TURKISH JOURNAL OF UROLOGY Turk J Urol 2017; 43(4): 566-70 • DOI: 10.5152/tud.2017.68639

UROONCOLOGY

Case Report

Bilateral renal cell carcinoma with leiomyomatous stroma: A rare entity diagnosed synchronously and treated surgically in a staged fashion

Murat Can Kiremit[1], Ömer Acar[1], Yeşim Sağlıcan[2], Tarık Esen[3]

Cite this article as: Kiremit MC, Acar Ö, Sağlıcan Y, Esen T. Bilateral renal cell carcinoma with leiomyomatous stroma: A rare entity diagnosed synchronously and treated surgically in a staged fashion. Turk J Urol 2017; 43(4): 566-70

ABSTRACT

Renal cell carcinoma (RCC) accounts for approximately 3% of adult malignancies and 90–95% of kidney neoplasms. Renal cell carcinoma with leiomyomatous stroma (RCCLS) is an extremely rare histopathological entity based on available literature data. Herein, we report a 31-year-old male with incidentally detected synchronous bilateral renal masses who was eventually found to harbor RCCLS after being operated sequentially via nephron-sparing surgery.

Keywords: Leiomyomatous stroma; nephron- sparing surgery; partial nephrectomy; renal cell carcinoma.

Introduction

Renal cell carcinoma (RCC) accounts for approximately 3% of adult malignancies and 90–95% of kidney neoplasms.[1-4] While the number of patients diagnosed with kidney cancer increases steadily, the incidence of bilateral renal tumors varies between 3-5%.[5-7] Description of the RCC subtype has been extremely revised based on morphological and genetic features in the 2016 World Health Organization (WHO) renal tumour classification.[8] Renal cell carcinoma with leiomyomatous stroma (RCCLS), which was not included in this new classification system. It is an extremely rare histopathological entity based on the available literature data which was firstly defined by Canzonieri et al in 1993.[9] Thereafter several case reports have been published by various authors.[10-13]

Herein, we report a case with incidentally detected synchronous bilateral renal masses who was eventually found to harbor RCCs with leiomyomatous stroma after being operated sequentially via nephron-sparing surgery (NSS).

Case presentation

A 31-year-old Caucasian male presented with nonspecific abdominal pain for two months. He was referred for an urological evaluation after the incidental discovery of bilateral renal masses both of which were suspicious for RCC upon ultrasonographic findings. He denied any episode of macroscopic hematuria. He was a moderate smoker, otherwise his past medical, surgical and family histories were unremarkable. Physical examination findings were within normal limits. Urinalysis demonstrated neither microscopic hematuria nor pyuria and urine culture was sterile. Complete blood count and serum biochemistry panel were within normal limits. Cross- sectional imaging modalities (computed tomography and magnetic resonance imaging) revealed bilateral and centrally located renal masses. The left sided mass (3cm in maximal diameter) originated from the posterior aspect of

[1]Department of Urology, Koç University Hospital, İstanbul, Turkey

[2]Department of Pathology, Acıbadem University, İstanbul, Turkey

[3]Department of Urology, Koç University, İstanbul, Turkey

Submitted: 31.10.2016

Accepted: 18.01.2017

Correspondence: Murat Can Kiremit E-mail: mckiremit@gmail.com

©Copyright 2017 by Turkish Association of Urology

Available online at www.turkishjournalofurology.com

the middle zone while the coexistent right-sided counterpart was smaller (2.5 cm in maximal diameter) and situated at the posteromedial part of the lower kidney pole (Figure 1). The R.E.N.A.L. nephrometry scores of the masses were 7p and 9p for the right and left sides, respectively. Both masses demonstrated significant contrast enhancement, which was suggestive of an underlying malignancy. The Hounsfield units of the right and left renal masses were calculated to be 1046±52 HU and 1105±93 HU, respectively after IV administration of contrast medium. Regional lymph node enlargement was not evident on cross-sectional images.

The masses were solid in nature and radiologic characteristics (contrast enhancement, size, heterogeneous architecture etc.) substantially raised the possibility of malignancy. Additionally this was a young patient without any comorbidity, which meant a long- life expectancy. Therefore, renal mass biopsy, histopathological results of which would not change our treatment plan, was not considered for either side.

