

### Olgu Sunumu–Case Report

## NON-METASTATIC SQUAMOUS CELL LUNG CARCINOMA: A RARE CASE REPORT

## NON-METASTATİK SKUAMÖZ HÜCRELİ AKCİĞER KANSERİ: NADİR BİR OLGU SUNUMU

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### Özet

Santral ve periferik skuamöz hücreli karsinom tipleri (SQCC) farklı klinik-patolojik özellikleri nedeniyle farklı kategorilerde sınıflandırılır. Histolojik paterne göre periferik SQCC; kombine, genişleyen ve alveoler-boşluk dolduran tip olarak üç alt gruba ayrılır. Bu üç alt tipten alveoler-boşluk dolduran tip ne lenf nodu metastazına ne de lenfatik damar invazyonuna neden olur ve en iyi klinik sonuçlara sahiptir. Bu olgu sunumu ile SQCC'nun tanı ve metastaz özelliklerini gözden geçirmeyi amaçladık. İlk tanıdan iki buçuk yıl sonra herhangi bir tedavi uygulanmamasına rağmen metastaz yapmayan nadir bir SQCC olgusu sunuldu. Bu tümörün histolojik paterni, metastaz davranışına göre en az invaziv alveoler boşluk-dolduran olabilir.

**Anahtar Kelimeler:** Skuamöz hücreli karsinom, akciğer kanseri, patoloji, metastaz

### Abstract

Central and peripheral types of squamous cell carcinoma (SQCC) are classified in different categories due to different clinical-pathological features. Peripheral SQCC is categorized into three subgroups as combined, expanding, and alveolar space-filling type according to the histological pattern. Of these three subtypes, the alveolar space-filling type neither causes lymph node metastasis nor lymphatic vessel invasion and has the best clinical outcomes. We aimed to review the diagnosis and metastasis features of SQCC by this case report. A rare case of squamous cell lung cancer that did not metastasis despite the absence of any treatment two and a half years from the initial diagnosis was presented. The histological pattern of this tumor may be the least invasive alveolar-space filling type according to its metastatic behavior.

**Key Words:** Squamous cell carcinoma, lung cancer, pathol, metastasis

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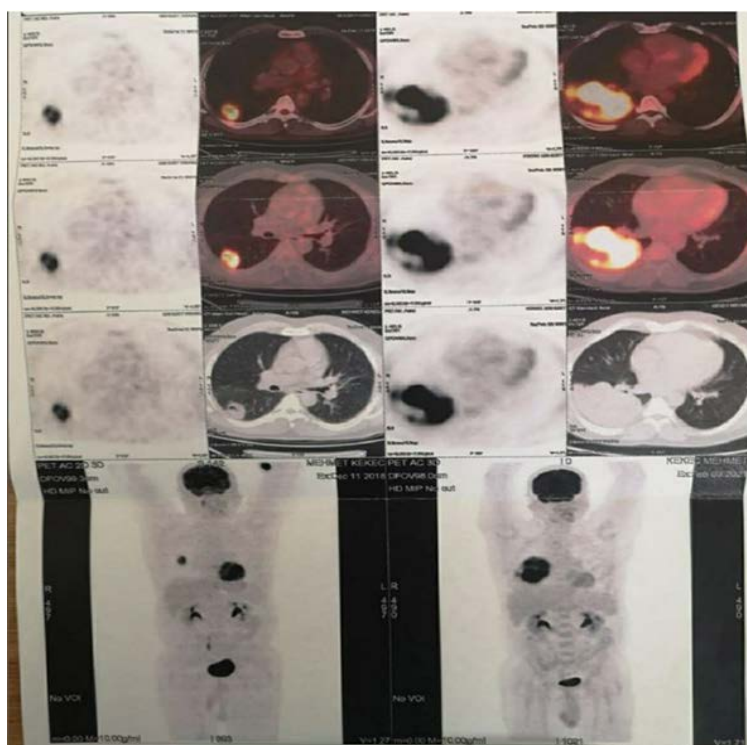
## 1. INTRODUCTION

