

## Pulmonary Metastasis from Renal Cell Carcinoma 21 Years after Nephrectomy

### Authors

Motohisa Kuwahara<sup>1</sup>,  
Nobutoshi Kawagoe<sup>2</sup>,  
Hiroshi Koga<sup>3</sup>, Hirohisa  
Yano<sup>4</sup>, Akinori Iwasaki<sup>5</sup>

<sup>1</sup>Department of Chest  
Surgery, Takagi Hospital,  
141-11 Sakami, Okawa-shi,  
Fukuoka, Japan, 831-0016

<sup>2</sup>Division of Urology,  
Saiseikai Futsukaichi  
Hospital, 3-13-1 Yu-machi,  
Chikushino-shi, Fukuoka,  
Japan, 818-8516

<sup>3</sup>Department of Urology,  
Harasanshin Hospital, 1-8  
daihaku-machi, Hakata-ku,  
Fukuoka-shi, Fukuoka, Japan,  
812-0033

<sup>4</sup>Department of Pathology,  
School of medicine, Kurume  
University, 67 Asahi-machi,  
Kurume-shi, Fukuoka, Japan,  
830-0011

<sup>5</sup>Department of General  
Thoracic Surgery, School of  
medicine, Fukuoka University,  
7-45-1 Nanakuma, Johnan-ku,  
Fukuoka-shi, Fukuoka, Japan,  
814-0180

Corresponding Author:

Motohisa Kuwahara, Department of General Thoracic  
Surgery, Takagi Hospital, 141-11 Sakami, Okawa-shi,  
Fukuoka, Japan, 831-0016, E-mail:  
KHC03152@nifty.com

### Abstract:

This research reports a case of pulmonary metastasis from renal cell carcinoma with a disease free interval of 21-years. The patient at 44-years old underwent a left nephrectomy for clear cell cancer from renal cell carcinoma. The patient who visited an outpatient clinic in our hospital due to hypnagogic pollakiuria was diagnosed of benign prostate hyperplasia and the neurologic bladder, and received medication till 61-years-old. The patient was thereafter diagnosed of degeneration of cerebral basal ganglions in another hospital and was suspected to have prostate cancer, hence systemic examination and transrectal prostate biopsy was performed. Computed tomography (CT) revealed a well-defined, homogeneous nodular shadow, 6.6 mm in size, at the right lower lobe. From the CT, the nodule had become enlarged to a maximal diameter 7.9 mm at age 65-years-old. Surgical biopsy was performed from 8 cm surgical wounds using a thoracoscope. The tumor was palpable and then resected by staplers, and were well defined and yellowish in color. The pathological examination revealed that almost all the tumor cell were clear cell cancer from renal cell carcinoma. A few cases of recurrent renal cell carcinoma after a long interval from initial diagnosis have been seen.

**Key Words:** Metastasectomy, Renal Cell Carcinoma, Clear cell carcinoma, Lung Metastasis

## Introduction

Although pulmonary metastases of renal cell carcinoma (RCC) constitute the majority of cancer recurrences following nephrectomy, an overall 5-year cancer specific survival (CSS) rate for RCC of all stages was 60.4% (1). Surveillance, epidemiology, and result stage-specific 5-year CSS rates were 87.0% for localized stage, 62.9% for regional stage, and 9.3% for distant stage. The most common sites of metastases were lung (45.2%), bone (29.5%), lymph nodes (21.8%), liver (20.3%), adrenal (8.9%) and brain (8.1%) (2). The median time to relapse was shown to be within 1–2 years, with most recurrences occurring <3 years after surgery (3, 4). Several case reports exist in the literature of recurrences occur 10 years or more after initial nephrectomy; however, recurrences occurring after a longer time interval generally. There is a fair number of literature reports of clinical studies of metastasectomy performed in these sites with several cases of these being in the lung. However, late recurrences were almost written for ten years. Over 20 year's pulmonary resection after renal surgery were evident in a few cases. Thus we report here a case of 20 year's pulmonary resection after renal surgery.