After thorough patient counseling, we elected to perform a 2-staged nephron-sparing approach with an initial open surgery for the left renal tumor due to its high R.E.N.A.L. nephrometry score and robot-assisted laparoscopic surgery for the right-sided kidney mass concerning its relative morphometric easiness.

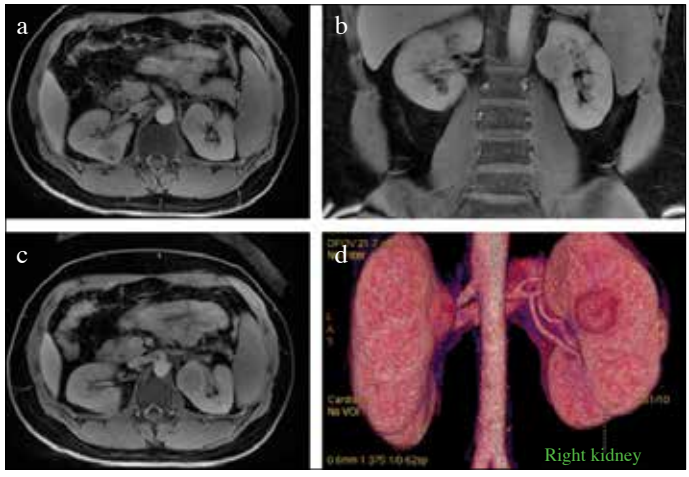


Figure 1. a-d. Axial fat-saturated post-contrast T1- weighted MRI images of the kidneys in nephrographic phase demonstrate bilateral heterogeneusly enhancing renal cortex masses. The masses are located at the posterior medial right interpolar and anterior medial upper pole cortex measuring 3 cm and 2.5 cm respectively. Other sequences (not shown) demonstrated these lesions to be hypointense relative to normal renal parenchyma on the precontrast T1 -weighted images and hypo-to-isointense on T2- weighted images. Delayed contrast washout was observed on dynamic contrast -enhanced images. Color volume surface rendered 3D image demonstrates the exophytic nature of the bilateral renal masses.

Procedure 1

A left open partial nephrectomy was performed through 11-12th intercostal incision. After entering the retroperitoneum, left renal artery was identified, dissected and controlled with vessel loop (without creating warm ischemic conditions) through posterior approach. Thereafter, the upper pole and lateral borders of the kidney were mobilized within Gerota's fascia, without dissecting the perirenal fat overlying the tumor. The mass was enucleoresected with a milimetric rim of normal looking renal parenchyma overlying its pseudocapsule. Frozen section evaluation of the surgical margin revealed benign findings. After repairing collecting system defects with 3/0 polyglactin sutures, the cortical edges were approximated by interrupted 2-0 monofilament sutures. Total operation and warm ischemia times were 97 and 19 minutes, respectively. Estimated blood loss was 150 cc. He was discharged after an uneventful course on the third postoperative day.

Procedure 2

One month later, transperitoneal robot-assisted laparoscopic right partial nephrectomy was performed. A total of 5 ports (3 for the robot, 2 for the assistant) were introduced. After mobilizing the colon, Gerota's fascia was opened and the central renal mass was exposed with its overlying perirenal fatty tissue. Renal pedicle was dissected free and within 15 minutes of warm ischemia time the renal mass was completely enucleoresected and the resultant corticomedullary defect was repaired using the sliding-clip renorrhapy technique.

Histopathological examination of both tumors revealed the same diagnosis, ie. renal cell carcinoma with leiomyomatous stroma (Figure 2). His postoperative serum creatinine level was 0.93 mg/dL and abdominal CT scan, which was conducted 6 months after the surgery, detected no local recurrence or distant metastasis (Figure 3). Written informed consent of the patient was obtained from the patient for the publication of the procedures as a case report.

Histopathological examination

Both left and right renal tumors revealed similar macroscopic features. Well-circumscribed, pale yellow, solid masses with diameters of 3.2 cm and 2.6 cm, were detected, respectively. Microscopically; tumors had a multinodular appearance, due to abundant fibroleiomyomatous stromal component intermingled with epithelial tumor cells. Epithelial component was composed of branching tubules, nests and glands lined by cells with clear cytoplasm and mild nuclear atypia (Fuhrman grade 2). Atypia, mitosis and necrosis were not identified.

