ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Management Strategies for Synchronous Primary Lung Tumors: A Retrospective Two-Centre Study

Senkron Primer Akciğer Tümörlerinde Tedavi Stratejileri: Retrospektif İki Merkezli Çalışma

Demet Yaldiz[1], Guntug Batihan[2], Arkin Acar[1]

[1]Department of Thoracic Surgery, Manisa Celal Bayar University Faculty of Medicine, Manisa; [2]Department of Thoracic Surgery, Kafkas University Faculty of Medicine, Kars, Türkiye

ABSTRACT

Aim: *Synchronous primary lung tumors are uncommon and diverse clinical entities. Distinguishing them from intrapulmonary metastases is essential for accurate staging, prognosis evaluation, and selecting the right treatment. This study seeks to describe the clinical, radiological, and histopathological features of synchronous primary lung tumors and to aid in the diagnostic and treatment decision-making process.*

Material and Methods: *Between January 2023 and January 2025, patients diagnosed with synchronous primary lung tumors and evaluated at two tertiary centers were retrospectively analyzed. Clinical, radiological, and histopathological data were reviewed, including smoking history, occupational or environmental exposures, and TNM staging. Treatment strategies and follow-up outcomes were recorded.*

Results: *Out of 250 patients undergoing diagnostic or therapeutic interventions for lung cancer during the study period, four patients (1.6%) met the criteria for synchronous primary lung tumors. Detailed case-based analyses highlighted the heterogeneity in histologic subtypes, anatomical locations, and treatment approaches.*

Conclusion: *Synchronous primary lung tumors are rare but clinically significant. Comprehensive clinical evaluation, detailed histopathologic assessment, and individualized management strategies are essential to optimize outcomes.*

Key words: *synchronous lung tumors; multiple primary lung cancers; surgical management; personalized therapy; thoracic oncology*

ÖZET

Amaç: *Senkron primer akciğer tümörleri, nadir görülen ve heterojen özellikler gösteren bir klinik tablodur. Bu tümörlerin intrapulmoner metastazlardan ayırt edilmesi, doğru evreleme, prognozun öngörülmesi ve uygun tedavi stratejisinin belirlenmesi açısından kritik öneme sahiptir. Bu çalışma, senkron primer akciğer tümörlerinin klinik, radyolojik ve histopatolojik özelliklerini sunarak tanı ve tedavi sürecine katkı sağlamayı amaçlamaktadır.*

Gereç ve Yöntem: *Ocak 2023 ile Ocak 2025 tarihleri arasında senkron primer akciğer tümörü tanısı alan ve iki üçüncü basamak merkezde değerlendirilen hastalar retrospektif olarak analiz edildi. Klinik, radyolojik ve histopatolojik veriler; sigara öyküsü, mesleki veya çevresel maruziyetler ve TNM evrelemesi dâhil edilerek incelendi. Uygulanan tedavi stratejileri ve takip sonuçları kaydedildi.*

Bulgular: *Çalışma döneminde akciğer kanseri nedeniyle tanısal veya terapötik girişim uygulanan 250 hastadan dört hasta (%1,6) senkron primer akciğer tümörü kriterlerini karşıladı. Olgu bazlı ayrıntılı analizler; histolojik alt tipler, anatomik lokalizasyonlar ve tedavi yaklaşımlarındaki heterojenliği ortaya koydu.*

Sonuç: *Senkron primer akciğer tümörleri nadir ancak klinik açıdan önemli bir durumdur. Optimal sonuçlar için kapsamlı klinik değerlendirme, ayrıntılı histopatolojik inceleme ve bireyselleştirilmiş tedavi stratejileri esastır.*

Anahtar kelimeler: *senkron akciğer tümörleri; çoklu primer akciğer kanserleri; cerrahi tedavi; kişiselleştirilmiş tedavi; torasik onkoloji*