## Case Report

A 67-year-old man underwent left nephrectomy and was Histopathologically diagnosed with RCC. The patient underwent medical checkups every 6 months for 4 years,

and was reported to be in good health. The patient visited an outpatient clinic in our hospital due to hypnagogic pollakiuria and was diagnosed of benign prostate hyperplasia with neurologic bladder, and received medication at age 61-years old. The patient was subsequently diagnosed of degeneration of cerebral basal ganglions in another hospital and was followed-up every two months by the urologist in our hospital, and his prostate specific antigen (PSA) was elevated to 5.175 ng/ ml at 63 years old. The patient was suspected to have prostate cancer, hence systemic examination and transrectal prostate biopsy was performed. No atypical cell in the biopsy specimens was observed. Therefore the chest CT revealed a well-defined, homogeneous nodular shadow, 6.6 mm in size, at the right lower lobe (Figure 1A). A half year later, the urologist followed-up on chest CT, which revealed that the tumor enlarged at 7.3 mm in size (Figure 1B). The urologist consulted a chest physician and bronchoscopy revealed no unusual finding, and bronchoscopic biopsy specimens showed no specific findings, and as a result the chest physician consulted a surgeon. The patient was moved into our examination room on a wheel chair as a reticent person suffering from the degeneration of cerebral basal ganglions. Additional examination was difficult, which was then followed by chest CT. Half a year after PSA was elevated to 5.939 ng/ml, the patient was admitted to our hospital for transrectal prostate biopsy, and

no atypical cell was detected in the biopsy specimens.

During the period of hospital admission, the patient was observed to live without any threat, disturbance or making any strange sound. The nodule had become enlarged to a maximal diameter 7.9 mm from the CT (Figure 1C). The patient was tolerable for partial resection of the lung by the previous admission status, thus the family consented to a surgical procedure. Surgical biopsy performed did not reveal the nodule thoracoscopically; hence additional 8 cm surgical wounds were made. The tumor was palpable and then resected by staplers, and were well defined and yellowish in color (Figure 2A). Intraoperative pathological examination revealed that almost the entire tumor cells were clear cell cancer and as a result, the resected tumor was diagnosed as a metastasis from probable RCC. The patient was discharged 9 days after partial resection without any unusual events and the confirmative pathological specimens were same result as confirmed by the hospital (Figure 2B, C). The summary and pathological records were kept; renal surgery was performed for the clear cell cancer of RCC and ten times cytokine therapies. The urologist notified the family of the choice of cytokine therapy, kinase inhibitor therapy or observation, and the family chose the observation without additional treatments. After pulmonary resection, follow-up care was provided at the urologist out-patient clinic for 6 months. The degeneration of

cerebral basal ganglions was evaluated, and aspiration pneumonia was detected. The patient thus received tracheostomy and then moved to a sanatorium.

### Discussion

Following surgery, total survival rates in patients whose RCC underwent surgery for localized and locally advanced disease were 96.1%, 88.2% and 78.3% for one, three and five years, respectively (3). Recurrent rate was calculated in patients who underwent surgery for localized or locally advanced disease. The total RRs at one, three, and five years were 4.5%, 13% and 22%, respectively. T-stage was a significant predictor of recurrence with HR 13.5, HR = 7.1, and HR = 3.9 for T-stage (T3-T4), T2 stage (T2a-T2b), and T1b compared with stage T1a, respectively.

In general, RCC behaves similarly to most malignancies, with the greatest risk of recurrence occurring early (4). The median time to relapse was shown to be within 1–2 years, with most recurrences occurring <3 years after surgery. Several case reports exist in the literature of recurrences occurring 10 years or more after initial nephrectomy; however, recurrences occurring after a longer time interval generally appeared to be associated with a better prognosis. RCC metastases most commonly appear in the lungs (38–80% of patients with metastasis), bone (most often in the axial skeleton; 20–49% of patients), liver (9–40% of patients), adrenal glands (8–

11% of patients), brain (2–15% patients), and skin and subcutaneous tissue (2–13% of patients)(5). Therefore, there is a fair number of literature reports of clinical studies of metastasectomy performed in these sites with several cases of these being in the lung. Previous studies have demonstrated 5-year survival rates of 36.9% after pulmonary metastasectomy from RCC (6). Previously investigated significant prognostic factors that influence survival include complete resection, number of metastases, DFI, and lymph node status. Whether chest surveillance should be performed using X-ray or CT scan is also debatable; many researchers have recommended the use of chest X-ray (5). It is well known that chest X-rays underestimate pulmonary metastases and detect them at a more advanced stage than CT scan; even if chest CT scan is more expensive than X-ray. In our case, the patient underwent frequent medical checkups for four years, and the patient had been healthy except the hypnagogic pollakiuria and degeneration of cerebral basal ganglions without recurrences for 21 years.