Turk J Urol 2017; 43(4): 566-70
DOI:10.5152/tud.2017.68639

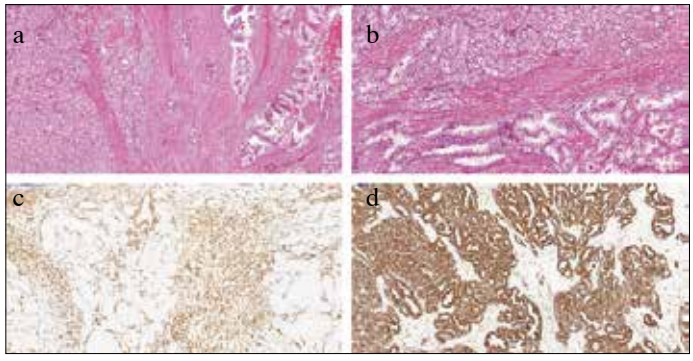


Figure 2. a-d. (a) Section of the tumor at the left kidney showing a circumscribed multinodular tumor composed of nests of clear cells embedded in abundant fibrous stroma (H&E, 3DHistech Panoramic Scanner 4.3x). (b) In this patient, higher magnification view of the tumor at the other (right) kidney shows a similar morphologic features as illustrated in Figure 1 (H&E, 3DHistech Panoramic Scanner 8.9x). (c) Stromal cells of both tumors are positive for smooth muscle actin. Immunostaining, comfirmed smooth muscle bundles between clear cells (3DHistech Panoramic Scanner 11.4x). (d) The same staining reaction for CK7 is observed in both tumors in addition to diffuse and strong positivity in clear cells (3DHistech Panoramic Scanner 7.6x).

The immunohistochemical study was performed using a Ventana BenchMark XT automated stainer (Ventana Medical System, Inc, Tuscon, AZ, USA). Formalin fixed, paraffin embedded tissues were immunostained. CK7 (OV-TL 12/30, monoclonal, RTU; Biocare Medical, CA, USA), pancytokeratin (multiple, monoclonal, RTU; ScyTek, Utah, USA), smooth muscle actin (1A4, monoclonal, RTU; ScyTek, Utah, USA) and desmin (D33, monoclonal, RTU; ScyTek, Utah, USA) were used as primary antibodies. Both tumors had similar immunohistochemical profiles namely epithelial cells showed diffuse and strong immunoreactivity for CK7 and pancytokeratin while the stromal component reacted positively for SMA and desmin.

Discussion

Leiomyomatous stroma may exist in various renal tumors, namely angiomyolipoma, renal angiomyoadenomatous tumor (RAT)/clear cell papillary renal cell carcinoma (CCPRCC) and "renal cell carcinoma with smooth muscle stroma" (RCCSMS).[9-11,13] RCCLS is an uncommon neoplasm, which has an intimate admixture of epithelial and stromal components.[14] Clear epithelial cells represent the epithelial component of this neoplasm and moderate nuclear atypia (mostly Fuhrman grade 2) that is evident in adenomatous structures encompassing a nested or tubular pattern admixed with focal papillary and solid areas constitute the main histopathological alterations observed in RCCLS.[14]

Petersson et al.[15] concluded that the leiomyomatous stroma that may be observed in RCC is not related to the neoplastic process.[15] The smooth muscle cells of this stroma are of polyclonal in origin and represent a reactive hyperplastic process possibly being derived from the muscular layer of large caliber veins located at the capsular periphery or within the tumoral septae. The proliferation of vessel-derived smooth muscle cells may be related to hypoxia induced factors as suggested by Kuhn et al.[10]

These tumors do not have unique genetic alterations.[16,17] On the other hand, some authors have reported molecular changes that resemble those encountered in clear cell RCCs (*VHL* gene mutation, VHL hypermethylation or loss of heterozygosity of 3p).[8,18] Considering these controversial findings about the relationship between genetic alterations and the development of renal cell carcinoma with leiomyomatous stroma (RCCLS) we did not performe molecular genetic evaluation either for the resected tissue specimen or peripheral blood sample.