Introduction

Synchronous lung tumors represent a rare and heterogeneous group of neoplasms that present significant diagnostic and therapeutic challenges. Accurate differentiation between multiple primary lung cancers (MPLCs) and intrapulmonary metastases is essential, as it directly influences staging, prognosis, and the overall treatment strategy[1–3]. This distinction can be complicated due to overlapping radiologic and histopathologic features, necessitating a multidisciplinary approach that integrates clinical findings, histology, and increasingly, molecular profiling. Current guidelines emphasize individualized management plans, often involving combinations of surgical resection,

İletişim/Contact: *Güntuğ Batıhan, Department of Thoracic Surgery, Faculty of Medicine, Kafkas University, Kars, Türkiye* • ***Tel:*** *0532 576 45 46* • ***E-mail:*** *guntugbatihan@gmail.com* • ***Geliş/Received:*** *21.04.2025* • ***Kabul/Accepted:*** *31.07.2025*

ORCID: *Demet Yaldız: 0000-0003-3774-9632 • Güntuğ Batıhan: 0000-0001-5258-2856 • Arkın Acar: 0009-0008-0877-*

systemic chemotherapy, immunotherapy, and targeted therapies guided by tumor histopathology and genetic alterations[4,5].

In this study, we present four illustrative cases of synchronous lung tumors, each highlighting the variability in clinical presentation, histologic patterns, and therapeutic decision-making, with a focus on practical considerations in real-world thoracic oncology practice.

Material and Methods

Between January 2023 and January 2025, patients who underwent diagnostic or therapeutic interventions for a preliminary diagnosis of lung cancer at two tertiary centers were retrospectively reviewed.

Inclusion Criteria

Only patients diagnosed with synchronous primary lung tumors, defined according to Martini–Melamed criteria and subsequent modifications, were included. The diagnosis required distinct histological types or, in cases of similar histology, anatomical separation without evidence of systemic or lymphatic spread.

Data Collection

For each patient, the following variables were systematically analyzed:

- Demographics: age, sex
- Smoking history (expressed in pack-years)
- Occupational and environmental exposure history, including asbestos or uranium (if available)
- Radiological and bronchoscopic findings
- Histopathology of all lesions
- Tumor size, TNM staging, and nodal involvement

Treatment and Follow-up

Therapeutic strategies, including surgical interventions, adjuvant or definitive chemoradiotherapy, and perioperative management, were recorded. Postoperative outcomes, recurrence, and survival were assessed based on follow-up visits. For cases with missing data, the lack of information was attributed to incomplete patient records.

Results

A total of 250 patients who underwent diagnostic or therapeutic interventions for suspected lung cancer between January 2023 and January 2025 were retrospectively reviewed. Among them, four patients (1.6%) fulfilled the criteria for synchronous primary lung tumors. Detailed clinical, radiological, and histopathological characteristics, as well as treatment and follow-up data, are summarized below.

The first patient was a 71-year-old male with a 65 pack-year smoking history and chronic obstructive pulmonary disease (COPD). There was no recorded occupational or environmental carcinogen exposure. Imaging revealed a spiculated mass in the left lower lobe and an irregular lesion with satellite nodules in the right upper lobe (Fig. 1). PET-CT demonstrated high FDG uptake in the left lesion and mild uptake in the right. Histopathological examination confirmed squamous cell carcinoma in the left lower lobe (T2bN0M0) and adenocarcinoma in the right upper lobe (T1cN0M0). A left lower lobectomy with mediastinal lymph node dissection was performed, followed by wedge resection of the right upper lobe lesion. The postoperative course was uneventful, and no adjuvant therapy was required. At 14 months of follow-up, no recurrence was observed.

