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Editorial

Scleroderma-Induced Renal Cell Carcinoma with Lung Metastasis

Attapon Cheepsattayakorn[1,2]*, Ruangrong Cheepsattayakorn[3] and Porntep Siriwanarangsun[1]

[1]Faculty of Medicine, Western University, Pathumtani Province, Thailand

[2]10th Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand

[3]Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

***Corresponding Author:** Attapon Cheepsattayakorn, 10th Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand.

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Systemic sclerosis (SSc; aka scleroderma), an autoimmune disease with hypothesized etiology of non-infectious, infectious, and genetic origins [1]. SSc is rarely associated with renal cell carcinoma (RCC-being diagnosed around 338,000 new cases annually worldwide [2]), whereas it may be associated with most commonly increased risk of lung (most common site [Figure 1-4]; [3-5], around 45-76% of metastatic RCC [5-7]), breast, and skin cancers [1] and metastases (being diagnosed around 20-30% of RCC patients at the time of diagnosis of RCC [3-5]) [8], including hematologic malignancies [9]. Clear cell RCC (being accounted for around 85% of renal cancer [10]) (with clear or eosinophilic cytoplasm [11]) originates from the proximal renal tubular cells, the most common subtype (accounting for 70-75% of patients at the surgical resection among the three major subtypes of RCC; clear cell, papillary, and chromophobe [Figure 5, 6]; [11-13] genetically involves the 3p chromosome [13], whereas around half of the tumors reveal somatic mutations in the von Hippel-Lindau tumor suppressor (vH-LTS) gene (or inactivation of vH-LTS gene in around 10-20% of RCC cases) [13].

Clinically, RCC patients with pulmonary metastasis who have endobronchial involvement may present with hemoptysis, lung atectasis, and post-obstructive pneumonia [14,15]. For patient following-up, the National Comprehensive Cancer Network suggest a baseline chest-computed tomography (CT) (Figure 2-4) within 3-6 months of the radical nephrectomy and following-up the chest radiography or chest CT every 3-6 months for at least 3 years, and should be followed by up-to-5-years of annual surveillance imaging [16]. Interferon-alpha is the principal pharmacotherapeutic option with response rate of 12% and high toxicity [4], whereas therapy with high-dose interleukin-2 gets complete response in around 5% of advanced-RCC patients [17] with severe cardiovascular toxicity limitation [18]. Local therapy for RCC includes surgical metastasectomy [19,20], percutaneous CT-guided thermal ablation [21], and radiation [22,23].

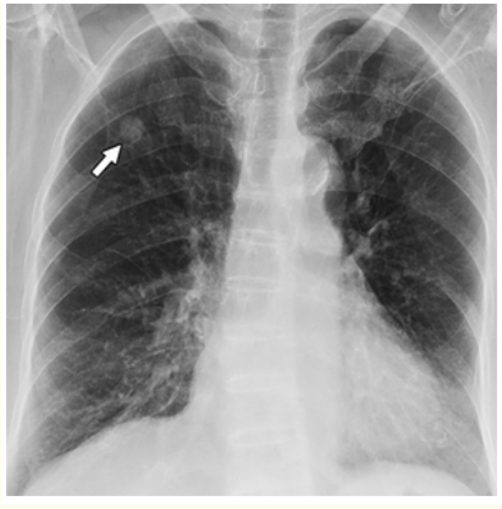

Figure 1: Demonstrating a 71-year-old woman with metastatic type 2 papillary renal cell carcinoma (RCC). Surveillance posteroanterior chest radiograph obtained 6 years after nephrectomy shows new nodular opacity (arrow) in right upper lobe.

(Source: Price M, Wu CC, Genshaft S, Sadow PM, Xie L, Shepard J-A O., *et al*. Imaging and manging of intrathoracic renal cell carcinoma metastases. AJR 2018; 210: 1181-1191. DOI: doi.org/10.2214/AJR.18.19645).

