

Case Report

## Mediastinal and Hilar Lymph Node Metastases from Renal Cell Carcinoma with Concomitant Lung Carcinoma: A Rare Case with Unique Diagnostic Challenges

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A 75-year-old man presented to our hospital 1 year after partial renal resection for clear cell carcinoma. A right lower lobe lung nodule noted at the time of surgery had increased to 3.0 cm in diameter and was confirmed as squamous cell lung carcinoma by bronchoscopic cytology. Computed tomography had also revealed paratracheal lymph node swelling. He underwent right lower lobectomy with lymph node dissection by video-assisted thoracic surgery. Pathological examination confirmed squamous cell carcinoma of the lung but diagnosed the right hilar and mediastinal lymph node metastases as clear cell carcinoma.

**Key words:** renal cell carcinoma, primary lung cancer, double cancer, mediastinal lymph node metastasis, hilar lymph node metastasis

Renal cell carcinoma (RCC) metastasis to the hilar or mediastinal lymph nodes is typically accompanied by lung or abdominal lymph node metastasis. Solitary metastasis to the mediastinal lymph nodes in the absence of lung metastasis or abdominal lymph node swelling is rare. In a case such as this with primary lung cancer, mediastinal and hilar lymph node swelling is more likely to represent lung cancer metastasis. We describe a case of concurrent primary lung cancer and solitary RCC metastasis to the mediastinal and hilar lymph nodes.

### Case Report

A 75-year-old man underwent partial right renal

resection for RCC that was pathologically diagnosed as clear cell carcinoma in 2019. The patient's comorbidities included hypertension, diabetes mellitus, and prostate enlargement, and he was undergoing hemodialysis due to chronic renal failure. In the pre-surgical computed tomography (CT) imaging, a nodule was found in the right lower lobe of the lung; hence, a transbronchial lung biopsy was performed. Malignancy was not found in the sample; therefore, the patient underwent regular follow-up CT scans after surgery. Within six months, the lung nodule had grown to approximately 3.0 cm in diameter (Fig. 1A); therefore, brush cytology by bronchoscopy was performed again and revealed squamous cell lung carcinoma. Lymphadenopathy of the right lower paratracheal lymph nodes (station 4R) was also noted (Fig. 1B). A whole-body fluorine-18-fluorodeox-

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ylucose positron emission tomography/CT (FDG-PET/CT) study revealed weakly positive focal FDG uptake (maximum standardized uptake value [SUVmax]=2.7) in the right lower lobe nodule, without significant FDG uptake in the hilar and mediastinal lymph nodes (Fig. 1C, D). No other lesions in the lungs or intraperitoneal lymphadenopathy were found. Compared with the tumor size on the PET/CT taken just before surgery for RCC (shown in Fig. 1C), the tumor on the CT taken 6 months following the PET/CT (Fig. 1A) was clearly enlarged. Laboratory data revealed renal failure, with elevated serum creatinine, hyperkalemia, hypoalbuminemia, and anemia. Tumor marker tests showed elevated levels of carcinoembryonic antigen (7.4 nanograms per milliliter [ng/mL]), squamous cell carcinoma-related antigen (6.7 ng/mL), and cytokeratin 19 fragment (7.0 ng/mL).

The preoperative clinical diagnosis was squamous cell lung carcinoma with mediastinal lymph node metastasis, TNM classification T1cN2M0, and clinical stage IIIA. Chemotherapy and induction therapy were not feasible owing to severe renal failure requiring hemodialysis, and we decided to perform only right lower lobectomy with lymph node dissection by video-assisted thoracoscopic surgery (right paratracheal stations 2R, 4R; subcarinal station 7; and right hilar stations 10R, 11i, and 12l).

Postoperative histopathological findings via hematoxylin and eosin (H & E) staining revealed that the lung and lymph node lesions were tumor tissue with clear eosinophilic cytoplasm. However, the lung lesion showed a high degree of nuclear atypia with desmosome bindings, whereas the lymph node lesions had relatively uniform nuclei and a fine stromal network with capillary vessels (Fig. 2A, B). Additionally, immunohistochemical staining of the lung tumor was positive for p40 (Fig. 2C) and high-molecular-weight cytokeratin (CKHMW), whereas the mediastinal and hilar lymph nodes were negative for p40 (Fig. 2D) and CKHMW. Moreover, the lung tumor was partially positive for CD-10 (Fig. 2E) and negative for vimentin, whereas the mediastinal and hilar lymph nodes were positive for vimentin and CD10 (Fig. 2F). These findings confirmed that the lung tumor was squamous cell carcinoma, and the lymph node lesions were metastases of clear cell RCC.

