily identifiable a bisected specimen, we believe it would be valuable to show our experience in recognizing and reporting the frequency of this finding in our practice.

Keywords Carcinoma, cell carcinoma, Pathology, Kidney Neoplasms, Renal veins

Background

A seminal work by Bonsib and Bhalodia in 2011 characterized the grossly identifiable pattern of retrograde venous invasion of renal cell carcinoma (Bonsib and Bhalodia 2011). Although previously described in case report (Hecht et al. 2010; Bonsib 2007), the authors clearly demonstrated the process as primarily intravascular and a retrograde pattern of dissemination. At gross examination, nodules between renal pyramids and in the corticomedullar junction reflect the involvement of interlobar and arcuate veins, respectively. Invariably, this pattern of dissemination is associated with invasion of the main renal vein invasion or at least of a renal sinus vein. Since it is a recently described phenomenon, easily identifiable a bisected specimen, we believe it would be valuable to show our experience in recognizing and reporting the frequency of this finding in our practice.

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Retrograde venous invasion results in intravascular emboli in renal sinus and intrarenal veins, and nodules in renal parenchyma (after extravascular spread). As recommended by International Society of Urologic Pathology, intravascular spread should not be considered for tumor size measurement (Trpkov et al. 2013). In addition, these nodules (intrarenal metastases) along renal parenchyma are not considered multifocality. It is important to distinguish multifocal tumors from a peculiar type of intravenous dissemination of one tumor. Multifocality may show different types of renal carcinoma and may infer familial predisposition in some instances. Proper recognition of retrograde venous invasion may avoid misinterpretation as multifocality or a larger tumor (Taneja et al. 2018).

Methods

We report our experience from January 2017 to November 2022 in as single private institution (204 renal resection specimens for renal cell tumor). Since all cases had the gross specimens evaluated by the same experienced uropathologist, we were able to estimate the proportion of retrograde venous invasion is this case series. One additional figure illustrates a from other academic institution where the first author works. Since not all cases

from that institution were reviewed by the same author of this work, we did not estimate the frequency of retrograde venous invasion in this institution.

Results

In our experience from January 2017 to November 2022 in a private Pathology Laboratory, we examined 204 renal resection specimens for renal cell tumor being the most common: clear cell carcinoma (166), papillary carcinoma (38), chromophobe carcinoma (36), clear cell papillary renal cell tumor (34) and oncocytoma (28). Retrograde venous invasion was observed in five cases: four in clear cell carcinoma (2.4%) and one in unclassified renal cell carcinoma (one of eight, 12.5%). Thirty-four clear cell carcinomas had pT3a disease due to renal vein invasion or its branches. Therefore, in the group of patients with clear cell carcinoma and documented major vein invasion, the rate of retrograde venous invasion was 4/34 (12%). One figure (Fig. 6) is an illustrative case from other academic institution where the first author works.

Case description

Case 1: A 47-year-old male patient with 6.9 cm clear cell carcinoma in the left kidney (Fig. 1). One year before, he removed the contralateral kidney due to a clear cell carcinoma (two independent foci). At 2 months of follow-up, the patient is alive without signs of disease recurrence.

Case 2: A 58-year-old male sought medical assistance due to weight loss and abdominal pain. Imaging studies showed a 10-cm kidney mass. The resected kidney showed a 10-cm clear cell carcinoma (Fig. 2). Immunohistochemistry showed diffuse and strong membranous expression of carbonic anhydrase IX while TFE3 was negative. At 20 months of follow-up, the patient is alive without signs of disease recurrence.

Case 3: A 57-year-old male patient with 6.0-cm kidney tumor incidentally detected by imaging studies. The resected kidney showed a 6-cm clear cell carcinoma (Fig. 3). Immunohistochemistry showed diffuse and strong membranous expression of carbonic anhydrase IX while TFE3 was negative. He developed a metastasis to soft tissue (lumbar region) after 19 months of follow up.

Case 4: A 75-year-old female patient with 4.0-cm kidney tumor incidentally detected by imaging studies. The resected kidney showed a 4-cm clear cell carcinoma (Fig. 4). At 14 months of follow-up, the patient is alive without signs of disease recurrence.

