Ipsilateral synchronous clear and papillary renal cell carcinoma: A case report and review of the literature

Muna Alhusban, Sohaib Alhamss, Bayan Alzumaili, Ali Al-Daghmin*

King Hussein Cancer Center, P. O. Box 1289, Al-Jubeiha, Amman 11941 Jordan

Abstract

Clear cell renal cell carcinoma and papillary renal cell carcinoma are the most common types of renal tumors. However, coexistence of both tumors in the same kidney is a rare condition.

We report a 56-year old male who was found to have ipsilateral synchronous clear cell and papillary renal cell carcinoma in the left kidney. Review of related literature is provided to estimate the prevalence of similar cases.

© 2017 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Renal cell carcinoma (RCC) accounts for 2–3% of all cancers.1 There is a 1.5:1 predominance of men over women, with peak incidence occurring at 60–70 years old. Etiology includes lifestyle factors, such as smoking, obesity, and hypertension, with cigarette smoking being a definite risk factor for RCC. On the other hand, obesity and hypertension roles as risk factors for RCC are still inconclusive.2,3

Clear cell (cc RCC) accounts for 75% of RCC cases, papillary RCC (pRCC) represents 10% of cases, and chromophobe RCC, 5% of cases.3 Clear cell papillary renal cell carcinoma (ccpRCC) has recently been reported and is considered a distinct subtype, composed of cells with clear cytoplasm lining cystic, tubular, and papillary structures.4

The incidence of sporadic multifocal tumors is 4–20% of patients at the time of diagnosis.5–8 Multiple synchronous renal tumors can be associated with genetic predisposition to RCC, as in hereditary familial RCC syndrome, or acquired conditions, like chronic kidney disease, which has the tendency to develop bilateral pRCC.9 Sorbellini et al. reviewed the literature to estimate the prevalence of multifocal RCC and revealed 6.8% incidence of ipsilateral multifocal RCC and 11.7% were bilateral.10

Several cases of multifocal RCC that had two or more tumors of different histologic subtypes have been reported.5,11–16

Herein, we report an unusual case of coexistence of two different synchronous ipsilateral renal tumors; clear-cell RCC and papillary RCC.

2. Case report

We report a case of a 56 year-old gentleman who underwent abdominal CT with IV contrast during evaluation of newly diagnosed high blood pressure which revealed a unilateral synchronous two kidney lesions and one renal cyst. The first lesion was in the upper pole left renal pole, measuring 5 cm and indenting the splenic surface with no definite invasion; the second lesion was invading the renal sinus fat; and the third lesion was hemorrhagic cyst in the lower pole of the left kidney measuring about 2 cm. There is an enlarged pathological left para-aortic lymph node measuring 2.2 × 1.6 cm. There is a separate enhancing soft tissue nodule in the left adrenal gland measuring 1.6 cm; this nodule might represent metastasis. Figs. 1 and 2.

A true cut biopsy of one of the nodules showed the histopathologic features of renal cell carcinoma, the conventional type while a fine needle aspiration of the second nodule came negative. Physical examination was normal. Hematological and biochemical tests were unremarkable.

Patient underwent laparoscopic left radical nephrectomy and adrenalectomy with para-aortic lymph nodes dissection and he was discharged from hospital after 3 days without events.

Grossly, the first nodule was in the upper pole, confined to the capsule and measuring 5 × 4.5 × 4cm with solid and cystic hemorrhagic cut surfaces; the second nodule was in the middle pole...
confined to the kidney, indenting the sinus fat and measuring 4.5 × 3.5 × 3.5 cm with solid cut surfaces. Benign hemorrhagic renal cyst found in the lower pole. Left adrenal showed a small nodule measuring 0.5 × 0.5 × 0.5 cm. Para-aortic lymph nodes showed one lymph node grossly positive for malignancy and measuring 2.5 × 2.5 × 2 cm.

