Urology Case Reports 51 (2023) 102588

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

TFE3-rearranged renal cell carcinoma with tumour thrombus in the ureter mimicking invasive transitional cell carcinoma

Arman Z. Chacko [a,*], Shweta Singh [b], Johann Boaz [a], Vikram Raj Gopinathan [c], M.P. Rajadoss [a]

[a] Department of Urology, Christian Medical College Vellore, India
[b] Department of Radiology, Christian Medical College Vellore, India
[c] Department of Pathology, Christian Medical College Vellore, India

ARTICLE INFO

Keywords:
TFE3 renal cell carcinoma
Immunohistochemistry
Urothelial carcinoma

ABSTRACT

Background: Renal cell carcinoma (RCC) occasionally breaches the urothelial tissue barrier and extends into the collecting system mimicking a transitional cell carcinoma. We present a case of a TFE3-rearranged renal cell carcinoma in a young patient that extended to fill the entire upper urinary tract leading to a pre-operative diagnosis of upper tract urothelial carcinoma (UTUC) based on CT imaging. A sequential algorithm of IHC/FISH assays led to the correct diagnosis of TFE3-rearranged RCC. Awareness of this potential misdiagnosis, particularly in young patients, can mitigate significant morbidity.

1. Introduction

Renal cell carcinoma (RCC) occasionally extends into the urinary passage mimicking a transitional cell carcinoma. We present a case of TFE3-rearranged renal cell carcinoma (TFE3RCC) that extended inferiorly to fill the entire ureter.

2. Case presentation

An 18-year-old male presented with multiple episodes of painless hematuria over 3 ½ years. Physical examination disclosed a mass in the left lumbar region and the contrast-enhanced computed tomogram confirmed left hydroureteronephrosis (21 × 10 cm), with a homogenously enhancing soft tissue mass filling the renal pelvis and ureter to its distal extent. Multiple enlarged para-aortic nodes were identified (Fig. 1). Urine cytology was not performed. A pre-operative diagnosis of an upper tract urothelial carcinoma was made. An open radical nephroureterectomy was performed with regional lymphadenectomy and excision of the bladder cuff. The 16.5 × 9x8.5 cm tumour had a variegated solid cut surface with numerous friable papillary projections and infiltrated the renal pelvis, ureter and renal parenchyma with complete occlusion of the ureteric lumen. There was no gross infiltration of the renal capsule or renal sinus pad of fat. Microscopic examination demonstrated branching papillae and alveolar nests of epithelioid cells with pleomorphic vesicular nuclei, conspicuous nucleoli and abundant clear to flocculent eosinophilic cytoplasm. The cells covering the papillae were a single layer thick. Several psammoma bodies were present (Fig. 2). The tumour infiltrated the renal pelvis and upper ureter, but further distally formed a thrombus within the lumen with no evidence of infiltration. The distal end of the ureter and hilar vessels were free of tumour. There was metastasis to the hilar and para-aortic nodes. The tumour showed strong nuclear immunopositivity for TFE3 and PAX8 (Fig. 3), cytoplasmic positivity for CD10 and focal weak positivity for cytokeratin. Cytokeratin 7, Cytokeratin 20, Vimentin, E cadherin, GATA 3, Melan A and HMB45 were negative. A diagnosis of *TFE3*-rearranged renal cell carcinoma was made. The patient did not continue with treatment at this hospital and reportedly died 6 months after surgery.

3. Discussion

Renal cell carcinoma (RCC) accounts for 3% of all adult malignancies, with nearly 50% of cases detected incidentally, the triad of hematuria, flank pain and palpable abdominal mass being seen in less than 15% of cases.[1] The most common histological subtype of RCC is clear cell carcinoma (70–80%), followed by papillary renal cell carcinoma (PRCC) comprising 15–20%, and lastly chromophobe RCC at 5–7%.[2] *TFE3*-rearranged renal cell carcinoma, is a relatively rare subtype of RCC, belonging to the category of molecularly defined renal cell carcinomas, as defined in the 5th edition of the WHO.[2]

* Corresponding author.
E-mail address: arman.chacko@gmail.com (A.Z. Chacko).

https://doi.org/10.1016/j.eucr.2023.102588
Received 8 September 2023; Received in revised form 3 October 2023; Accepted 13 October 2023
Available online 15 October 2023