Due to the rare incidence of RCCLS, the prognosis of this entity has not been thoroughly evaluated. Nevertheless a good clinical behaviour is likely, given the small sized lesions and relatively lower tumor grades published up to now. Shannon et al.[11] reported that all of their patients (n: 3) were alive with no evidence of disease after 18 months to 5 years of follow-up. In this publication[11], patients'ages ranged between 48-65 years. One patient was female and the others were male. Despite their small size (2.4-2.6 cm) these solid masses were managed by radical nephrectomy. Our case was a relatively young male patient and had bilateral cT1a masses (2.6 and 3.2 cm), which were treated by NSS. Fuhrman grades of these masses, including the ones reported by Shannon et al.[11], were ≤2. In another study, all 3 patients remained well and alive after 20-52 months of follow-up.[13] Despite the relatively short follow-up period, which is one of the major drawbacks of the present study, our patient still remains disease free.

In conclusion, RCCLS is a rare subtype of RCC. Its histopathological diagnosis needs a meticulous immunohistochemical work-up. Genetic evaluation, which was not done in our patient, can be considered in selected cases, however there is limited data to support its routine application. Nephron-sparing surgery, which was inevitable in our case given the young age of the patient and synchronous bilateral presentation, should be the treatment modality of choice whenever its technically feasible. Despite limited data about its natural his-

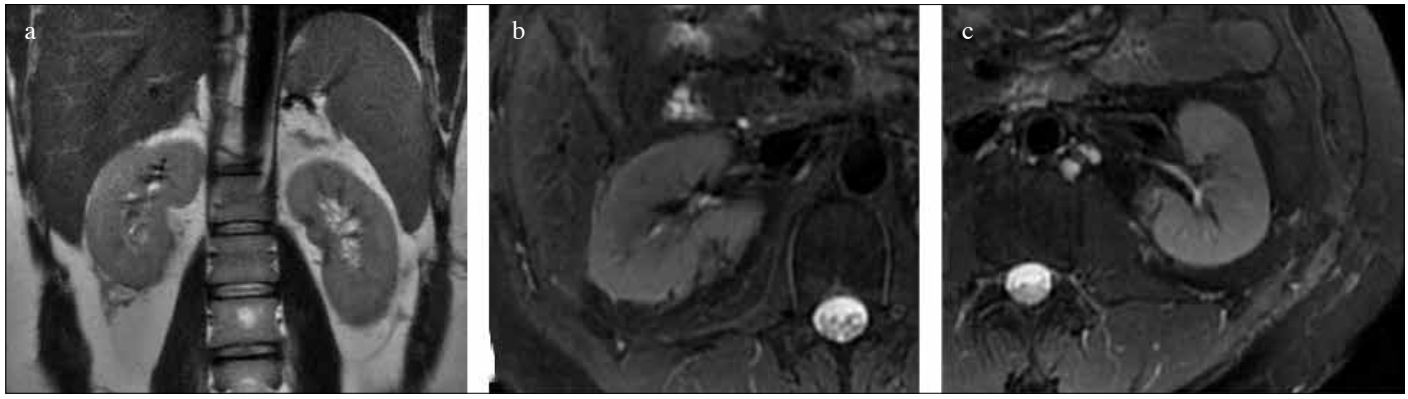


Figure 3. a-c. (a) Postoperative abdominal MRI, coronal section, demonstrating absence of residual/recurrent mass on either side. (b) Axial MRI section of the right kidney showing nothing remarkable other than postoperative changes. (c) Axial MRI section of the left kidney demonstrating nothing remarkable other than postoperative changes

tory, this tumor portends a favorable prognosis once excised completely with surgically negative margins.

