

# Lung Metastasis From Renal Cell Carcinoma 16 years After Nephrectomy: A Case Report and Review of the Literature

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## Abstract

Recurrence rate of renal cell carcinoma in the lungs after five years of nephrectomy is 93%. The occurrence of RCC after 16 years of nephrectomy as pulmonary metastasis is rare and needs to be considered in patient presenting with pulmonary nodules after a long interval since nephrectomy.

## INTRODUCTION

Renal Cell Carcinoma (RCC) accounts for 3% of all adult cancers and 85% of all kidney tumors making it the most common renal malignancy [1]. With an incidence rate of 14.5 per 100,000, RCC is the seventh most common solid cancer and comprises 3-5% of all adult malignancies[1, 2]. It has a high recurrence rate of 93% in the first five years after nephrectomy[3]. Lungs are the most common site for distant metastasis (50-60%). The median time to recurrence is 15-18 months after nephrectomy. Eighty-five percent of the relapse cases occur within 3 years of nephrectomy[4].

Here we report a rare case of RCC that presented with lung metastasis 16 years after nephrectomy. Based on our literature review, we found only ten reported cases with intervals longer than in our case between nephrectomy for RCC and lung metastasis: 17 years [5], 19 years[6], six cases with 20-28 years intervals [7], 31 years[8], and 37 years[9].

## CASE REPORT

A 70-year-old male presented with mild throat and chest discomfort for four months. A chest x-ray was performed which demonstrated a left upper lobe opacity. On further imaging, contrast-enhanced computed tomography (CECT) chest demonstrated a heterogeneously enhancing oval soft tissue density lesion (3x3x2.9 cm) with a lobulated outline and slight speculation at places involving the apicoposterior segment of the upper lobe of the left lung. Bronchoscopy demonstrated normal findings. He had a history of renal cell carcinoma for which he underwent a right nephrectomy 16 years ago, vertebral fusion surgery 24 years ago, and cholecystectomy 17 years ago. He did not have a history of smoking. The patient was then re-evaluated at our center with a CECT chest and abdomen which showed a 3x3x3.2 cm lesion in the left upper lobe of the lung without enlarged mediastinal lymph nodes. There was no visible recurrence in the right kidney bed. (Figure-1)

CT-guided tru-cut biopsy from the upper lobe of the left lung lesion was diagnosed as clear cell tumor favoring clear cell carcinoma. Later after a month, wedge resection of the left upper lobe of lung was done (Figure-2). Grossly, circumscribed tumor of maximum dimension of 3.5 cm was noted (Figure 3). Histologic sections showed tumor cells arranged in solid sheets and nests. These tumor cells were pleomorphic, polygonal in shape with delineated cell membrane, central nuclei with vesicular chromatin and abundant clear to eosinophilic cytoplasm. Some of the cells showed prominent eosinophilic nucleoli (Figure 4A and 4B). Immunohistochemistry was done to further confirm the diagnosis. On, immunohistochemistry, tumor cells were positive for cytokeratin (CK AE1/AE3), paired box gene (PAX8), cluster of differentiation 10 (CD10), vimentin, and weakly focal positive PAX2 and negative for CK7, CK20, thyroid transcription factor 1 (TTF1) and P40 (Figure 5). The histomorphological features along with immunohistochemical analysis favored the diagnosis of metastatic clear cell renal cell carcinoma.

The postoperative period was uneventful. The patient was stable without any new symptoms at seven months of follow-up.

## DISCUSSION

RCC is the sixth most common malignant tumor in males and the tenth most common malignant tumor in females[10]. RCC recurs after more than 10 years of nephrectomy in 10% of the cases[11]. The most common sites of metastasis include lungs, bones, lymph nodes, adrenal glands, liver, brain contralateral kidney, and pancreas[5]. Metastatic clear cell RCC has a poor prognosis with a median overall survival of 12 months only which has improved in the last decade[12]. Pulmonary metastasis from RCC after a long interval is rare. This is the first case of lung metastasis from renal cell carcinoma that we have encountered in our institution. To our knowledge, this is the first case of lung metastasis secondary to clear cell renal cell carcinoma reported from Nepal to date.

Shiono et al. reported a case with repeated metastasectomy for lung metastasis 16, 24, and 25 years after RCC treatment[7]. Shiono et al. also reported a mini-review of 5 cases of RCC with lung metastasis after 20-28 years of resection of primary neoplasm throughout 1973-1998[7]. Watanabe et al. reported pulmonary metastasectomy after 10 years of nephrectomy. Left upper lobectomy was performed in an 82-year-old patient who was consequently disease-free at 9 months follow-up[8]. Tamburrini et al. reported lung metastasis after 37 years of RCC resection. The patient had a central hilar mass which was suspected as primary lung cancer but histological examination revealed metastatic RCC. Left pneumonectomy was performed in this patient. The patient was recurrence-free at 3 years follow-up[9]. Genand et al. reported solitary lung metastasis in a patient 17 years after nephrectomy for RCC[13].