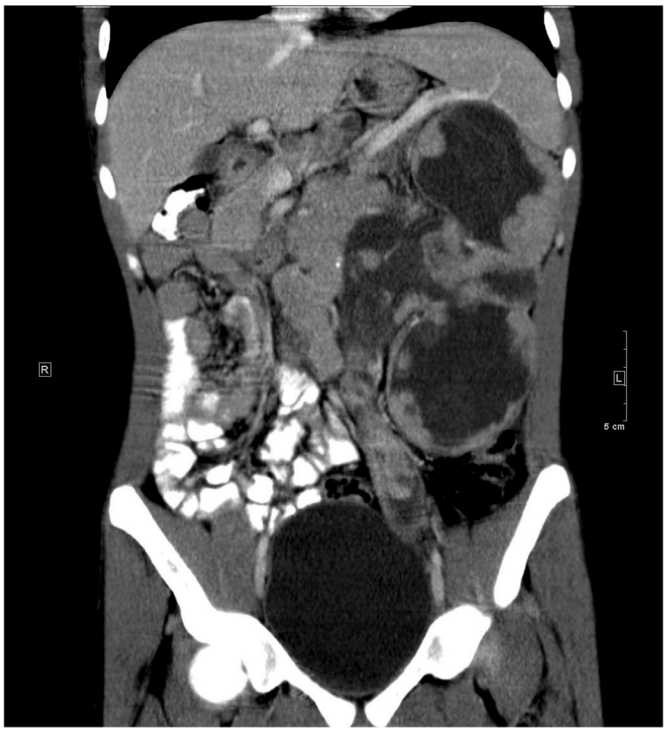

Fig. 1. Coronal sections of contrast enhanced (venous phase) images show an enlarged left kidney whose renal parenchyma is almost entirely replaced by endophytic nodular solid components lining the pelvi-calyceal system and the ureteric endothelium up to the level of the junction of the mid and distal ureter with associated hydroureteronephrosis.

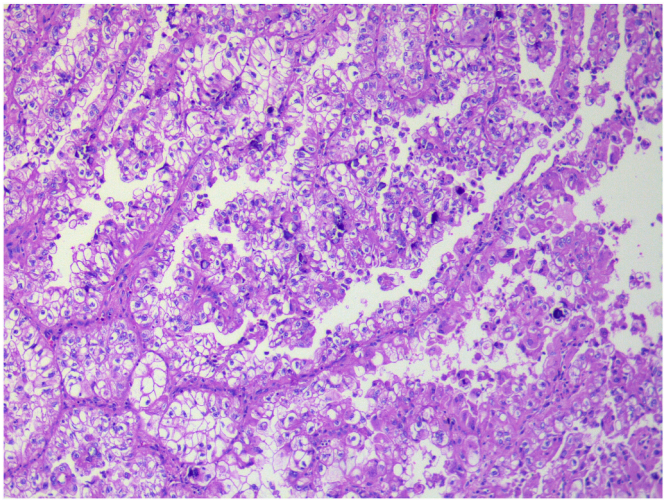

Fig. 2. Photomicrograph illustrating the papillary neoplasm with epithelioid cells having hybrid clear and eosinophilic cytoplasm. A few psammoma bodies are also seen. (H&E x90).

About 50% of paediatric RCCs and 1.6–4% of adult RCCs are *TFE3*-rearranged RCCs.[3] Tumours are usually diagnosed during a routine examination in adults (48.7%), but children tend to present with hematuria (38.1%) or an abdominal mass (23.8%)[4] as did our patient. The present tumour had a papillary architecture with predominantly clear cell morphology and psammoma bodies. The initial differentials considered were papillary renal cell carcinoma (PRCC), *TFE3*-rearranged renal cell carcinoma (*TFE3*RCC), clear cell carcinoma (CCRCC) and clear cell papillary renal cell carcinoma (CCPRCC). The young age of the patient and the presence of psammoma bodies

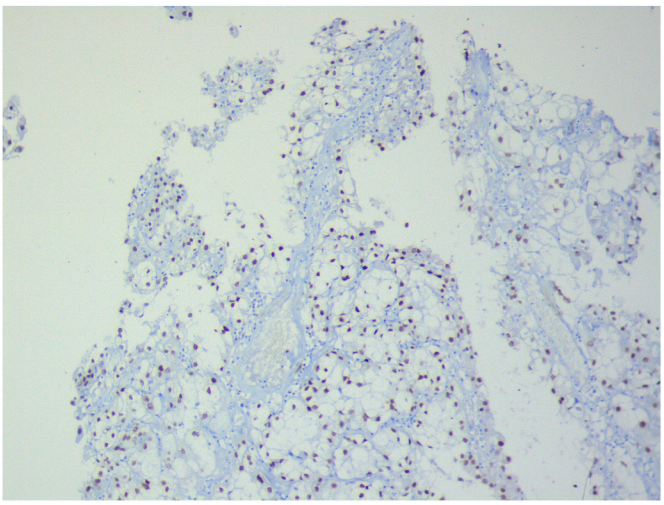

Fig. 3. Strong nuclear immunopositivity for TFE 3 (Avidin peroxidase x90).

indicated that *TFE3*-rearranged renal cell carcinoma was the more likely possibility. The immunonegativity for cytokeratin 7 and GATA3, eliminated both PRCC and CCPRCC and the immunonegativity for CK20 and GATA3 helped exclude papillary urothelial carcinoma. Nuclear positivity for PAX8 and TFE3 favoured a *TFE3*-rearranged renal cell carcinoma. Cytoplasmic positivity for CD10 and immunonegativity for E-cadherin provided further corroboration.