Case 5: A 42-year-old male sought medical attention due to hematuria. Imaging studies detected a large kidney mass. The kidney tumor measured 8 cm (Fig. 5) and

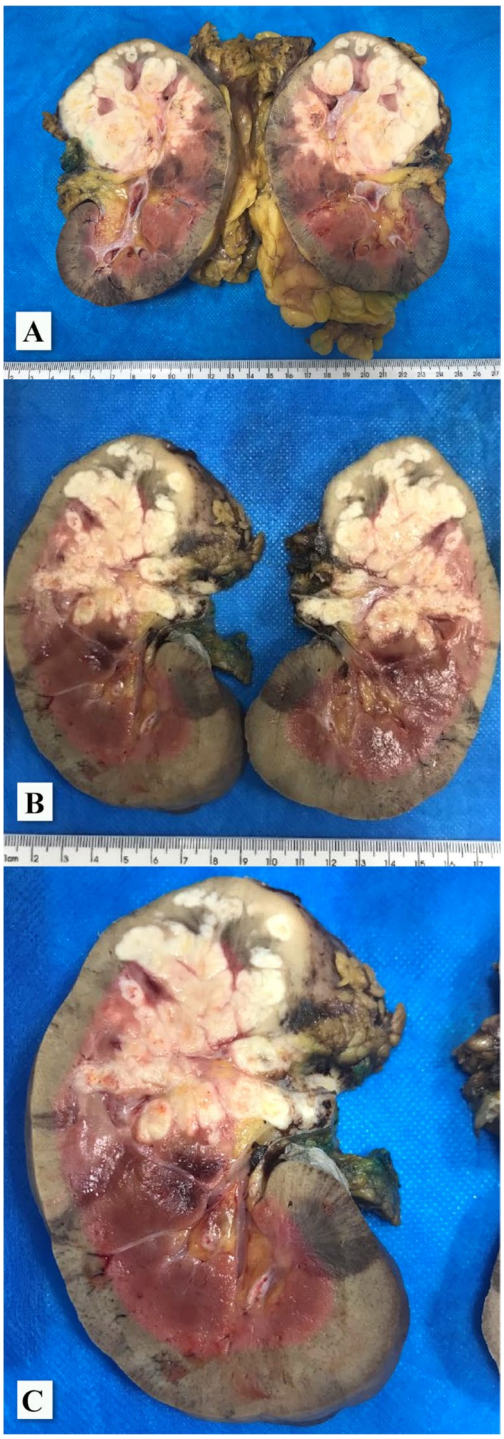

Fig. 1 Case 1. A 47-year-old male patient with clear cell carcinoma. One year before, he removed the contralateral kidney due to a clear cell carcinoma (two independent foci). White small nodules are distributed along the corticomedullar junction in the upper lobe. Invasion of major renal vein is evident in (**B** and **C**)

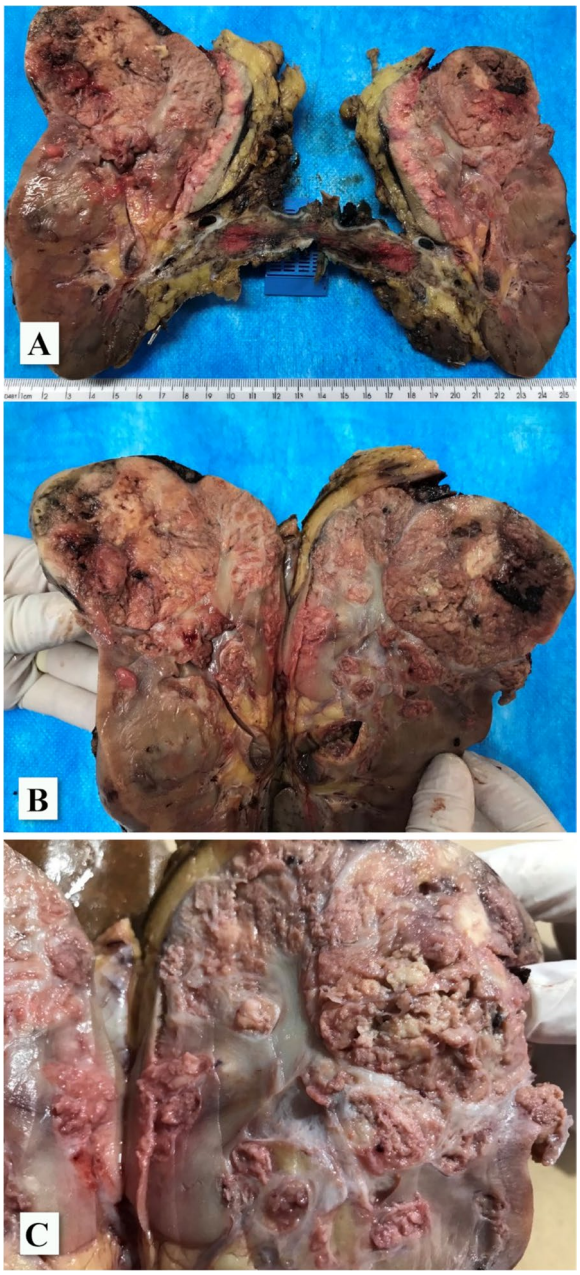

Fig. 2 Case 2. A 58-year-old male patient with clear cell carcinoma. **A** shows obvious invasion of major renal vein. **B** shows a primary tumor in the upper lobe and smaller nodules along corticomedullar junction and between renal pyramids. **C** closer view