Disease recurrence likelihood for RCC depends on several known and unknown factors including host and tumor factors[5]. Prognostic indicators for RCC include complete resection of all metastasis, low number of metastasis, long disease-free interval between primary tumor diagnosis and lung lesions, lymph node involvement, and size of pulmonary nodule[9]. Host immune response has been hypothesized to play a role to determine the time for the presentation of RCC metastasis. Duration decreases with compromised immune response[9]. The five and 10-year overall survival rate following pulmonary metastasectomy for metastatic renal cancer was 83% and 41.7% respectively according to Chen et al. [14] and 75% and 59% respectively according to Meacci et al.[15].

## CONCLUSION

Though rare, renal cell carcinoma can present with metastases after a prolonged interval following nephrectomy. In the evaluation of pulmonary nodules, the possibility of metastasis from RCC should be considered in a patient even after a long time with a history of primary RCC. Even though enough data is lacking, metastasectomy is the preferred treatment for pulmonary metastases from RCC.

## ACKNOWLEDGEMENTS

We gratefully acknowledge the work of members of our hospital and the patient.

## ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The hospital research board(HRB) of Nepal Cancer Hospital and Research Center, Harisiddhi, Lalitpur, Nepal provided approval.

## CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient before the submission of the report. The signed Institutional Consent Form is on file.

## CONFLICTS OF INTEREST STATEMENT

The authors declare that there is no potential conflict of interest with respect to the research, authorship, and /or publication of this article.

## FUNDING/FINANCIAL OUTCOMES

None

## AUTHOR'S CONTRIBUTION

ST was involved in counseling, treatment of the patient, and collection of the surgical images and CT-scan chest images. HPD and MS examined and interpreted the pathology. MS and VA collected the required case information, images, slides, reports and contributed to writing manuscripts. MS, VA, ASD, KN, and HPD reviewed the literature and contributed to both writing and editing the manuscript. All authors read and approved the final manuscript.

## DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## LEGENDS

**Figure 1:** CT Scan of the Chest shows a minimally enhancing lesion measuring 3.3x3.2 cm with lobulated margins.

**Figure 2 :** Surgical specimen of the resected lung mass.

**Figure 3 :** Gross specimen: On the cut section, the tumor is circumscribed, nodular and yellowish in appearance.

**Figure 4:** (A) 10x magnification photomicrograph showing clear cell renal cell carcinoma(ccRCC) in lung. (B) 40x photomicrograph showing tumor cells arranged in nests, have a polygonal shape with clear cytoplasm and separated by thin-walled blood vessels.

**Figure 6:** Tumor cells show positivity for pancytokeratin (CK AE1/ AE3), PAX 8, CD10 and vimentin.

## FIGURES :

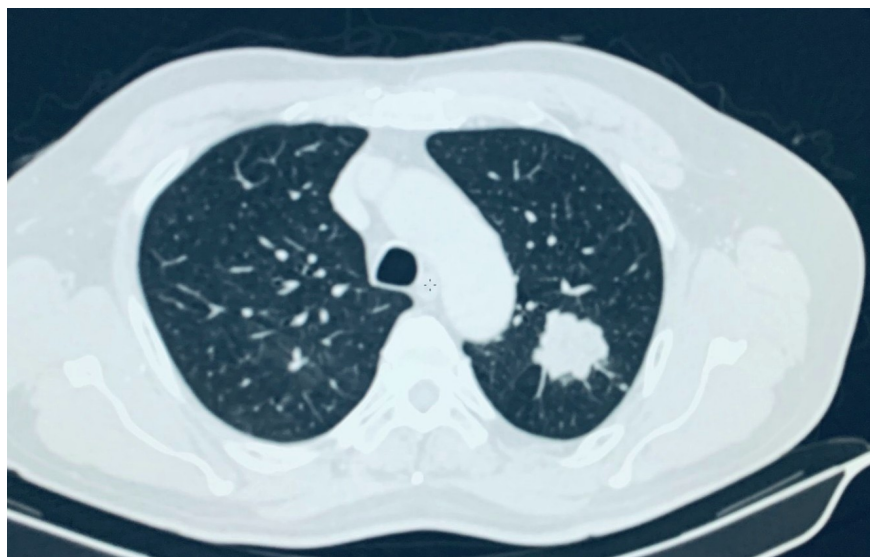


Figure 1: CT Scan of the Chest shows a minimally enhancing lesion measuring 3.3x3.2 cm with lobulated margins(as indicated by white arrow).