The 5th edition of the WHO defines strong nuclear labelling for TFE3 by immunohistochemistry in a clean background, or *TFE3* rearrangement identified by break-apart FISH, or *TFE3* gene fusion identified by RNA sequencing as an essential criterion for making a diagnosis of *TFE3*-rearranged renal cell carcinoma. A mixed histological pattern, including clear cells, papillary architecture, and psammoma bodies are considered desirable criteria.[2] Although the rearrangement was not demonstrated in the present case by molecular techniques, the crisp nuclear immunopositivity for TFE3, together with the mixed histological pattern, clinched the diagnosis.

The outcome for patients with *TFE3*RCC varies from indolent to rapidly aggressive behaviour. Survival of patients with *TFE3*RCC is similar to clear cell RCC but reported to be worse than papillary RCC[2] These tumours tend to present at an advanced stage and take on an aggressive clinical course, with metastasis in up to one-third of patients at diagnosis, the most common sites being para-aortic lymph nodes, mediastinal lymph nodes and lung.

The incidence of urinary collecting system invasion (UCSI) has ranged from 7.5% to 14.5% in different series.[5] The majority of reports indicate a non-infiltrative tumour thrombus extending into the ureter to varying extents and all were clear cell renal carcinoma on histopathological examination. The present case infiltrated the pelvicalyceal system and upper ureter but distally involved the ureter only in the form of a non-infiltrative tumour thrombus.

The optimal therapy for MiT family tRCCs is yet to be determined. Surgery is the treatment of choice for localized tumours even when involving regional lymph nodes. Involvement of the collecting system with renal tumour can mimic the radiological features and gross appearance of upper tract urothelial carcinoma (UC). Differentiating between these two entities can alter the surgical plan as UC warrants nephroureterectomy and removal of the entire ureter, most often with a cuff of the bladder. In the present case, the tumour thrombus extending into the distal ureter led us to mistakenly consider upper tract urothelial carcinoma (UC) and directed radical nephroureterectomy and excision of the bladder cuff. A negative preoperative urine cytology or an intraoperative frozen section would have helped avoid this surgical strategy as the histology of urothelial carcinoma and renal cell carcinoma are distinct.

4. Conclusion

This report highlights the potential pitfall of misdiagnosis of locally invasive *TFE3* rearranged carcinoma as urothelial carcinoma of the upper tract. Timely urine cytology and intraoperative frozen section consultation, awareness of the classic histological picture and the fact that metastases to regional lymph nodes do not adversely affect outcome, can result in an optimal treatment strategy.

Ethical statement

Informed consent was taken from the patient for publication of this case report and the associated images.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

All authors made substantial contributions to conception and design. They have all agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Declaration of competing interest

The authors have no conflicts of interest.

References

1. Cohen HT, McGovern FJ. Renal-cell carcinoma. *N Engl J Med*. 2005;353(23): 2477–2490. https://doi.org/10.1056/NEJMra043172.
2. Publication of the WHO Classification of Tumours, fifth ed., Volume vol. 8: Urinary and Male Genital Tumours – IARC. Accessed March 26, 2023. https://www.iarc.who.int/news-events/who-classification-of-tumours-5th-edition-volume-8-urinary-and-male-genital-tumours/.
3. Cheng X, Gan W, Zhang G, Li X, Guo H. Clinical characteristics of XP11.2 translocation/TFE3 gene fusion renal cell carcinoma: a systematic review and meta-analysis of observational studies. *BMC Urol*. 2016;16(1):40. https://doi.org/10.1186/s12894-016-0154-6.
4. Ma W, Liu N, Zhuang W, et al. Comparative clinicopathologic characteristics and outcomes of paediatric and adult Xp11 translocation renal cell carcinomas: a retrospective multicentre study in China. *Sci Rep*. 2020;10(1):1–11. https://doi.org/10.1038/s41598-020-59162-5.
5. Verhoest G, Avakian R, Bensalah K, et al. Urinary collecting system invasion is an independent prognostic factor of organ confined renal cell carcinoma. *J Urol*. 2009; 182(3):854–859. https://doi.org/10.1016/j.juro.2009.05.017.