



Solitary, Endobronchial Metastasis from Renal Cell Carcinoma 20 Years after Nephrectomy

신절제술 20년 후에 발생한 신세포암종의 단발성 기관지 내 전이

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Late recurrence over 10 years after surgery and endobronchial metastasis are some of the specific biological behaviors of renal cell carcinoma (RCC). The current report describes a case of solitary endobronchial metastasis at a subsegmental bronchus that developed 20 years after curative nephrectomy for RCC. A 71-year-old male was admitted to our hospital for pneumonia. Chest radiography showed multifocal ill-defined nodular opacities in the right lower lung zone, suggesting pneumonia. Subsequent chest CT confirmed pneumonic infiltration in the right lung. However, a 4.3-cm, well-defined, elongated mass with a branching pattern was also identified in the right lower lobe, and a right nephrectomy scar was detected on the covered upper abdomen. The patient had undergone right nephrectomy 20 years ago due to clear cell RCC. After right lower lobectomy, the postoperative pathological diagnosis was endobronchial metastatic clear cell RCC. Endobronchial metastasis should be considered in a patient with a history of RCC who presents with a suspected endobronchial tumor, even decades after curative surgery.

Index terms Carcinoma; Renal Cell Carcinoma; Metastasis

INTRODUCTION

Non-metastatic renal cancer carries a 5% risk of very late recurrence, even after at least 10 years of uneventful follow up, and pathological stage is the main predictor, as related to latency from surgery (1). Endobronchial metastases from extrathoracic malignancies are quite unusual, although the lungs are the most common organ of metastatic deposits. In particular, breast cancer, colorectal cancer, and renal cell carcinoma

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(RCC) are most commonly associated with endobronchial metastasis. The challenge posed by endobronchial metastasis is that it is difficult to recognize because of unremarkable clinical manifestations and normal chest radiographs in the majority of patients. Here, we report a case of solitary, ultra-late endobronchial metastasis from RCC that developed 20 years after nephrectomy and discuss not only ultra-late endobronchial metastasis, but possible mechanisms for this behavior.

CASE REPORT

A 71-year-old male visited our hospital with complaints of fever, cough, and sputum for 4 days prior. Laboratory examinations showed increased level of white blood cell (13570/ μ L) with elevated neutrophil segment (81%) and C-reactive protein (24.3 mg/dL). Chest radiograph showed both nodular opacity and ill-defined patchy increased opacity in right lower lung zone (Fig. 1A). Chest CT revealed multiple centrilobular nodules with ground glass opacities in the right middle lobe and right lower lobe (RLL), which were suggestive of pneumonia (Fig. 1B). Notably, a 4.3 cm, elongated mass whose long axis ran parallel to the bronchus was also identified in the RLL (Fig. 1C, D). The mass obstructed the subsegmental bronchus of the anterior basal segment of the RLL and showed a branching pattern adapting to the airway (Fig. 1C, D). Considering the CT findings and a right nephrectomy scar observed on the upper abdomen, both of primary endobronchial tumor and endobronchial metastasis were primarily suspected.

At 51 years of age, the patient had undergone the right nephrectomy due to RCC clear cell type (T3aN1M0, Fuhrman grade 3) at an outside hospital. The patient had been evaluated annually for five years with no evidence of recurrent disease, and no significant urological event had been reported for the subsequent 15 years between 2003 and 2018. Given that RCC occasionally presents delayed metastasis and it is one of the major neoplasms that causes endobronchial metastasis, we considered the possibility of very late endobronchial metastasis of previous RCC despite the long disease-free interval of 20 years.

CT-guided percutaneous transthoracic needle biopsy confirmed metastatic clear cell RCC. The patient underwent right lower lobectomy with video-assisted thoracoscopic surgery. The tumor cells consisted of abundant clear cytoplasm and hyperchromatic nucleoli and were surrounded by ciliated respiratory epithelium (Fig. 1E). In immunohistochemistry analysis, the tumor cells were negative for CK7, CK20 and TTF-1 and positive for EMA and vimentin. The final diagnosis was metastatic clear cell RCC with Fuhrman grade 3. The patient received medical treatment with sunitinib and was followed for 2 years with no evidence of recurrent disease.