Lung cancer is the first among cancers and is still 2-fold lethal than common cancers such as liver and lower gastrointestinal tract cancers, reported by World Health Organization (WHO) (Brambilla & Travis, 2014, p.17; World Health Organization, 2018, <http://www.who.int/news-room/fact-sheets/detail/cancer>). Non-small cell lung cancer (NSCLC) accounts for 85-90% of lung cancer cases, with a current 5-year survival rate of only 25% (American cancer society, 2021, <https://www.cancer.org>). The median survival time of patients with untreated metastatic NSCLC is only four to five months, with a 1-year survival rate of only 10% (Rapp et al., 1988, pp 633–661). The diagnosis and metastasis features of squamous cell lung cancer (SQCLC), a subtype of NSCLC, were reviewed by the present case presentation.

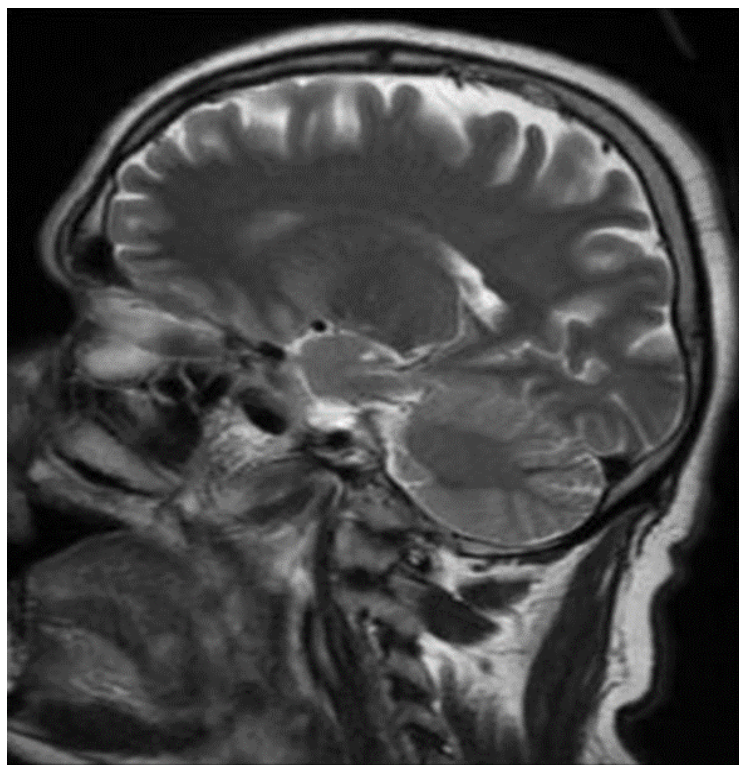
## 2. CASE REPORT

A 56-year-old male patient applied to the chest diseases outpatient clinic with the complaint of right chest pain on February 2021. The patient who quit smoking two years ago had a smoking history of 70 pocket/year. It was learned that the patient with a cardiac stent and depression had applied to the chest diseases outpatient clinic on November 2018, firstly. Whole-body computed tomography and positron emission tomography (PET-CT) dated 2018, had revealed a hypermetabolic, juxtapleural, 3.5-cm mass lesion containing necrotic tissue in the lower lobe of the right lung. Thereupon, he had undergone transthoracic fine-needle aspiration biopsy and the cytopathologic result had been reported as squamous lung cancer. When the patient's history was questioned in detail, it was learned that he had an acute myocardial infarction and could not be consulted by a pulmonologist for the biopsy result while he was dealing with his cardiac problems. Thus, PET-CT for staging was ordered for the patient who was diagnosed with SQCLC, but who had not applied any treatment modality of surgery, chemotherapy, and radiotherapy.