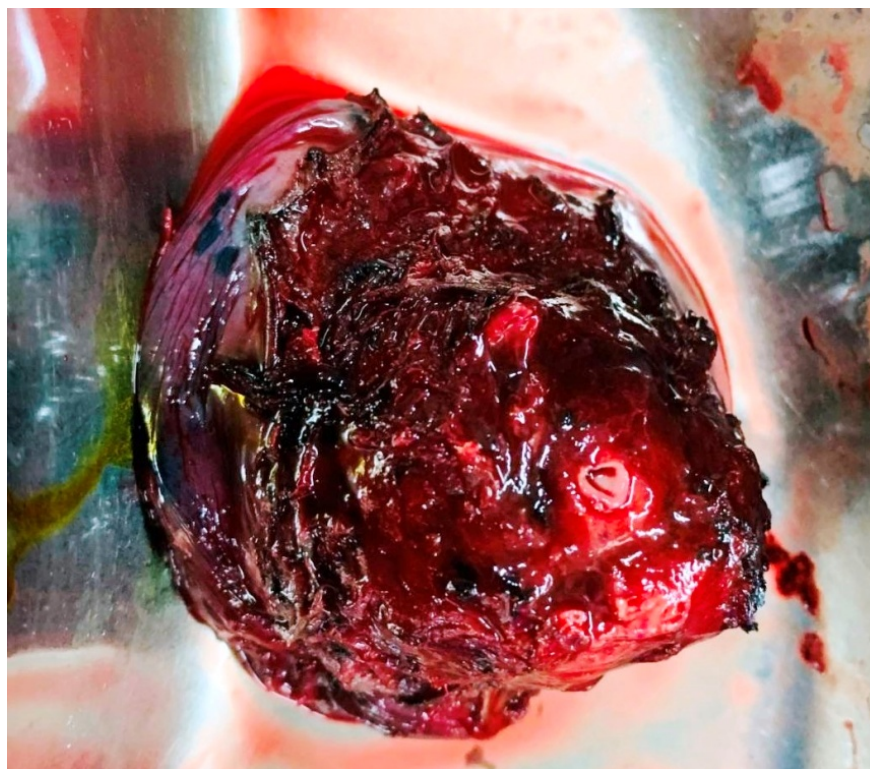


Figure 2: Surgical specimen of the resected lung mass.

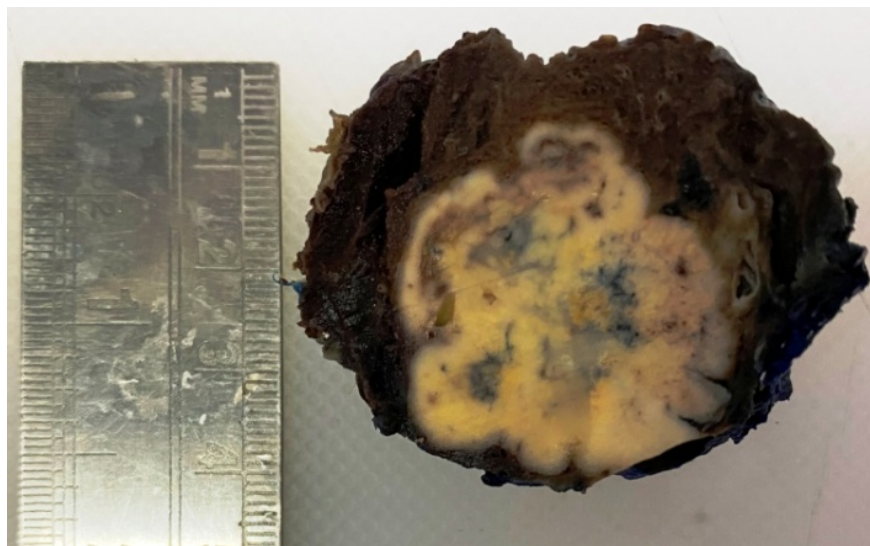
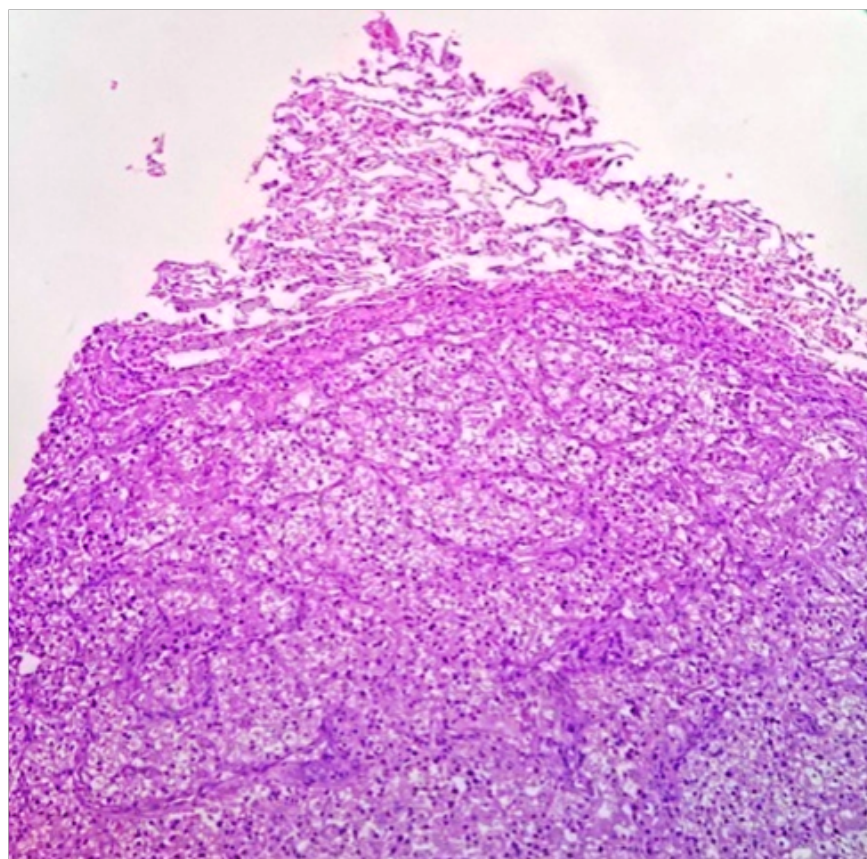