The patient recovered uneventfully and was discharged from the hospital 14 days after the surgery.

Unfortunately, 4 months after the surgery, a follow-up FDG-PET/CT revealed swelling of the left lower paratracheal lymph nodes with intense focal FDG uptake. We diagnosed the patient with mediastinal and right hilar lymph node metastasis of RCC and administered 60-Gy radiation therapy. After radiotherapy, he received immunotherapy (combined nivolumab and ipilimumab) and was doing well at the 9-month follow-up visit.

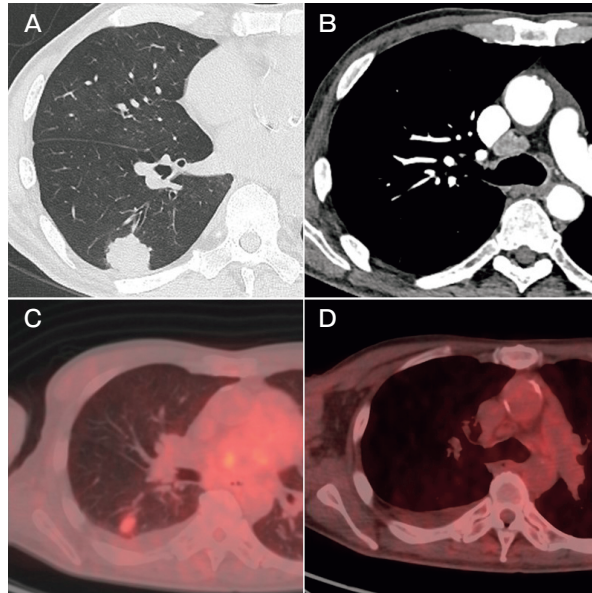
Informed consent was obtained from the patient for the publication of the data and images.

## Discussion

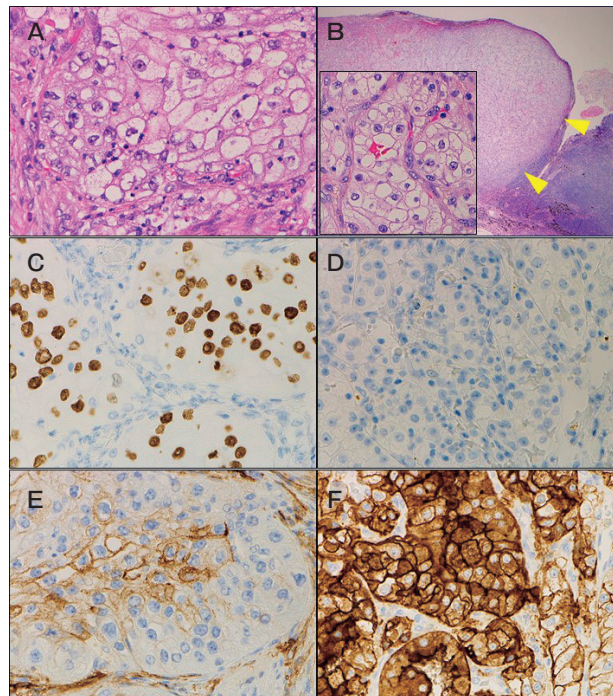
In this case, a man with previous surgery for RCC underwent surgery for squamous cell lung carcinoma in the right lower lobe and mediastinal lymphadenopathy. Contrary to expectations, postoperative pathological findings revealed that the lesions of the mediastinal lymph nodes (right paratracheal station #4R and subcarinal station #7) and right hilar lymph nodes (station #11i) did not match the squamous cell carcinoma of the resected lung tumor, but were metastases from the RCC. To the best of our knowledge, a case of primary lung cancer combined with RCC metastasis to the hilar and/or mediastinal lymph nodes has never been reported.