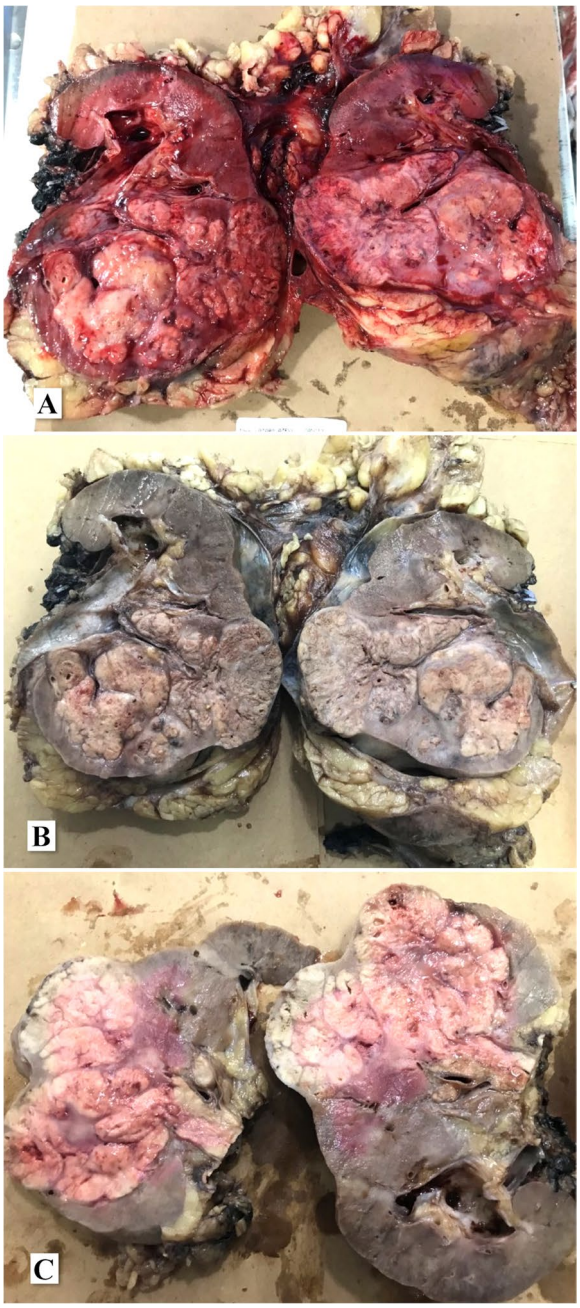

Fig. 3 Case 3. A 57-year-old male patient with clear cell carcinoma. Figure **A** shows a large primary tumor in lower lobe. The bisected kidney show, in each half, obvious invasion of the renal vein. In **B**, the same specimen after fixation shows small nodules along corticomedullar transition. In **C**, cut surface of renal vein invasion that is continuous to a primary tumor. Mid lobes show smaller nodules

was predominantly composed of clear cells but showed different growth patterns and cytology. Tumor cells expressed PAX8 but were negative for cytokeratin 7, carbonic anhydrase IX and TFE3 (by immunohistochemistry). A diagnosis of unclassified renal cell carcinoma was rendered. At 2 months of follow-up, the patient is alive without signs of disease recurrence.

Case 6: A 65-year-old male patient sought medical attention due to hematuria. Imaging studies detected a large kidney mass. The resection specimen showed a 3.5 cm clear cell carcinoma (Fig. 6). He developed pulmonary metastases 18 months after the kidney surgery.

Fig. 4 Case 4. A 75-year-old female patient with clear cell carcinoma. A strikingly hemorrhagic tumor in mid pole. The tumor involves main renal vein, renal sinus veins and satellite nodules are seen in upper and lower lobes along corticomedullar transition and between renal pyramids

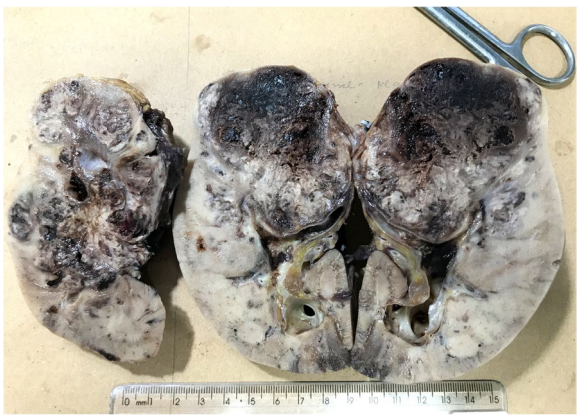

Fig. 5 Case 5. A 42-year-old male patient with an unclassified renal cell carcinoma. The cut surface of a sliced kidney. The slice in the right, shows a tumor in the upper lobe and gross renal invasion. In all sections, small nodules are seen in between renal pyramids