Figure 3: Gross specimen: On the cut section, the tumor is circumscribed, nodular and yellowish in appearance.



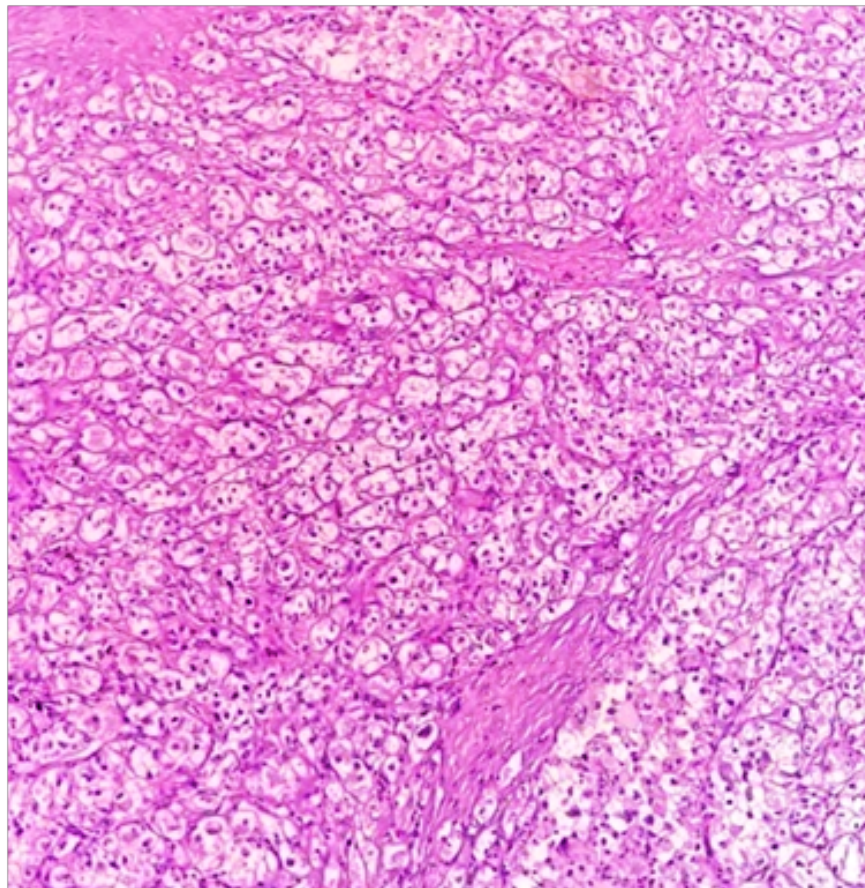


Figure 4: (A) 10x magnification photomicrograph showing clear cell renal cell carcinoma(ccRCC) in lung. (H&E stain). (B) 40x photomicrograph showing tumor cells arranged in nests, have a polygonal shape with clear cytoplasm and separated by thin-walled blood vessels. (H&E stain)

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## literature

Figure 5: Tumor cells show positivity for (A) CD10, (B) pancytokeratin (CK AE1/ AE3), (C) vimentin, and (D) PAX 8.