DISCUSSION

An estimated 18% of patients with RCC have metastasis at diagnosis, and more than 50% will develop metastasis after nephrectomy during follow-up, with 85% metachronous metastasis occurring within the first 3 years and 93% within the first 5 years (2). Late recurrence more than five years after initial curative resection is one of the specific characteristics of

RCC. Five cases of late pulmonary metastasis of RCC with a disease-free interval over 20 years after curative resection have been reported in the English literature, and a disease-free interval of 37 years after nephrectomy is the maximum record (3, 4). Interestingly, tumor size

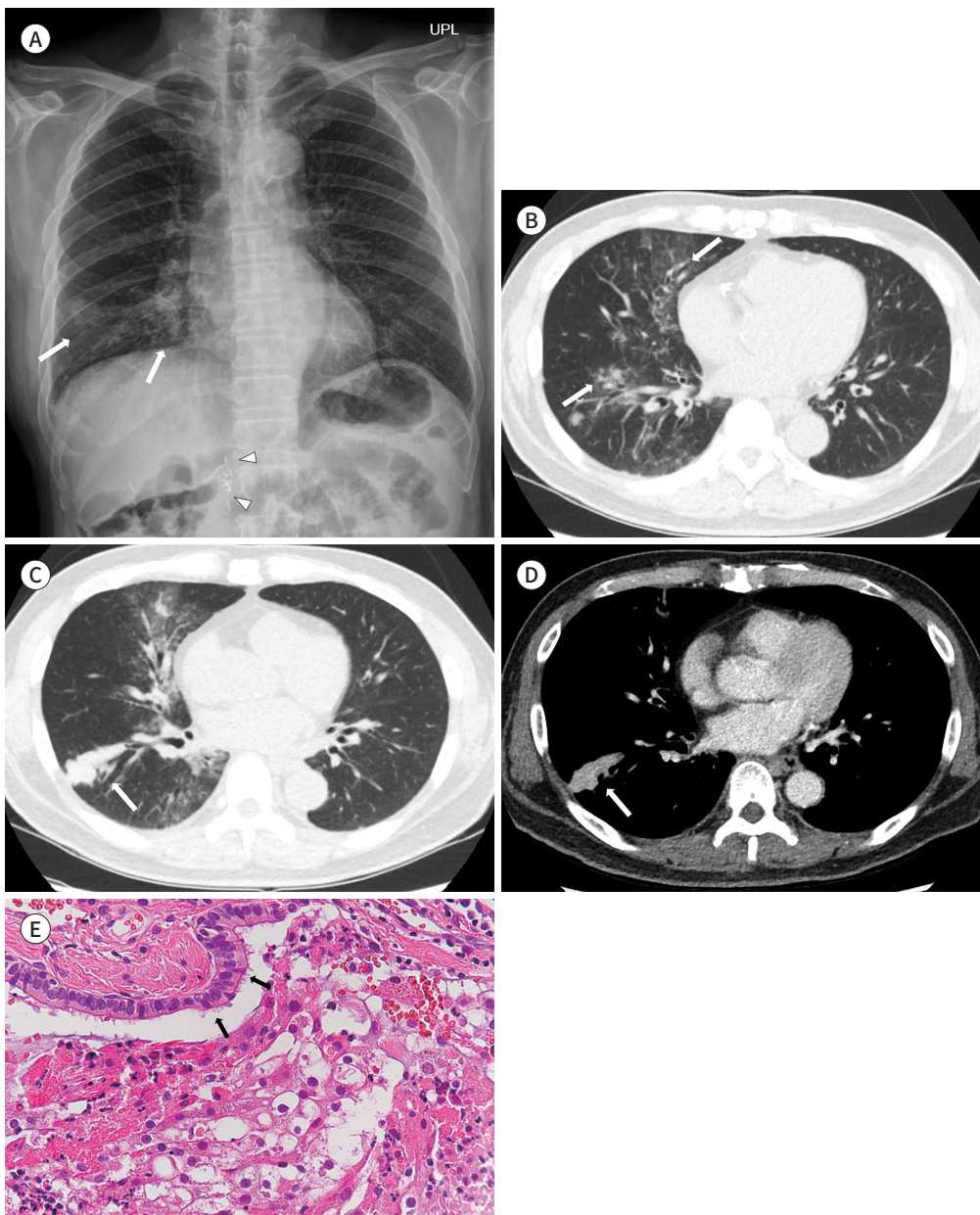
Fig. 1. Late endobronchial metastasis from renal cell carcinoma in a 71-year-old male, which was incidentally detected 20 years after nephrectomy.

A. Chest radiograph shows both nodular opacity and ill-defined patchy increased opacities in the right lower lung field (arrows) and surgical clips at the right nephrectomy bed (arrowheads).

B. Chest CT scan with lung window setting exhibits ill- and well-defined centrilobular nodules and ground-glass opacities (arrows) at the right middle and lower lobes.

