Case Report

Management of Renal Cell Carcinoma in Von Hippel-Lindau Syndrome: Case Report and Review of Literature

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Abstract

Renal cell carcinoma (RCC) is the one of the most common type of of cancer of the kidneys affecting adults. A 35-year-old man, with Von Hippel Lindau (VHL) syndrome was referred for bilateral renal mass in a follow up CT for evaluation. Open partial left nephrectomy was performed and the final histopathological report confirmed the diagnosis. One of the most important genetic and hereditary risk factor for RCC is Von Hippel-Lindau syndrome (VHL). RCC in VHL may occur bilaterally in some cases, so preserving renal parenchymal function is a major therapeutic goal and nephron sparing surgery provides a favorable patient outcome.

Keywords: Renal cell carcinoma, Von Hippel Lindau syndrome, kidney dialysis, risk factor, neoplasm

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Introduction

RCC (Grawitz' tumour) is the most common type of cancer of the kidneys, contributing to 90-95% cases of kidney cancers. RCC is seen in 3% of total cancer cases in adults and usually occurs in people aged more than 55 years (mean age is 64 years) (1). One of the most important genetic and hereditary risk factor for RCC is Von Hippel-Lindau syndrome (VHL) whereby the risk is estimated to be 40% and manifestations become apparent in a younger age group (2). With the advent of improved detection techniques (CT, US , and MRI) the incidence of RCC seems to be on the rise (3). Historically, TN was done to prevent or reduce the risk of disease progression which led to patient being dependent on dialysis. Since, RCC has a low pathological grade, slow growth and metastatis, the treatment is aimed at conserving renal parenchymal function. Hence presently, nephron sparing surgery (NSS) has become the gold standard of treatment compared to radical nephrectomy (RN) (2).

Case Report

A 35-year-old Malay man with VHL syndrome who had cereberal haemangioblastoma, was referred for incidental findings of bilateral renal mass suggestive of RCC in a follow up CT scan. The scan showed solid mass in the lower pole of right and left kidneys, measuring 1.6 cm and 4.6 cm, respectively. He also had multiple renal cysts bilaterally and also pancreatic cysts. He was asymptomatic and had normal renal function. An extra-peritoneal approach open partial left nephrectomy was done and the histopathological report revealed clear cell RCC (Fuhrman nuclear grade 2). However, a tumour free resected margin was not obtained. He was being followed-up with regular CT scans with a plan of partial nephrectomy of the contralateral kidney later once he recovered well.

Discussion

RCC usually presents above the age of 55 years. Hematuria, abdominal pain, and a palpable abdominal

mass are classic symptoms of RCC. But this triad of symptoms is seen only in 10% patients. Upto a quarter of the cases show metastatsis at presentation. Half of diagnosed RCC cases develop metastasis or local recurrence after treatment for the primary tumour during follow up visit. One fifth of the cases show common paraneoplastic syndromes like hypercalcemia, liver dysfunction, polycythemia, amyloidosis, fever and weight loss (3).

Incidental detection by employing CT scan, US, and MRI have been steadily increasing over the years due to advancement in detection techniques. More than half of RCC cases can be identified incidentally by imaging techniques. The use of CT scan in the diagnosis of RCC increases accuracy to 95%. The tumours detected by CT scan are usually smaller, picked up in the earlier stages, and with improved survival for which partial nephrectomy can be carried out instead of radical nephrectomy (4).

The above patient has RCC, despite falling into a younger age group and being asymptomatic (does not show the classic symptoms of the triad). This can be explained due to a strong correlation of RCC with VHL syndrome.

Von Hippel Lindau (VHL) syndrome is a rare autosomal dominant genetic condition resulting from a mutation in the VHL tumour suppressor gene on chromosome 3p25.3. This disease is characterised by occurrence of cancers of central nervous system, retinal hemangioblastomas, pheochromocytomas, pancreatic neurondocrine tumours, pancreatic cysts, endolymphatic sac tumours, epididymal papillary cystadenomas, clear cell RCC and presents with an increased risk of malignant transformation (5).

Nephron sparing surgery in the form of partial nephrectomy is the gold standard of treatment whenever feasible for enhancing solid renal masses (6) considering the fact that there is bilateral involvement in 2-4 % of cases. In approximately one half cases with bilateral tumours, there is synchronous involvement with the risk of RCC occurring in the original contralateral kidney at a later point in the patient ranging from 1-2% . In our patient, NSS was considered since there were bilateral tumours. NSS can also be considered in patients whose renal function is of clinical concern especially in patients with a sole functioning kidney or patients with renal dysfunction. In these subset of patients, if the entire kidney were to be removed then these patients would be dependent on dialysis for their entire lifespan.

Patients aged 40-44 years undergoing dialysis, the average survival rate is 8 years. Patients aged 60-64 years the average survival rate being 4.5 years and this decrease in survival rate is mostly due to cardiovascular compromise (7). This consideration is most obvious in younger patients and those with hereditary history (2).

Various retrospective studies comparing PN and RN showed no difference in cancer specific survival and rate to distant metastasis at long-term followup. But there was greater renal function preservation with PN (8) along with a lower risk of recurrence rates. Earlier there was some concern over local recurrence and the need for a wider resection margin with PN. But it was found that local recurrence rates with PN was rare and occurred only in the presence of grossly positive surgical margins and these concerns were no longer found to be valid (8). Hence, PN was found to provide equivalent oncological outcomes to RN for renal tumours < 4cm (T1a) and tumours < 7cm (T1b) (9).