Informed Consent: Written informed consent of the procedures and publication as a 'case report' was obtained from the patient.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.C.K., Ö.A.; Design – M.C.K., Ö.A.; Supervision – Y.S., T.E.; Materials – M.C.K., Y.S., T.E.; Data Collection and/or Processing – M.C.K., Ö.A.; Analysis and/or Interpretation – M.C.K., Ö.A.; Literature Review – M.C.K.; Writer – M.C.K., Ö.A., Y.S.; Critical Review –T.E.; Other – Ö.A., T.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, et al. Cancer statistics 2006. CA Cancer J Clin 2006;56:106-30. [CrossRef]
2. Lam JS, Leppert JT, Belldegrun AS, Figlin RA. Novel approaches in the therapy of metastatic renal cell carcinoma. World J Urol 2005;23:202-12. [CrossRef]
3. Mickisch GH, Mattes RH. Combination of surgery and immunotherapy in metastatic renal cell carcinoma. World J Urol 2005;23:191-5. [CrossRef]
4. Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. N Engl J Med 1996;335:865-75. [CrossRef]
5. Marshall FF, Stewart AK, Menck HR. The National Cancer Database: report on kidney cancers. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer 1997;80:2167-74. [CrossRef]
6. Grimaldi G, Reuter V, Russo P. Bilateral non-familial renal cell carcinoma. Ann Surg Oncol 1998;5:548-52. [CrossRef]
7. Klatte T, Wunderlich H, Patard JJ, Kleid MD, Lam JS, Junker K, et al. Clinicopathological features and prognosis of synchronous bilateral renal cell carcinoma: an international multicentre experience. BJU Int 2007;100:21-5. [CrossRef]
8. Moch H, Cubilla AL, Humphrey PA, Reuter VE, Ulbright TM. The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs-Part A: Renal, Penile, and Testicular Tumours. Eur Urol 2016;70:93-105. [CrossRef]
9. Canzonieri V, Volpe R, Gloghini A, Carbone A, Merlo A. Mixed renal tumor with carcinomatous and fibroleiomyomatous components, associated with angiomyolipoma in the same kidney. Pathol Res Pract 1993;189:951-6. [CrossRef]
10. Kuhn E, De Anda J, Manoni S, Netto G, Rosai J. Renal cell carcinoma associated with prominent angioleiomyoma-like proliferation: Report of 5 cases and review of the literature. Am J Surg Pathol 2006;30:1372-81. [CrossRef]
11. Shannon BA, Cohen RJ, Segal A, Baker EG, Murch AR. Clear cell renal cell carcinoma with smooth muscle stroma. Hum Pathol 2009;40:425-9. [CrossRef]
12. Iczkowski KA, Shanks JH, Burdge AH, Cheng L. Renal cell carcinoma with clear cells, smooth muscle stroma, and negative for 3p deletion: a variant of renal angiomyoadenomatous tumour? A case report. Histopathology 2013;62:522-4. [CrossRef]
13. Martignoni G, Brunelli M, Segala D, Gobbo S, Borze I, Atanesyan L, et al. Renal cell carcinoma with smooth muscle stroma lacks chromosome 3p and VHL alterations. Mod Pathol 2014;27:765-74. [CrossRef]
14. Hes O, Compérat EM, Rioux-Leclercq N. Clear cell papillary renal cell carcinoma, renal angiomyoadenomatous tumor, and renal cell carcinoma with leiomyomatous stroma relationship of 3 types of renal tumors: a review. Ann Diagn Pathol 2016;21:59-64. [CrossRef]
15. Petersson F, Branzovsky J, Martinek P, Korabecna M, Kruslin B, Hora M, et al. The leiomyomatous stroma in renal cell car-

Turk J Urol 2017; 43(4): 566-70
DOI:10.5152/tud.2017.68639

cinomas is polyclonal and not part of the neoplastic process. Virchows Archiv 2014;465:89-96. [CrossRef]

16. Williamson SR, Cheng L, Eble JN, True LD, Gupta NS, Wang M, et al. Renal cell carcinoma with angioleiomyoma-like stroma: clinicopathological, immunohistochemical, and molecular features supporting classification as a distinct entity. Mod Pathol 2015;28:279-94. [CrossRef]
17. Hakimi AA, Tickoo SK, Jacobsen A, Sarungbam J, Sfakianos JP, Sato Y, et al. TCEB1-mutated renal cell carcinoma: a distinct genomic and morphological subtype. Mod Pathol 2015;28:845-53. [CrossRef]
18. Allory Y, Culine S, de la Taille A. Kidney cancer pathology in the new context of targeted therapy. Pathobiology 2011;78:90-8. [CrossRef]