C, D. Chest CT scans show an elongated mass (arrow, **C**) whose long axis ran parallel to that of the bronchus in the right lower lobe, and the mass shows a branching pattern and mild homogenous contrast enhancement (arrow, **D**).

E. The tumor cells with abundant clear cytoplasm are surrounded by ciliated respiratory epithelium (arrows) ($\times 100$, hematoxylin and eosin staining).



observed in late metastasis usually is larger with an increase of disease-free interval. Exceptionally late onset metastasis is likely related to slow growth and late detection. However, longer disease-free interval does not always imply slow tumor growth or absence of other metastases (5).

To date, the mechanism behind these extraordinary late recurrences of localized RCC has not been fully understood. Micrometastasis at the time of surgery, which is related with vascular invasion by the primary tumor, and their comparably lower malignant potential could contribute to late recurrence (5). The immune mechanism of patient and tumor dormancy was hypothesized to play a critical role in this setting. Especially in RCC, late relapses after nephrectomy as well as a few cases of spontaneous regression suggest that host immune reactions may be important in regulating tumor growth (6). The case report by Cozar et al. (7) in which multiple late pulmonary metastases 8 years after radical nephrectomy provoked immediately after an immunosuppressive treatment could support this hypothesis.

Endobronchial metastasis, one type of atypical lung metastasis, occurs in 2–5% of autopsies performed on patients with extrapulmonary malignancy (8). RCC is the most common extrapulmonary tumor to metastasize to the central airways, followed by colorectal carcinoma. There are two possible mechanisms for endobronchial metastasis: a) direct metastasis to the bronchus and b) invasion of the bronchial wall by tumor cells in the lymph nodes or lung parenchyma (9). A recent study by Marchioni et al. (10), in which epidemiologic and clinicopathologic features of 174 patients with endobronchial metastasis were examined, revealed a significantly longer overall median latency period between detection of primary tumor and occurrence of endobronchial metastasis in breast or renal carcinoma than colorectal carcinoma (median 86 or 82 months vs. 53 months). Although RCC is associated with a substantially long latency period, the solitary, late endobronchial metastasis in the present case that was detected over 20 years later is extraordinary.

Endobronchial metastasis and bronchogenic carcinoma have similar CT findings, rendering differential diagnosis a challenge. Endobronchial tumor should be considered when an elongated tumor whose long axis runs parallel to that of the bronchus and also shows a branching pattern adapting to the airway is observed on CT. Detection of an endobronchial tumor is also considerably challenging because it can simulate bronchitis, pneumonia, and primary lung cancer. Furthermore, when endobronchial tumor exists with concurrent pneumonia and involves the distal peripheral airway, such as our case, endobronchial metastasis with a branching pattern could be easily skipped. Early detection of recurrence is crucial, because surgical removal can lead to regression of the disease in a significant proportion of patients and, in a minority, be truly curative.

In conclusion, given the propensity of RCC to develop very late metastasis and endobronchial metastasis, it is important to consider the possibility of endobronchial metastasis for a lung mass with a branching pattern in a patient with history of RCC, even decades ago.

Author Contributions

Conceptualization, K.J.I.; investigation, K.M.J., K.J.I., W.K.Y.; project administration, K.J.I.; supervision, K.J.I.; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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신절제술 20년 후에 발생한 신세포암종의 단발성 기관지 내 전이

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수술 이후 10년 이상이 경과된 후 발생하는 후발성 전이와 더불어 기관지 내 전이는 신세포암의 특징적인 소견이다. 본 증례 보고는 신절제술 20년 후에 세분절 기관지에서 발생한 신세포암의 단일성 기관지 내 전이의 사례를 보고하고 문헌을 고찰하고자 한다. 71세의 남자가 폐렴을 주소로 병원에 입원하였다. 흉부 단순촬영에서 우하폐야의 다발성 결절성 병변을 보여 흉부 컴퓨터단층사진을 촬영하였고 우폐의 염증성 침윤과 함께 우하엽에 4.3 cm 크기의 경계가 좋은 길쭉한 고형성 종괴를 발견하였다. 포함된 상복부에 우측 신절제술의 흔적으로 20년 전에 투명 신세포암으로 우측 신장 절제술을 받았던 기왕력을 확인하였다. 병변은 폐우하엽 절제술로 제거하였고, 병리학적으로 기관지 내 전이성 투명신세포암으로 진단되었다. 신세포암의 병력이 있다면 절제술 후 수십 년이 지난 후라도 기관지 내 종양에 대하여 신세포암의 기관지 내 전이 가능성을 고려하여야 한다.

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