The pulmonary metastasis of 7.9 mm in maximum diameter at the time of the last checkup by chest CT was, however, resectable because of being a solitary tumor and having no other metastasis

including lymph node adenopathy.

In RCC, late relapses after nephrectomy, as well as a few cases of spontaneous regressions, suggest that host immune reactions may be important in regulating tumor growth. The host immune reactions may vary in long-term views in this case, affected by repeated aspiration pneumonia causes. Therefore, it is necessary to carefully follow up cases of RCC, even two of the promising preliminary results obtained with cytokine treatments emphasize the need for early identification of recurrence and thus for rational follow-up protocols; but in this case, four years follow up were insufficient. There is the group pulmonary metastasis needing lobectomy and lymphadenectomy but we believe that partial resection is sufficient for a small size metastasis (7).

The late recurrences were almost written for ten years (8). Over twenty year's pulmonary resection after renal surgery were evident in a few cases (9-12) and diagnosed cases were rare (13, 14).

#### **Conflict of Interest Statement**

The authors declare that they have no conflicts of interest.

## References

1. Gandaglia G, Ravi P, Abdollah F, Abd-El-Barr AE, Becker A, Popa I, et al. Contemporary incidence and mortality rates of kidney cancer in the United States. *Canadian Urological Association journal = Journal de l'Association des urologues du Canada*. 2014;8(7-8):247-52.
2. Bianchi M, Sun M, Jeldres C, Shariat SF, Trinh QD, Briganti A, et al. Distribution of metastatic sites in renal cell carcinoma: a population-based analysis. *Annals of oncology : official journal of the European Society for Medical Oncology*. 2012;23(4):973-80.
3. Azawi NH, Tesfalem H, Mosholt KS, Hoyerup P, Jensen ES, Malchau E, et al. Recurrence rates and survival in a Danish cohort with renal cell carcinoma. *Danish medical journal*. 2016;63(4):A5208.
4. Williamson TJ, Pearson JR, Ischia J, Bolton DM, Lawrentschuk N. Guideline of guidelines: follow-up after nephrectomy for renal cell carcinoma. *BJU international*. 2016;117(4):555-62.
5. Rouviere O, Bouvier R, Negrier S, Badet L, Lyonnet D. Nonmetastatic renal-cell carcinoma: is it really possible to define rational guidelines for post-treatment follow-up? *Nature clinical practice Oncology*. 2006;3(4):200-13.
6. Pfannschmidt J, Hoffmann H, Muley T, Krysa S, Trainer C, Dienemann H. Prognostic factors for survival after pulmonary resection of metastatic renal cell carcinoma. *The Annals of thoracic surgery*. 2002;74(5):1653-7.
7. Shiono S, Matsutani N, Okumura S, Nakajima J, Horio H, Kohno M, et al. The prognostic impact of lymph-node dissection on lobectomy for pulmonary metastasis. *European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery*. 2015;48(4):616-21; discussion 21.
8. Miyao N, Naito S, Ozono S, Shinohara N, Masumori N, Igarashi T, et al. Late recurrence of renal cell carcinoma: retrospective and collaborative study of the Japanese Society of Renal Cancer. *Urology*. 2011;77(2):379-84.
9. Donaldson JC, Slease RB, DuFour DR, Saltzman AR. Metastatic renal cell carcinoma 24 years after nephrectomy. *Jama*. 1976;236(8):950-1.
10. Shiono S, Yoshida J, Nishimura M, Nitadori J, Ishii G, Nishiwaki Y, et al. Late pulmonary metastasis of renal cell carcinoma resected 25 years after nephrectomy. *Japanese journal of clinical oncology*. 2004;34(1):46-9.

11. Watanabe Y, Harada A, Aoki M, Kamimura G, Wakida K, Nagata T, et al. Pulmonary Metastasectomy 31 Years After Surgery for Renal Cell Carcinoma. The Annals of thoracic surgery. 2015;99(6):2195-7.
12. Kaneko M, Matsumoto S, Tahara H, Ishii T, Uemura H. [Pulmonary metastasis of renal cell carcinoma 20 years after nephrectomy]. Hinyokika kiyo Acta urologica Japonica. 2006;52(12):929-31.
13. Piscioli F, Pojer A, Pusioli T, Luciani L. Diagnosis by aspiration biopsy of lung metastasis of renal cell carcinoma 24 years after nephrectomy. European urology. 1984;10(5):358-60.
14. Bradham RR, Wannamaker CC, Pratt-Thomas HR. Renal cell carcinoma metastases 25 years after nephrectomy. Jama. 1973;223(8):921-2.