PET-CT revealed a 10-cm gross malignant lesion which was accompanied by markedly progressive intense hypermetabolism (SUVmax:16.79), extending from the right lower lobe superior segment to the right upper lobe posterior segment (Figure–1). And no metastatic mass lesion was detected on PET-CT. There was no metastatic lesion on the brain magnetic resonance imaging, too (Figure–2).

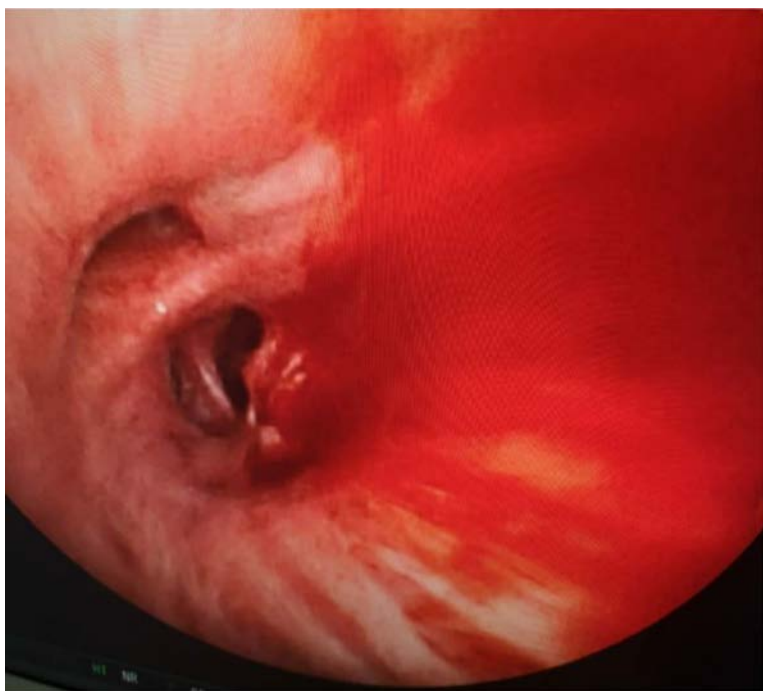


**Figure-1:** PET-CT scan showing the progression of a 3,5-cm hypermetabolic mass to a 10-cm hypermetabolic mass after approximately two and a half years.



**Figure-2:** No metastases were detected in the brain magnetic resonance imaging.

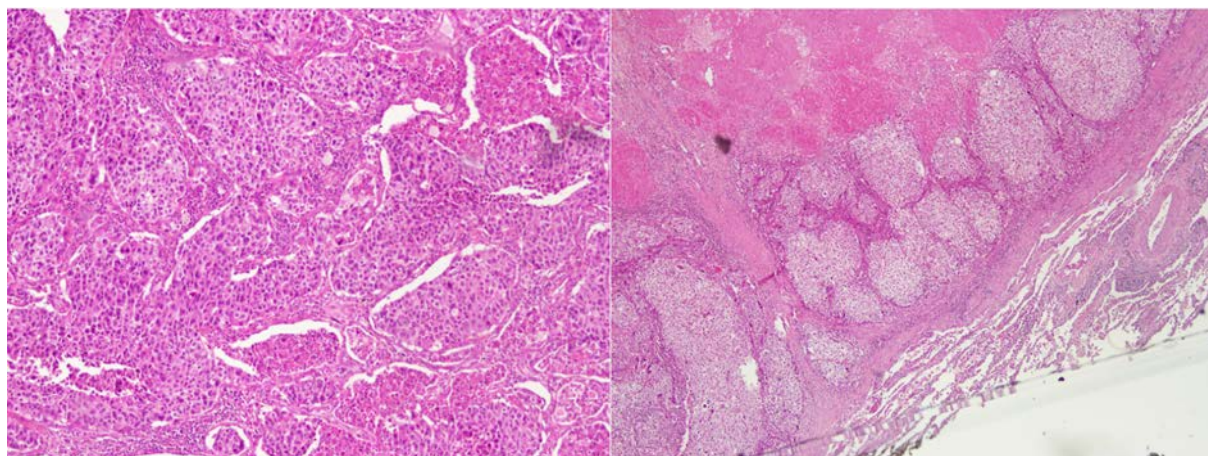
Fiberoptic bronchoscopy was applied to evaluate the operability. A vegetative “popcorn” tumor that extended into the right main bronchus from the right lower lobe superior segment was observed and punch biopsies of the tumor were performed. Hemorrhage occurred following the biopsies (Figure–3). The histochemical staining of the biopsy specimen was positive with Anti-pankeratin (AE1/AE3/PCK26) and Anti-p40 (BC28). The histopathological result of the biopsy was reported as squamous cell carcinoma (SQCC).