Microscopic examination of the specimen showed one tumor in the upper pole consistent with the histopathological subtype clear cell of renal cell carcinoma, with the pathologic stage: pT1bN0 (Fig. 3). The second tumor was in the middle pole and it was the subtype papillary renal cell carcinoma, type 2 and its stage was pT1bN1 (Fig. 4). Sarcomatoid features were absent. Histologic Grade (Fuhrman Nuclear Grade) was 2. Para-aortic lymph nodes revealed metastatic papillary renal cell carcinoma in one out of the twenty lymph nodes that were dissected and adrenal gland with focal hyperplasia.

3. Review of the literature

Methods

We underwent a review of the English-written literature using PubMed looking for these terms: “synchronous clear cell papillary RCC” and “multifocal RCC”. Besides, we reviewed the references of the available articles. Papers that did not mention the frequency of multifocal RCC or its laterality were excluded. 10 articles fulfilled our criteria, plus 3 case reports.

Results

About 47 cases of ipsilateral synchronous clear cell renal cell carcinoma and papillary renal cell carcinoma were reported in literature (Table 1). Ipsilateral multifocal renal tumors occur in 0.5–5.4% of the total number of renal tumor patients. About 13–14% of this small subset of patients will develop cases of ipsilateral synchronous ccRCC + pRCC tumors as shown by four series.11–13,16 Capaccio et al. reported a higher percentage, 42.8%, while Minervini reported a lower one, 5.9%.14,15

4. Discussion

Awareness of the coexistence of multiple synchronous tumors of different histology within the same kidney is important in managing such cases, especially when planning for nephron-sparing surgery.
needle biopsy was not successful in determining the histological subtype, lymph node metastasis, advanced tumor stage (pT4), and different prognosis rates and will vary in aggressiveness. Using needle biopsy was not successful in determining the histological subtype of renal masses with much reliability. In our case; the true cut biopsy was successful in diagnosing the ccRCC, while the fine needle aspiration failed to diagnose the pRCC component.

In fact, depending on preoperative imaging to identify multifocal tumors will lead to missing some of the multifocal lesions. Thus complete mobilization and inspection on the entire kidney is implied that if biopsy is indicated preoperatively, or in intra-operative setting for frozen section biopsy, each of the multiple nodules should be biopsied; because different tumors will carry different prognosis rates and will vary in aggressiveness. Using needle biopsy was not successful in determining the histological subtype of renal masses with much reliability. In our case; the true cut biopsy was successful in diagnosing the ccRCC, while the fine needle aspiration failed to diagnose the pRCC component.

In fact, depending on preoperative imaging to identify multifocal tumors will lead to missing some of the multifocal lesions. Thus complete mobilization and inspection on the entire kidney is justified when performing NSS to identify multifocal disease.

In this reported case, two factors may help in predicting the presence of multifocality. They are the papillary subtype and lymph node metastasis. Richstone, who reviewed 1071 radical nephrectomies and performed multivariate analysis of this population, showed significant associations between multifocality with papillary subtype and lymph node metastasis, advanced tumor stage (pT4), and bilateral disease. On the other hand, tumor size had not been a significant factor. Furthermore, he revealed that there is no significant difference in 5 year disease-free and overall survival between patients with multifocal and those with solitary RCC. However, 2 series with large number of patients concluded that 5%–6% of the patients with multiple ipsilateral renal tumors develop a contralateral metachronous recurrence and this risk is 5 times that of patients with a sporadic single tumor. In addition, when they compared the 2 main surgical options for managing this subset of patients, similar tumor-specific survival was observed for patients treated with nephron-sparing surgery NSS and radical nephrectomy RN in carefully selected patients.

We conclude that multiple ipsilateral synchronous RCC of different histological subtypes are a special entity that is needed to be considered preoperatively even though they have low incidence rates.