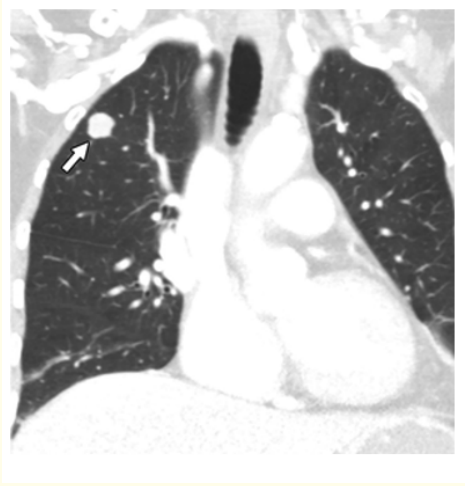

Figure 2: Demonstrating a 71-year-old woman with metastatic type 2 papillary renal cell carcinoma (RCC). Coronal CT image shows corresponding solid 1.5-cm nodule (arrow) in right upper lobe, which was biopsy-proven to represent RCC metastasis. Patient subsequently underwent right upper lobectomy.

(Source: Price M, Wu CC, Genshaft S, Sadow PM, Xie L, Shepard J-A O., *et al*. Imaging and manging of intrathoracic renal cell carcinoma metastases. AJR 2018; 210: 1181-1191. DOI: doi. org/10.2214/AJR.18.19645).

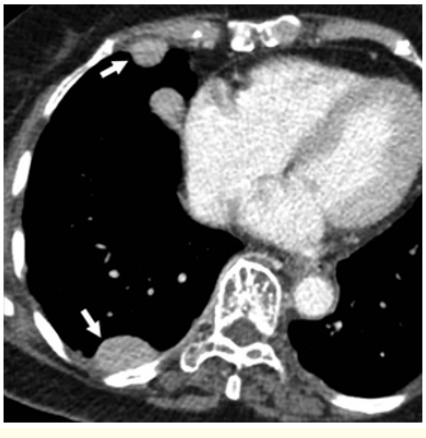

Figure 3: Demonstrating a 71-year-old woman with metastatic type 2 papillary renal cell carcinoma (RCC). Axial CT image obtained approximately 12 months after lobectomy shows that patient developed new enhancing pleural metastases (arrows).

(Source: Price M, Wu CC, Genshaft S, Sadow PM, Xie L, Shepard J-A O., *et al*. Imaging and managing of intrathoracic renal cell carcinoma metastases. AJR 2018; 210: 1181-1191. DOI: doi. org/10.2214/AJR.18.19645).

Figure 4: Demonstrating RRC with Lung Metastasis with a sub-carinal lymph node demonstrated by coronal chest CT prior the endobronchial ultrasound fine needle aspiration (EBUS FNA) (A) (arrow), resolution of the subcarinal lymph node 3 weeks following the EBUS FNA (B), pulmonary nodule in the upper right lung prior to the EBUS FNA of the subcarinal lymph node (C) (arrow), and resolution of the pulmonary nodule 3 weeks following the EBUS FNA (D).

(Source: Shields LBE, Kalebasty AR. Spontaneous regression of delayed pulmonary and mediastinal metastases from clear cell renal cell carcinoma. Case Rep in Oncol 2020; 13: 1285-1294).

Figure 5: Demonstrating a 71-year-old woman with metastatic type 2 papillary renal cell carcinoma (RCC). Photomicrograph from lobectomy specimen (H and E, low power) shows that tumor nodule (arrow) is well demarcated from surrounding lung parenchyma.

(Source: Price M, Wu CC, Genshaft S, Sadow PM, Xie L, Shepard J-A O., *et al*. Imaging and manging of intrathoracic renal cell carcinoma metastases. AJR 2018; 210: 1181-1191. DOI: doi. org/10.2214/AJR.18.19645)

Figure 6: Demonstrating a 71-year-old woman with metastatic type 2 papillary renal cell carcinoma (RCC). Photomicrograph (H and E, high power) shows that tumor cells have large irregular nuclei and abundant eosinophilic cytoplasm admixed with tubular and papillary architecture.

(Source: Price M, Wu CC, Genshaft S, Sadow PM, Xie L, Shepard J-A O., *et al*. Imaging and manging of intrathoracic renal cell carcinoma metastases. AJR 2018; 210: 1181-1191. DOI: doi.org/10.2214/AJR.18.19645).

In conclusion, it is unlikely that scleroderma-related fibrosis or immunosuppressant exposures that made by the short scleroderma-RCC diagnosis interval would explain the increased malignancy risk. A significantly increased possibility of pulmonary-metastasis progression in radical- or partial-nephrectomy-RCC patients with pulmonary nodules should be aware.

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