The second patient was a 68-year-old male with a 40-pack-year smoking history and a past occupational history in construction, where asbestos exposure was likely but not definitively documented. Thoracic CT revealed a centrally located mass in the left upper lobe causing partial atelectasis and minimal pleural effusion (Fig. 2), and bronchoscopy incidentally identified an endobronchial lesion in the right upper lobe. Pathology confirmed adenocarcinoma in the left upper lobe (T3N2M0) and squamous carcinoma in situ (Tis) in the right upper lobe. The right-sided lesion was excised bronchoscopically, while the left-sided tumor was treated with definitive concurrent chemoradiotherapy due to limited pulmonary reserve. The patient remained clinically stable with no evidence of progression at the 12-month follow-up.

The third patient was a 64-year-old female, a nonsmoker with no known occupational or environmental exposure. A right upper lobe mass and an additional endobronchial lesion in the right lower lobe bronchus were detected radiologically (Fig. 3). Histopathology revealed adenocarcinoma in the

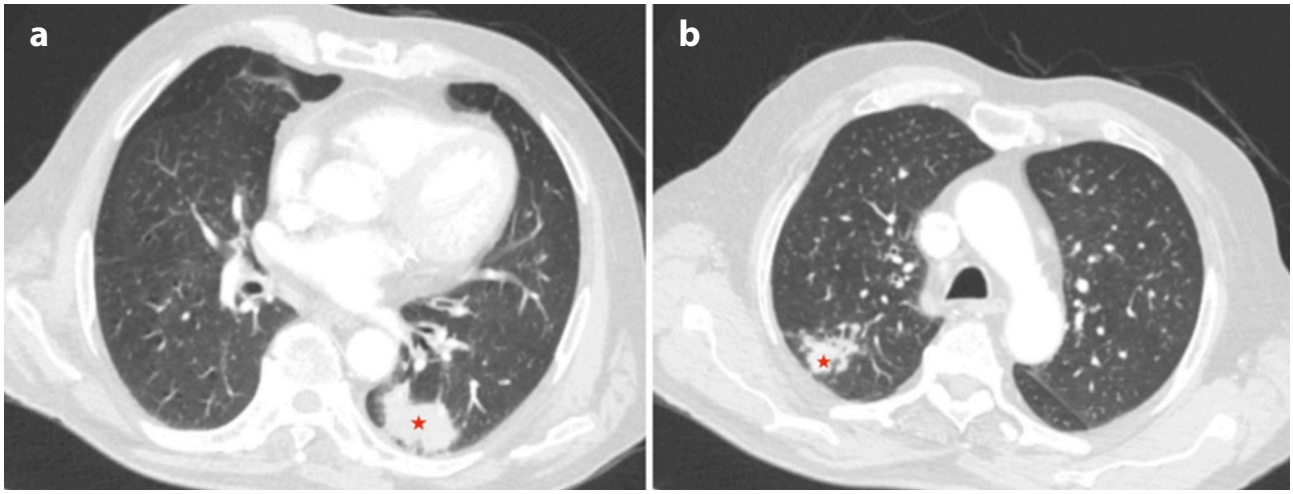

Figure 1. *Synchronous tumors located in the right upper lobe and left lower lobe are marked with arrows on thoracic CT images*