**Figure–3:** Bronchoscopic image of the endobronchial vegetative “popcorn” tumor and the hemorrhage following the biopsy.

The case was discussed in the thoracic surgery council and right pneumonectomy afterward adjuvant chemotherapy was decided. The pathological diagnosis of the 13-cm tumor resected during pneumonectomy operation was reported as grade III non-keratinized SQCC. The histological pattern of this peripheral tumor was examined and reported as “alveolar space-filling” type in the pathology department (Figures–4 a,b). The surgical margins of the tumor were negative. The patient whose adjuvant chemotherapy was completed has been still followed up by the oncology department.





**Figures– 4a.** Squamous cell carcinoma infiltration, through filling and extending alveolar spaces (H & E 10X10); **4b.** Squamous cell carcinoma infiltration, through filling and extending alveolar spaces (H &E 4X10).

### 3. DISCUSSION

The incidences of NSCLC subtypes are as follows: Adenocarcinoma (AC) (40%), SQCC (25-30%), and large cell carcinoma (10-15%). These subtypes differ in origin and patient characteristics; SQCC is associated with smoking and originates from bronchial epithelial cells, while AC arises mainly from alveolar-bronchial cells (Langer et al., 2010, pp. 5311–5320). 11-36% of patients with NSCLC have any distant organ metastasis at the first outpatient clinic presentation, and autopsy studies showed that tumor spread increased up to 93% of patients (Matthews et al., 1973, pp. 63–67). Regardless of the histologic subtype, the most common sites for NSCLC organ distant metastases are bone, brain, adrenal glands, and liver, respectively. Interactions between cancer-cell-surface proteins and capillary lining-endothelial cell receptors explain the most common distant metastases in these organs (Quint et al., 1996, pp. 246–250). Brain metastases are observed in 50% of patients with NSCLC at any stage (Gavrilovic & Posner, 2005, pp. 5–14).

The diagnosis of SQCC is based on the presence of keratin production by tumor cells and/or intercellular desmosomes (intercellular bridges) and/or immunohistochemistry (IHC) staining consistent with SQCC (i.e. p40, p63, CK5 or CK5 / 6, desmoglein expression). The p53 IHC marker, which also shows reactivity in AC, is not specific for squamous differentiation, therefore WHO recommends using p40 instead of p63. While SQCC variants in the 2004 WHO classification system included papillary, clear cell, small cell, and basaloid carcinoma, these variants were replaced by nonkeratinized, keratinized, and basaloid subtypes with the acceptance of non-cancer cell change as a cytological feature (Travis et al., 2015, pp. 1240–1242; Travis et al., 2015, pp. 1243–1260). Most of SQCCs (60-80%) differentiate into squamous metaplasia-dysplasia-carcinoma in situ, respectively in the proximal parts of the tracheobronchial tree, and gradually grow into a peripheral lesion. Central and peripheral types of SQCC have different clinical-pathological features, so they are classified in different categories. Peripheral SQCC is classified into three subtypes combined, expanding, and alveolar space-filling type according to the histological pattern. Of these three subtypes,



alveolar space-filling type has the best clinical outcomes because this type does not cause a lymphatic vessel invasion and a lymph node metastasis (Funai et al., 2003, pp. 978–984).