### Table 1

| Study Year | Total number of cases reviewed n | Ipsilateral multifocal tumors n (%) | ccRCC + pRCC ipsilateral synchronous tumors n (%) | Notes |
|------------|---------------------------------|------------------------------------|-------------------------------------------------|-------|
| Beaugerie et al. 2017 | 216 | 50 | unavailable | combinations of subtypes are not mentioned |
| Harlow et al. 2016 | 2817 | 15 (0.5%) | 2 (13.3%) | Plus 3 cases of mixed ccRCC + pRCC in single tumors |
| Mano et al. 2015 | 333 | 128 | unavailable | combinations of subtypes are not mentioned |
| Simhan et al. 2013 | 2569 | 97 (3.8%) | unavailable | Plus 8 cases of mixed ccRCC + pRCC in single tumors |
| Capaccio et al. 2009 | 381 | 7 (1.8%) | 3 (42.8%) | _ |
| Crispin et al. 2008 | 1113 | 60 (5.4%) | 8 (13.3%) | _ |
| Minervini et al. 2008 | 960 | 34 (3.5%) | 2 (5.9%) | _ |
| Krambeck et al. 2008 | >4000 | 140 (~3.4%) | 20 (14.3%) | Same institution registry as Blute et al. |
| Richstone et al. 2004 | 1071 | 51 (4.8%) | 9" | Extra new ccRCC + pRCC cases are only 3 |
| Blute et al. 2003 | 118 | 118 | 17 (14.4%) | A total of 57 multifocal cases; both unilateral & bilateral |
| Single case reports [20–23] | _ | 3 | 3 | Plus a case of ccRCC + pRCC + papillary adenoma |

**a** Only multiple synchronous renal masses were included.

**b** 9 cases of synchronous ccRCC + pRCC out of the total number of multifocal 57 cases.

**c** Only multiple ipsilateral tumors were included.

### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eucr.2017.11.020.

### References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. CA Cancer J Clin. 2016;66(1):7–30. https://doi.org/10.3322/caac.21332.

2. Ljungberg Borje, Hanbury Damian C, Kuczyk Marcus A, Merseburger Axel S, Mulders Peter FA, Patard Jean-Jacques. Renal cell carcinoma guideline. Eur Urol. 2007;51:1502–1510. https://doi.org/10.1016/j.eururo.2007.03.035.

3. Cohen HT, McC Vollmer FJ. Renal-cell carcinoma. N Engl J Med. 2005;353:2477–2490. https://doi.org/10.1056/NEJMra043172.

4. Williamson Sean R, Eble John N, Cheng Liang, Grignon David J. Clear cell papillary renal cell carcinoma: differential diagnosis and extended immunohistochemical profile. Mod Pathol. 2013;26:697–708. https://doi.org/10.1038/modpathol.2012.204.

5. Richstone L, Scherr DS, Reuter VR, et al. Multifocal renal cortical tumors: frequency, associated clinicopathological features and impact on survival. J Urol. 2004;171(2 Pt 1):615–620. https://doi.org/10.1016/j.juro.2004.01.016.

6. Dimarco DS, Lohse CM, Zincke H, Cheville JC, Blute ML. Long-term survival of patients with unilateral sporadic multifocal renal cell carcinoma according to histologic subtype compared with patients with solitary tumors after radical nephrectomy. Urology. Sep 2004;64(3):462–467. https://doi.org/10.1016/j.urol.2004.04.016.

7. Lang H, Lindner V, Martin M, et al. Prognostic value of multifocality on progression and survival in localized renal cell carcinoma. Eur Urol. 2004;45:749–753. https://doi.org/10.1016/j.eururo.2004.02.006.

8. Ballca Li, Orhan D, Soyupek S, Beduk Y, Tulunay O, Gogus O. Influence of tumor stage, size, grade, vascular involvement, histological cell type and histological pattern on multifocality of renal cell carcinoma. J Urol. Jul 2000;164(1):36–39. https://doi.org/10.1016/S0022-5347(05)67443-5.

9. Breda A, Lohse CM, Zincke H, et al. Clinical and pathological outcomes of renal cell carcinoma (RCC) in native kidneys of patients with end stage renal disease: a long-term comparative retrospective study with RCC diagnosed in the general population. World J Urol. 2015;33:1–7. https://doi.org/10.1007/s00345-014-1248-y.

