Solitary Liver Metastasis of Renal Cell Carcinoma 8 Years After Nephrectomy

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Case Report

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Abstract

Background: Renal cell carcinoma (RCC) is the most common renal malignancy in adults. RCC can metastasize to various organs of the human body, including lung, bone, brain, liver, and adrenal gland. However, solitary metastases are relatively rare in clinical practice, and surgical treatment is still the preferred treatment.

Case report: We present a 68-year-old male patient who was performed laparoscopic radical left nephrectomy for RCC 8 years ago. Postoperative routine examination revealed an occupying lesion in the liver. Further PET-CT suggested hepatic metastasis of RCC thus undergoing laparoscopic left hepatectomy. Pathology confirmed metastatic RCC in the liver. The patient recovered well after the operation, and there was no sign of recurrence during the follow-up for six months after the operation.

Conclusion: Patients with renal carcinoma can still have recurrence and metastasis after radical nephrectomy for many years. Therefore, long-term close follow-up is beneficial to patients with radical nephrectomy.

Introduction

RCC is a malignancy that is prone to early metastasis, with approximately 33% of RCC patients having distant metastases by the time they are detected [1]. RCC usually metastasizes to the lungs (45.2%), bones (29.5%), lymph nodes (20.8%), liver (20.3%), adrenal glands (8.9%), and brain (8.1%) [1]. Distant metastases occur in more than 50% of patients after surgery for RCC over a 5-year follow-up period [2]. Patients with advanced RCC have a poor prognosis, with an average survival time of 16 months; the 1-year survival rate is 73%, but the 5-year survival rate is only 10% [3]. Patients with metastatic RCC often have larger tumors, a higher number of metastases, and the invasion of multiple organs makes them inoperable, resulting in a poor prognosis for patients.

It has been proven that RCC is insensitive to chemotherapy, radiotherapy and hormone therapy; it responds well to immunotherapy, especially interferon combined with interleukin can significantly prolong the survival time of patients with renal carcinoma [4]. For patients with renal carcinoma combined with a single metastasis, surgical resection is preferred treatment. We report a case of a patient with laparoscopic resection of liver metastases who underwent nephrectomy for renal carcinoma 8 years ago.

Case Report

This patient, a 68-year-old male, had a history of "hypertension" for 40 years; he underwent laparoscopic left nephrectomy for clear cell renal carcinoma 8 years ago. The patient's abdominal CT, chest CT and tumor markers were reexamined every six months for five years after surgery and no abnormalities were found. Color Ultrasound of the liver at last visit revealed a liver low-density space occupying (no images could be taken); an enhanced MR of the upper abdomen then suggested a solitary mass in segment 4 of the liver (Figure 1). PET-CT, showed changes of clear cell carcinoma after resection, found no clear signs
of recurrence in the area of surgery, but an occupying lesion in the left lobe of liver with elevated PDG metabolism, which was considered a liver metastasis (Figure 2). The patient was administered a laparoscopic left liver resection (Figure 3). Postoperative immunohistochemistry staining was negative for Hepacyte and positive for vimentin, CD10 and CK (Figure 4), suggesting that the liver tumor originated from the clear cell carcinoma of kidney that had been excised 8 years ago. The patient recovered well after the operation, and there was no sign of recurrence during the follow-up for six months after the operation.

**Discussion**

It is estimated that there are approximately 295,000 new cases of RCC worldwide, with only 134,000 patients able to be diagnosed [5-7]. The ratio of male to female is close to 2:1 [8]. The average age of patients diagnosed is 64 years [9]. The incidence of kidney cancer is increasing every year along with the increase in obesity rate [10]. A third of new kidney cancer patients already have distant metastases, and another third still develop subsequent multiple metastases that are untreatable after RCC resection. In fact, the 5-year survival rate for patients with renal carcinoma is only 13% due to multiple metastases and underlying disease [11]. Clinical data show that patients with delayed metastases have a better prognosis than patients with concurrent metastases in renal carcinoma. The median survival time of patients with untreated advanced kidney cancer is 4 months, while the one-year survival rate is only 10% [12]; therefore, primary and metastatic lesions should be treated as much as possible [13, 14]. Clinical data from Talarico and Skinner showed a median survival was 33 months for patients with metastases within 1 year of kidney cancer resection; and 55 months for patients with metastases after 1 year [15, 16]. Kozlowski et al. reported that only 2-4% of patients with liver metastases from kidney cancer had access to surgery [17]. In 1939, Barney first reported lung metastasis occurred in patients with renal cancer after resecting primary lesion by surgical treatment for 23 years [18].