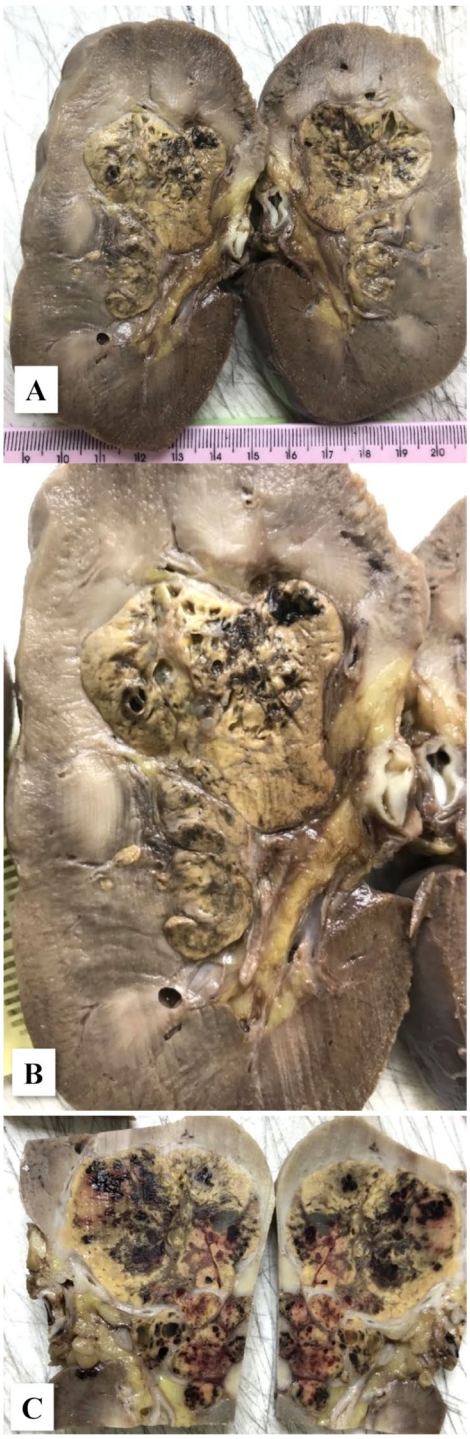

Fig. 6 Case 6. A 65-year-old male patient with clear cell carcinoma. In the bisected kidney, small yellow nodules between renal pyramids are seen in mid-pole (**A** and **B**). All photos show invasion of sinus veins. In **C**, yellow nodules within renal sinus indicate vein invasion

Discussion

Bonsib and Bhalodia identified retrograde venous invasion in 9 of 115 kidney specimens with renal cell carcinoma (8%). Seven of them were of clear cell type (7/72% or 10%) and two were unclassified (Bonsib and Bhalodia 2011). In a recent series of 300 renal cell carcinomas, this

pattern of dissemination was documented in 15 cases (5%) and 13 out of 15 were of clear cell type. The other two cases were one chromophobe and one TFEB-rearranged renal cell carcinoma (Taneja et al. 2018).

Renal cell carcinomas associated with retrograde venous invasion are associated with larger size of primary tumor and higher grade (Taneja et al. 2018).

Since it has been recently described, there is not enough data to support that retrograde venous invasion has prognostic implication among patients who already has tumor staged as pT3a disease due to renal vein invasion. Proper recognition of this finding will surely enhance our ability to measure the prognostic relevance of this pattern of dissemination. Anterograde extension of renal cell carcinomas that invade segmental or main renal veins is associated with poor survival (Ball et al. 2016). It is reasonable to expect that future studies may find the same effect for retrograde pattern of dissemination.

Conclusion

Renal cell carcinoma, notably clear cell renal cell carcinoma in particular, show impressive predisposition for intravenous growth. Proper recognition of retrograde venous invasion is important for correct staging and recognition of nature of dissemination observed in the specimen. It should be carefully evaluated in gross specimens especially on those showing tumor invasion of main renal vein or renal sinus veins.

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None.

Authors' contributions
DAA conceived the idea. DAA was the major contributor to the writing of the manuscript. DAA, MFS and MEPA diagnosed the cases. MSF and MEPA were major contributors for critically revising the manuscript for important intellectual content. The authors read and approved the final manuscript.

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Availability of data and materials
Supplementary data is available upon request.

Declarations

Ethics approval and consent to participate
This work was approved by Ethics Committee of Federal University of Bahia, Faculty of Medicine, number 3.709.267.
Written informed consent was obtained from the patients.

Consent for publication
The authors agree with the publication of these results in its current form.

Competing interests
The authors declare that they have no competing interests.

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