Central and peripheral SQCCs may show extensive central necrosis resulting in cavitation. A small subset of central, well-differentiated SQCC is observed as exophytic, endobronchial, papillary lesions. The clinics of patients with this unusual variant of SQCC are persistent cough, recurrent hemoptysis, or recurrent pulmonary infections due to airway obstruction. Most exophytic endobronchial SQCCs are less invasive and have better prognoses with 5-year survival rates above 60% (Dulmet-Breder et al., 1986, pp. 1358–1364).

Clinicians should not be surprised when they encounter Squamous Cell Lung Cancer (SQCLC) that does not metastasize to lymph nodes and distant organs in the long term. As this rare case demonstrates, it may be a SQCLC with a histological pattern of alveolar space-filling that has no lymphovascular invasion and has a high survival-rate.

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#### 4. REFERENCES

- American cancer society. (2021). Lung cancer survival rates. Online <https://www.cancer.org>.
- Brambilla, E., Travis, WD. (2014). Lung cancer. In: World Cancer Report, Stewart BW, Wild CP (Eds), World Health Organization, Lyon. p.17.
- Dulmet-Breder, E., Jaubert, F., Huchon, G. (1986). Exophytic endobronchial epidermoid carcinoma. *Cancer*. 57(7): 1358–1364.
- Funai, K., Yokose, T., Ishii, G., Araki, K., Yoshida, J., Nishimura, M., Nagai, K., Nishiwaki, Y., Ochiai, A. (2003). Clinicopathologic characteristics of peripheral squamous cell carcinoma of the lung. *Am J Surg Pathol*. 27(7): 978–984.
- Gavrilovic, IT., Posner JB.(2005). Brain metastases: epidemiology and pathophysiology. *J Neurooncol*. 75(1): 5–14.
- Langer, CJ., Besse, B., Gualberto, A., Brambilla, E., Soria, JC. (2010). The evolving role of histology in the management of advanced non-small-cell lung cancer. *J Clin Oncol*. 28(36): 5311–5320.
- Matthews, MJ., Kanhouwa, S., Pickren, J., Robinette, D. (1973). Frequency of residual and metastatic tumor in patients undergoing curative surgical resection for lung cancer. *Cancer Chemother Rep* 3. 4(2): 63–67.
- Quint, LE., Tummala, S., Brisson, LJ., Francis, IR., Krupnick, AS., Kazerooni, EA.,



Lannettoni, MD., Whyte, RI., Orringer, MB. (1996). Distribution of distant metastases from newly diagnosed non-small cell lung cancer. *Ann Thorac Surg.* 62(1): 246–250.

Rapp, E., Pater, JL., Willan, A., Cormier, Y., Murray, N., Evans, WK., Hodson, DI., Clark, DA., Feld, R., Arnold, AM. (1988). Chemotherapy can prolong survival in patients with advanced non-small-cell lung cancer--report of a Canadian multicenter randomized trial. *J Clin Oncol.* 6(4): 633–661.

Travis, WD., Brambilla, EW., Burke, AP., Marx, A., Nicholson, AG. (2015). WHO Classification of Tumours of the Lung, Pleura, Thymus, and Heart. *J Thorac Oncol.* 10(9): 1240–1242.

Travis, WD., Brambilla, E., Nicholson, AG., Yatabe, Y., Austin, JHM., Beasley, MB., Chirieac, LR., Dacic, S., Duhig, E., Flieder, DB., Geisinger, K., Hirsch, FR., Ishikawa, Y., Kerr, KM., Noguchi, M., Pelosi, G., Powell, CA., Tsao, MS., Wistuba, I., WHO panel. (2015). The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification. *J Thorac Oncol.* 10(9): 1243–1260.

World Health Organization. (2018). Fact sheets: Cancer. Online <http://www.who.int/news-room/fact-sheets/detail/cancer>.