Another advantage of PN is the significant reduction in risk of inducing chronic renal failure when NSS was performed (9). Studies comparing radical and partial nephrectomy, have demonstrated a significantly reduced risk of chronic renal insufficiency using nephron-sparing surgery (10). In the event of recurrence, and patient needing systemic drug treatment, a satisfactory renal function is essential and here the PN may be favoured over RN (10).

RCC in VHL where the tumours are small can be monitored by imaging and for tumours ranging in size from 2.5-3cm, NSS in the form of partial nephrectomy can be performed (11).

PN is generally performed with regional ischemia to allow tumor resection to be performed in a nearly bloodless field. Several techniques have been described for tumor resection with limited ischemic duration or without ischemia. Nevertheless, for more complex situations regional ischemia is required and may exceed the 30-min limit that has commonly been considered the safe duration for warm ischemia. Ischemia intervals of less than 20 mins have been associated with improved outcomes for OPN performed in functionally solitary kidneys. There is a slight decrease in the expected nadir GFR when the warm ischemia is more than 20-25 mins. However, further prolonging the ischemic time can decrease the renal function by the minute. Early unclamping significantly decreases ischemia time by more than 50% with a trend toward decreased post-operative complications (12).

The risk of local tumour recurrence is one of the major disadvantage following NSS. For smaller sized tumours (3-4 cm in diameter), the local recurrence is found to be lower. It has been reported to have an incidence of 4-6% mostly and some even as high as 16% (11). The possible reasons for tumour recurrence are incomplete surgical margin, multifocal preexisting tumours, tumour spillage, and new tumour growth. RN has a major advantage in this issue as local recurrence rate is uncommon for localised RCC (9).

Microscopic PSMs on final pathology can be managed expectantly without immediate additional treatment or compromised long term outcome. 5-year freedom from local recurrence for patients with negative margins is 97% and for those with positive margins 98%. A 10-year probability of freedom from metastatic progression is 93% for patients with negative margins and 95% for those with positive margins. PSMs should not be used as a measure of oncological outcome and moreover they have not been found to increase the long-term risk of local recurrence nor metastasis. Patients with positive surgical margins can be safely monitored and will not have any bearing on the long-term disease-free survival (13). Though NSS might show improved outcomes in good hands, there may be some surgical morbidities like increase incidence of urine leakage, postoperative bleeding, obstruction of pelviureteric junction (8) which can be minimised by performing laparoscopic partial nephrectomy (14), but for which no difference was observed in the oncological outcomes.

Conclusion

With the advent of improved imaging techniques, the diagnosis of RCC in VHL in early stages can be made much before the actual onset of metastasis. Hence, NSS in bilateral involvement is gold standard of treatment of small RCC to preserve renal function.

References

1. Jonasch E, Matin S, Wood CG, Pagliaro LC. Renal Cell Carnicoma. In: MD Anderson Manual of Clinical Oncology. McGraw-Hill. New York, 2000, p- 757-84.

2. Mario Alvarez Maestro, Luis Martinez-Piñeiro and Emilio Rios Gonzalez. Renal Tumors in Patients with von Hippel-Lindau Disease: “State of Art Review”. In: Renal Cell Carcinoma. Edited by Dr. Hendrik Van Poppel. In Tech Publishers, December 2011, p- 93-110.

3. Pepper K, Jaowattana U, Starsiak MD, et al. Renal Cell Carcinoma presenting with paraneoplastic hypercalcemic coma: a case report and review of the literature. J Gen Intern Med 2007; 22(7): 1042-6.

4. Pavesi G, Feletti A, Berlucchi S, et al. Neurosurgical treatment of von Hippel-Lindau-associated hemangioblastomas: benefits, risks and outcome. J Neurosurg Sci 2008; 52(2): 29-36.

5. Andonian S1, Janetschek G, Lee BR. Laparoscopic partial nephrectomy: an update on contemporary issues. Urol Clin North Am 2008; 35(3): 385-96.

6. Joniau S, Vander Eeckt K, Van Poppel H. The indications for partial nephrectomy in the treatment of renal cell carcinoma. Nat Clin Pract Urol 2006; 3(4): 198-205.

7. United States Renal Data System. Excerpts from USRDS 2009 Annual Data Report. U.S. Department of Health and Human Services. The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Am J Kidney Dis 2010; 55(Supply 1): S1.

8. Medina-Polo J, Romero-Otero J, Rodríguez-Antolín A, et al. Can partial nephrectomy preserve renal function and modify survival in comparison with radical nephrectomy? Scand J Urol Nephrol 2011; 45(2): 143-50.

9. Ljungberg B. Nephron-sparing surgery–strategies for partial nephrectomy in renal cell carcinoma. Scand J Surg 2004; 93(2): 126-31.

10. Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H. Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. Mayo Clin Proc 2000; 75(12): 1236-42.

11. Volpe A, Cadeddu JA, Cestari A, et al. Contemporary management of small renal masses. Eur Urol 2011; 60(3): 501-15.

12. Lane BR, Fergany AF, Weight CJ, Campbell SC. Renal functional outcomes after partial nephrectomy with extended ischemic intervals are better than after radical rephrectomy. J Urol 2010; 184(4): 1286-90.

13. Yossepowitch O, Thompson RH, Leibovich BC, et al. Positive surgical margins at partial

nephrectomy: predictors and oncological outcomes. J Urol 2008; 179(6): 2158-63.

14. Pietzak EJ, Guzzo TJ. Advancements in laparoscopic partial nephrectomy: expanding the feasibility of nephron-sparing. Adv Urol 2012; 148952.