According to the data reported in various articles, although surgical resection is the basic treatment for liver metastasis of renal carcinoma, the therapeutic effect has not been fully affirmed. This uncertainty is mainly due to the small number of reported cases and a large number of variables. The 3-and 5-year survival rates of patients with single metastatic tumor after surgical resection were 45% and 34%, respectively [19]. The perioperative mortality rate in each center ranged from 3 to 31%, depending on the number of metastases and the surgical approach.

With the development of targeted therapy in recent years, RCC treatment has become one of the most successful cases in cancer research. These drugs include VGF and MTOR, as well as new immunooncology drugs [20]. Patients with metastatic RCC have spontaneously resolved metastases after surgical removal of the primary tumor, suggesting that RCC may be a good immunotherapy disease [21, 22]. Cytokines, interleukin-2 and interferon can effectively treat some patients. These new immunotherapies are becoming more and more important in the treatment of renal carcinoma. Although these methods are still in clinical trials, their successful applications in other types of cancer suggests that they may ultimately be beneficial for renal carcinoma patients. Immunotherapy, particularly immune
monitoring site inhibitors such as PD1 antibodies and anti-PDL1 antibodies, has shown promising results in the treatment of renal carcinoma [23-25]. The therapeutic efficacy of metastatic renal carcinoma has been improved significantly in the past decade or so due to the emergence of new tumor therapies. Although various treatments are still in the experimental stage, the results are inspiring. Surgical resection combined with immunotherapy significantly increased survival in patients with metastatic renal cancer.

In this article, we first report the application of laparoscopic techniques in the surgical treatment of patients with single liver metastases of RCC. Interferon and PD1 antibody were given after operation. At present, no obvious recurrence or metastasis was observed during the 6-month follow-up. With the development of endoscopic technology, more treatment options will be available for patients with less trauma and faster recovery. Due to the small number of cases and lack of more clinical observation data, its long-term effects need further observation.

Conclusion

RCC patients can still have recurrence and metastasis many years after radical nephrectomy. Therefore, it is beneficial to carry out long-term close follow-up for patients with renal cancer after radical surgery. Any space-occupying lesion found in each organ should be further examined for metastases. In addition, patients have less pain and faster recovery after laparoscopic treatment.

Abbreviations

RCC
Renal cell carcinoma

Declarations

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Consent for publication: The parents of patient agreed to publication of this case.