Figures legends

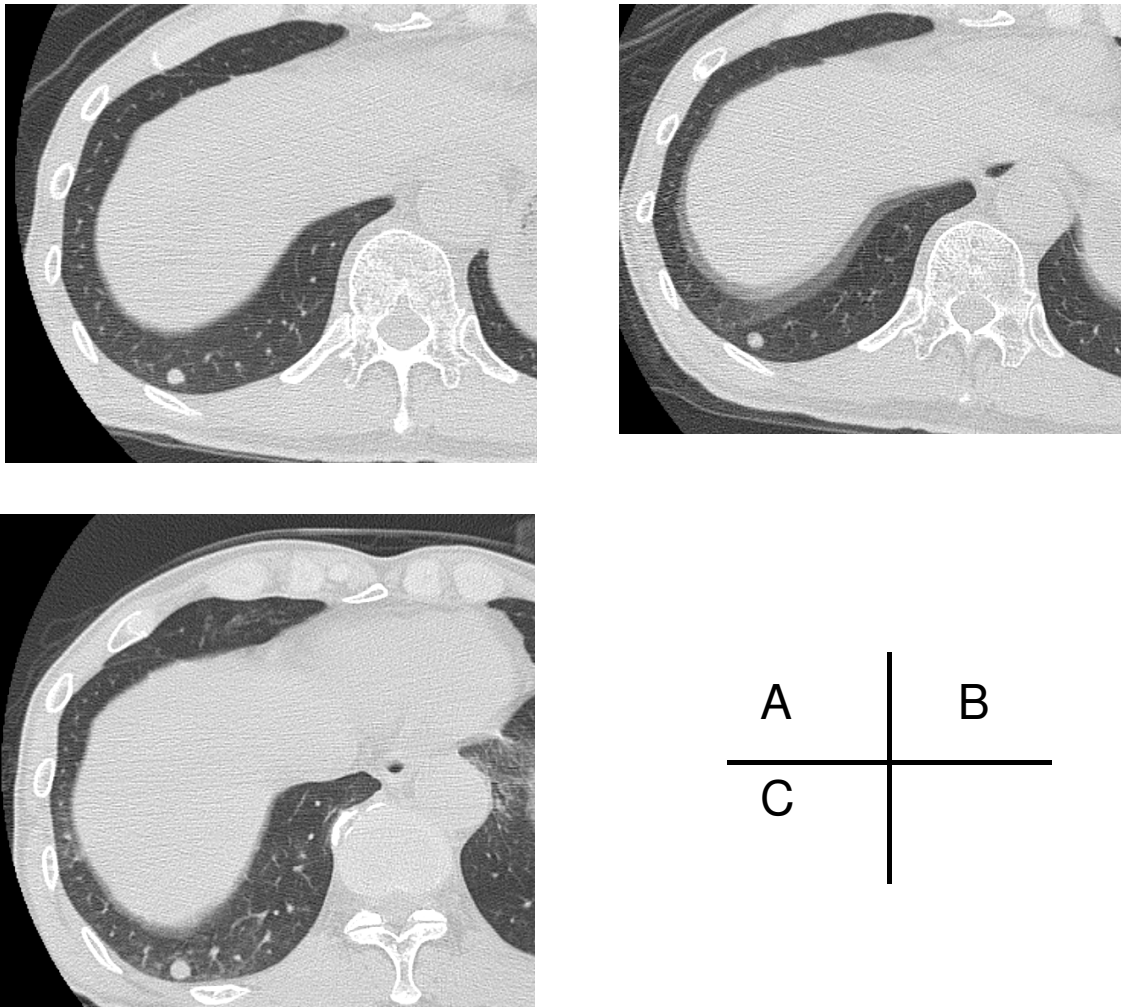


Figure 1

About 6 months interval follow up, CTs demonstrated a well-defined, homogeneous nodular shadow, 6.6 mm in size at the right lower lobe (A), 7.3 mm (B), which become enlarged to a maximal diameter 7.9 mm (C).