The occurrence of multiple cancers has recently increased due to increases in life expectancy, developments in diagnostic technologies, and improvement in treatment outcomes. In some cases, the co-occurrence of multiple cancers makes it difficult to provide patients with an accurate diagnosis and precise treatment. When a lung tumor with swelling of the mediastinal lymph nodes is found, as in this case, lung cancer with mediastinal lymph node metastases is first considered; however, if the patient has a history of other cancers, the possibility of other metastases should also be considered.

Lung metastasis of RCC is not uncommon. However, Kanzaki *et al.* [1] stated that mediastinal lymph node metastases of RCC are usually accompanied by lung metastases, whereas mediastinal lymph node metastasis in the absence of lung metastases is rare. Arkless *et al.* [2] reported mediastinal lymph node metastases in 11 of 152 patients with RCC; in all 11 cases, lung metastases were also present. Saitoh *et al.* [3] reported that 75 of 1451 patients with RCC had mediastinal lymph node metastases, and more than 90% of



**Fig. 1** Contrast-enhanced chest computed tomography (CT) image and whole-body fluorine-18-fluorodeoxyglucose (FDG) positron emission tomography/CT study. (A), A 31 × 26-mm mass is seen in the right lower lobe; (B), An axial CT section shows a right lower paratracheal lymph node lesion measuring 22 × 15 mm; (C), Weakly positive focal FDG uptake is seen in a nodule in the right lower lobe (maximum standardized uptake value = 2.7); (D), No significant uptake is observed in the right mediastinal lymph nodes.



**Fig. 2** Microscopic pathological findings. (A), Hematoxylin and eosin (H&E) staining reveals that the lung tumor has clear eosinophilic cytoplasm with a high degree of nuclear atypia and desmosome bindings; (B), H&E staining reveals a metastatic tumor (arrowhead) in the mediastinal lymph node; the lesion has eosinophilic cytoplasm with relatively uniform nuclei and a fine stromal network with capillary vessels; (C, D), Immunohistochemical staining reveals that the lung tumor is positive for p40 while the mediastinal lymph node is negative for p40; (E, F), Immunohistochemical staining reveals that the lung tumor is partially positive for CD10 while the mediastinal lymph node is strongly positive for CD10.

these 75 patients had concomitant lung metastases.

RCC with hilar or mediastinal lymph node metastases without lung involvement has occasionally been found. However, most of these cases also involve metastases to the retroperitoneal or abdominal lymph nodes. Cases of RCC metastasis to the hilar [4,5] or mediastinal lymph nodes [1,6] without lung, abdominal, or retroperitoneal lymph node metastases have been reported, but none of these cases had concomitant lung cancer.

The metastasis of RCC to the intrathoracic lymph nodes can be explained by two pathways. Metastasis may occur via the lymphogenous pathway through the thoracic duct or the inferior pulmonary ligament. First, lymphogenous reflux via the thoracic duct may result from the dysfunction of lymphatic valves, allowing cancer cells to reach the hilar-mediastinal lymph nodes [7]. Second, metastasis through the retroperitoneum into the inferior pulmonary ligament is also known. Another possibility is that lymph node metastasis of RCC occurs after micrometastasis of RCC in the lung [8].

Before obtaining the cytology results in this case, we considered a diagnosis of lung cancer with metastasis to the mediastinal lymph nodes or RCC metastasis to the lung and mediastinal lymph nodes. Exact clinical diagnosis was important owing to differences in the treatment regimens of the two types of cancer. In this case, we probably should have considered performing CT-guided biopsy for the lung tumor and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for mediastinal lymphadenopathy to obtain a precise diagnosis before surgical intervention. In general, the standard treatment for metastatic lung cancer is chemotherapy or chemoradiotherapy. While chemotherapy is the primary recommendation even for metastatic RCC, it has been reported that complete resection of RCC metastases to the mediastinal lymph nodes significantly improved the overall survival [9,10]. Therefore, even if a definite diagnosis had been procured by CT-guided biopsy and EBUS-TBNA, lobectomy of the lung with mediastinal lymph

node dissection would still have been considered an option.

**Conclusion.** This rare case of lung cancer combined with solitary RCC metastasis to the mediastinal lymph nodes highlights the importance of accurate diagnosis in lung cancer patients with mediastinal or hilar lymphadenopathy. Rapid and accurate diagnosis of metastases is critical to providing the best treatment for patients with multiple cancers.

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