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

References

1. Bianchi M, Sun M, Jeldres C, et al. Distribution of metastatic sites in renal cell carcinoma: a population-based analysis. Ann of Oncol. 2012;23(4):973–80.
2. Matveev VB, Gurari LL, Began-Bogatskii KM. Surgical treatment of late metastases of kidney cancer. Urol Nefrol (Mosk). 1999;2:51–2.
3. Giuliani L, Giberti C, Martorana G, et al. Radical extensive surgery for renal cell carcinoma: Long-term results and prognostic factors. J Urol. 1990;143(3):468–73.
4. Flanigan RC, Salmon SE, Blumenstein BA, Bearman SI, Roy V, McGrath PC, Caton JR Jr, Munshi N, Crawford ED. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. N Engl J Med. 2001;345:1655–659.
5. Hsieh JJ, Purdue MP, Signoretti S, et al. Renal cell carcinoma. Nat Rev Dis Primers. 2017 Mar 09;3:17009. [PMC free article] [PubMed].
6. Méndez-Vidal MJ, Molina Á, Anido U, et al. Evidence review and clinical practice in the management of advanced renal cell carcinoma. BMC Pharmacol Toxicol. 2018 Nov 26;19(1):77. [PMC free article] [PubMed].
7. Trotta AM, Santagata S, Zanotta S, et al. Mutated Von Hippel-Lindau-renal cell carcinoma (RCC) promotes patients specific natural killer (NK) cytotoxicity. J Exp Clin Cancer Res. 2018 Dec 04;37(1):297. [PMC free article] [PubMed].
8. Mancini M, Righetto M, Baggio G. Gender-Related Approach to Kidney Cancer Management: Moving Forward. Int J Mol Sci. 2020 May 10;21(9) [PMC free article] [PubMed].
9. Maher ER. Hereditary renal cell carcinoma syndromes: diagnosis, surveillance and management. World J Urol. 2018 Dec;36(12):1891–8. [PMC free article] [PubMed].
10. Gati A, Koudhi S, Marrakchi R, et al. Obesity and renal cancer: Role of adipokines in the tumor-immune system conflict. Oncoimmunology. 2014 Jan 01;3(1):e27810. [PMC free article] [PubMed].
11. Stief CG, Jähne J, Hagemann JH, et al. Surgery for metachronous solitary liver metastases of renal cell carcinoma. J Urol. 1997;158(2):375–77.
12. Rafla S. Renal cell carcinoma: Natural history and results of treatment. Cancer. 1970;25:26–40.
13. O’dea MJ, Zincke H, Utz DC, et al. The treatment of renal cell carcinoma with solitary metastasis. J Urol. 1978;120:540–42.
14. Talarico F, Buli P, Iusco D, et al. Synchronous right nephrectomy, left kidney tumorectomy, right lateral hepatic sectorectomy and inferior vena cava thrombectomy for metastatic clear cell renal carcinoma: Report of a case and review of the literature. Ann Ital Chir. 2013;84:209–12.
15. Talarico F, Buli P, Iusco D, et al. Synchronous nephrectomy and right hepatectomy for metastatic chromophobe renal cell carcinoma: Report of a case and review of the literature. Chir Ital. 2007;59(2):257–61.
16. Skinner DG, Colvin RB, Vermillion CD, et al. Diagnosis and management of renal cell carcinoma. A clinical and pathologic study of 309 cases. Cancer. 1971;28:1165–177.
17. Kozlowski JM. Management of distant solitary recurrence in the patient with renal cancer. Contralateral kidney and other sites. Urol Clin North Am. 1994;21(4):601–24.
18. Barney JD, Dellinger Barney J, Churchill EJ. Adenocarcinoma of the kidney with metastasis to the lung: cured by nephrectomy and lobectomy. J Urol. 1939;42:269–76.
19. Tolia BM, Whitmore WF Jr. Solitary metastases from renal cell carcinoma. J Urol. 1975;114(6):836–38.
20. Graham J, Heng DYC, Brugarolas J, et al. Personalized management of advanced kidney cancer. Am Soc Clin Oncol Educ Book. 2018;23:330–41.
21. Guttermann JU, Fine S, Quesada J, et al. Recombinant leukocyte A interferon: pharmacokinetics, single-dose tolerance, and biologic effects in cancer patients. Ann Intern Med. 1982;96:549–56.
22. Scanlan M, Gordan JD, Williamson B, et al. Antigens recognized by autologous antibody in patients with renal-cell carcinoma. Int J Cancer. 1999;83:456–64.
23. Drake CG, Lipson EJ, Brahmer JR. Breathing new life into immunotherapy: review of melanoma, lung and kidney cancer. Nat Rev Clin Oncol. 2014;11:24–37.
24. Hammers H. Immunotherapy in kidney cancer: the past, present, and future. Curr Opin Urol. 2016;26:543–7.
25. Nazzani S, Bazinet A, Karakiewicz PI. Role of immunotherapy in kidney cancer. Curr Opin Support Palliat Care. 2018;12:325–33.

Figures
Figure 1

The left lobe of liver showed occupied solitary mass by enhanced MR, as indicated by the arrow.

Figure 2

PET-CT showed no clear signs in the area of surgery, and elevated PDG metabolism in the left lobe of liver, as indicated by the arrow.

Figure 3

Laparoscopic left hemihepatectomy
Figure 4

Pathological findings revealed metastatic renal clear renal cell carcinoma in the liver

Supplementary Files

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