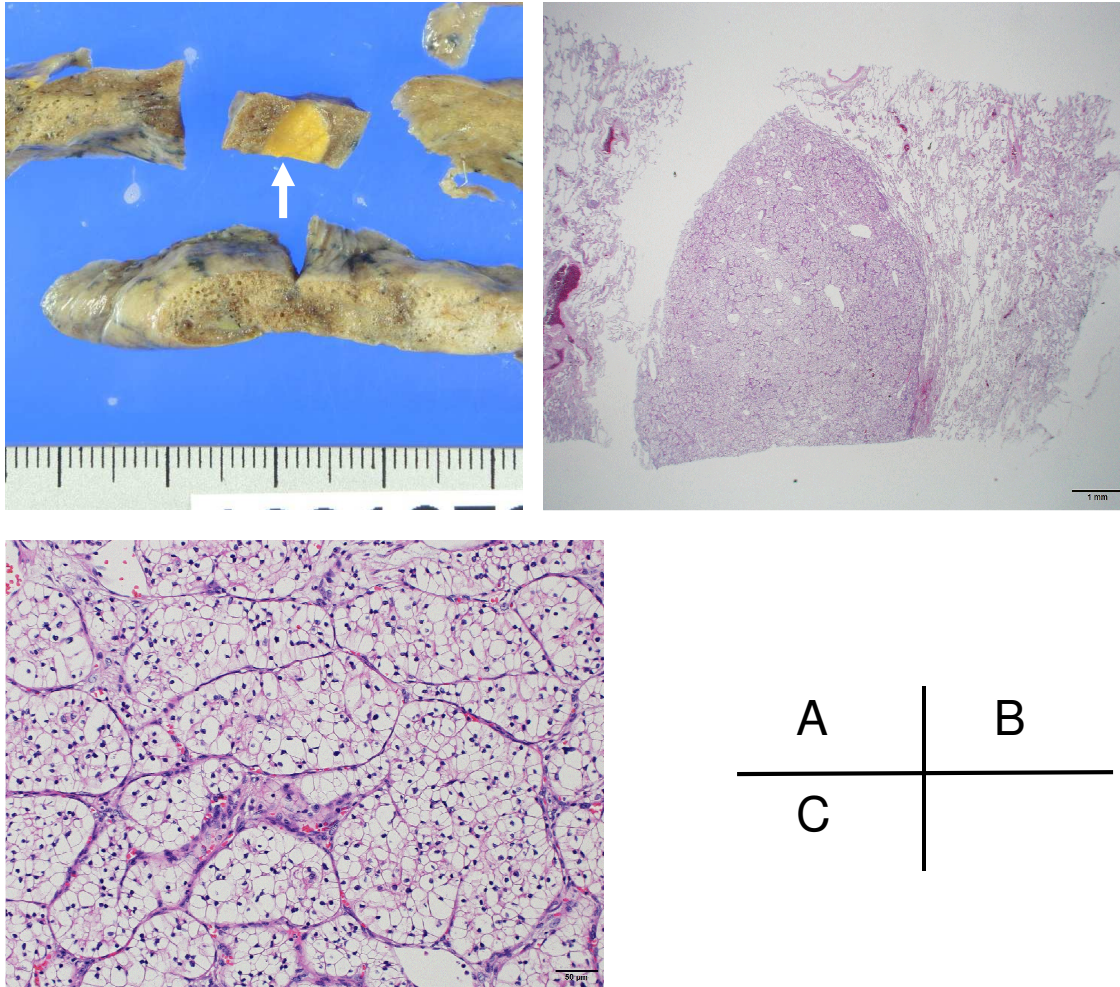


Figure 2

The tumor was well defined and yellowish in color (A), the tumor cell were clear cell cancer and as a result the resected tumor was diagnosed as a metastasis from renal cell cancer (B, C).



Author	Year	Period	Diagnosis	Resection
Bradham, R. R.	1973	25	Bronchoscope	none
Donaldson, J. C.	1976	24	Surgery	left lower lobectomy right wedge resection
Piscioli, F.	1984	24	Fine needle aspiration cytology	none
Shiono, S.	2004	25	Surgery	wedge resection
Kaneko, M.	2006	20	Surgery	wedge resection
Watanabe, Y.	2015	31	Surgery	wedge resection
Our case	2017	21	Surgery	wedge resection

Table: Over twenty year's pulmonary metastases from renal cell cancer