10. Maximiliano Sorbellini and Gennady Bratslavsky. Decreasing the indications for radical nephrectomy: a study of multifocal renal cell carcinoma. Front Oncol. 2012;2:84. https://doi.org/10.3389/fonc.2012.00084.

11. Blute ML, Thibault GP, Leibovich BC, Cheville JC, Lohse CM, Zincke H. Multiple ipsilateral renal tumors discovered at planned nephron sparing surgery: importance of tumor histology and risk of metachronous recurrence. J Urol. 2003;170:760–763. https://doi.org/10.1097/01.ju.0000081422.47894.e6.
12. Krambeck A, Iwaszko M, Leibovich B, Cheville J, Frank I, Blute M. Long-term outcome of multiple ipsilateral renal tumours found at the time of planned nephron-sparing surgery. BJU Int. 2008;101(11):1375–1379. https://doi.org/10.1111/j.1464-410X.2008.07588.x.

13. Crispen PL, Lohse CM, Blute ML. Multifocal renal cell carcinoma: clinicopathologic features and outcomes for tumors <4 cm. Adv Urol. 2008;518091. https://doi.org/10.1155/2008/518091.

14. Capaccio E, Varca V, Simonato A, Toncini C, Carmignani G, Derchi LE. Synchronous parenchymal renal tumors of different histology in the same kidney. Acta Radiol. 2009;50(10):1187–1192. https://doi.org/10.3109/02841850903236120.

15. Minervini A, Serni S, Guibilei G, et al. Multiple ipsilateral renal tumors: retrospective analysis of surgical and oncological results of tumor enucleation vs radical nephrectomy. EJSO. 2009;55:521–526. https://doi.org/10.1016/j.ejso.2008.06.003.

16. Harlow Brittani L, Klaassen Zachary, Holzman Sarah, Reinstatler Lael, Franken Alicia A, Kavuri Sravan K. Multiple discordant histology after nephrectomy: descriptive analysis and outcomes. Clin Genitourin Cancer. 2016 Apr;14(2):e171–e175. https://doi.org/10.1016/j.clgc.2015.10.013.

17. Beaugerie Aurélien, Audenet François, Verkarre Virginie, Delavaud Christophe, Le Guilchert Thomas, Hurel Sophie. Pathological heterogeneity in sporadic synchronous renal tumors: is the histological concordance predictable? Urol Oncol. 2017 Oct 6. https://doi.org/10.1016/j.urolonc.2017.09.002. pii: S1078–1439(17)30465-9.

18. Mano R, Kent M, Larish Y, et al. Partial and radical nephrectomy for unilateral synchronous multifocal renal cortical tumors. Urology. 2015;85:1404–1410. https://doi.org/10.1016/j.urology.2015.02.032.

19. Simhan J, Canter DJ, Sterious SN, et al. Pathological concordance and surgical outcomes of sporadic synchronous unilateral multifocal renal masses treated with partial nephrectomy. JUrol. 2013;189:43–47. https://doi.org/10.1016/j.juro.2012.08.092.

20. Andreou A. Synchronous ipsilateral conventional and papillary renal cell carcinoma. Pathology. 2012;44. https://doi.org/10.1016/S0031-3025(16)32772-6, S68–S68.

21. Ustuner M, Yaprak B, Teke K, et al. Coexisting papillary and clear renal cell carcinoma in the same kidney. Case Rep Urol. 2014. https://doi.org/10.1155/2014/575181, 575181.

22. Shankar Tele Jyoti, Shah Anita, Kushwaha Harshul. A case of synchronous papillary and clear cell carcinoma in the same kidney. Int J Res Med Sci. 2015 May;3(5):1288–1292. https://doi.org/10.2455/2320-6912-ijrms20150549.

23. Tait L, Coleman P, Grantham M, Abaghotu C. Mixed renal cell carcinoma with metastasis to the ipsilateral ureter, a case report. Internet J Urol. 2012;9(3).