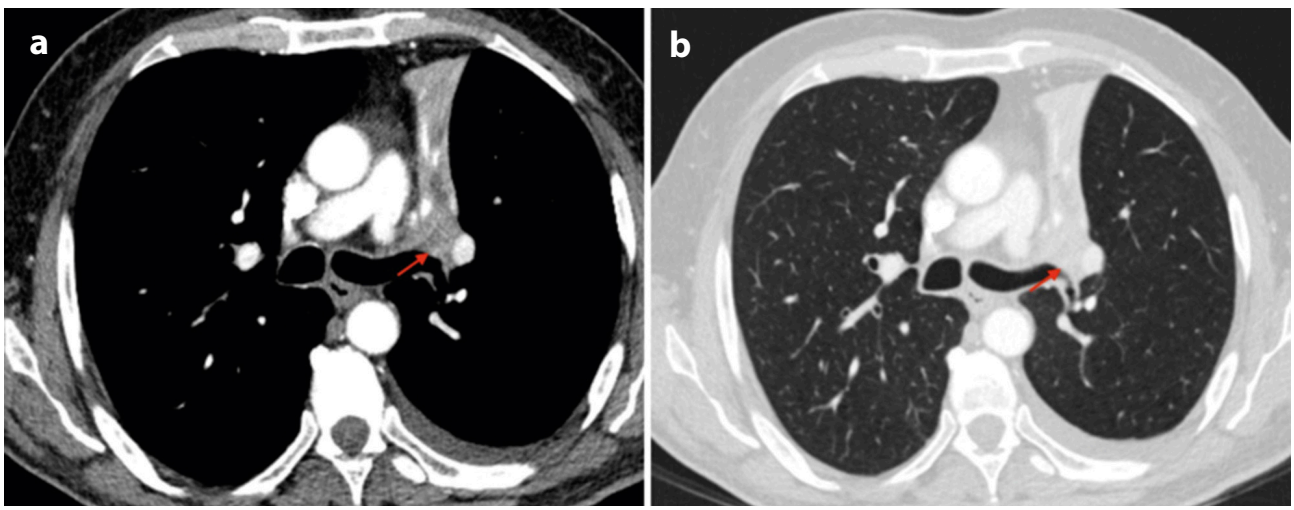

Figure 2. *Thoracic CT images showing a centrally located tumor in the left lung causing complete atelectasis of the upper lobe. The arrow indicates the centrally located mass.*

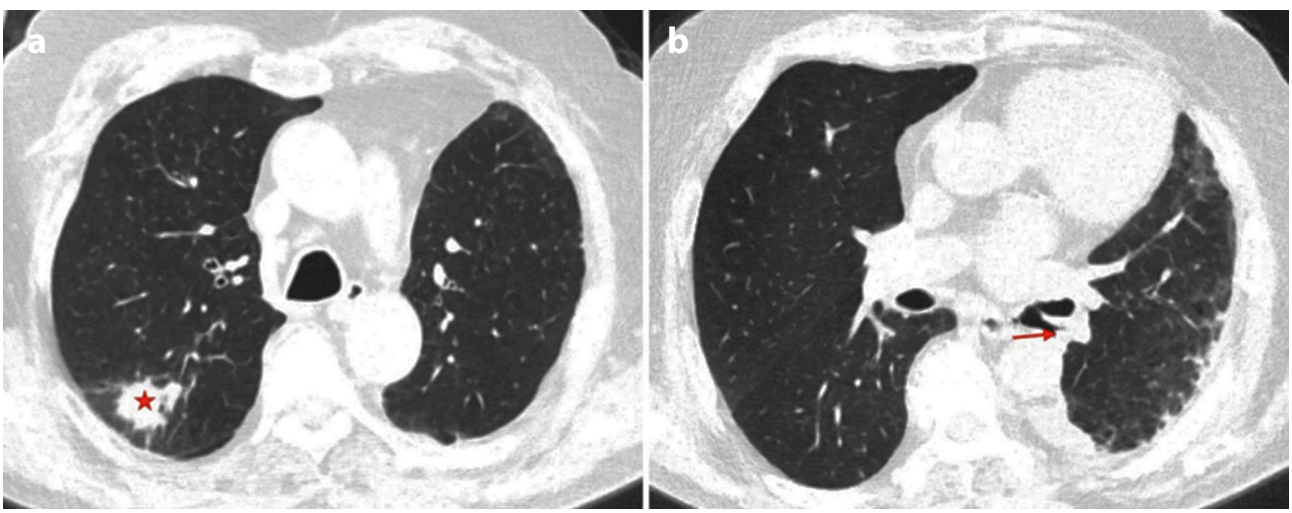

Figure 3. *Thoracic CT sections demonstrating synchronous tumors located in the periphery of the right upper lobe (asterisk) and within the left lower lobe bronchus (arrow).*

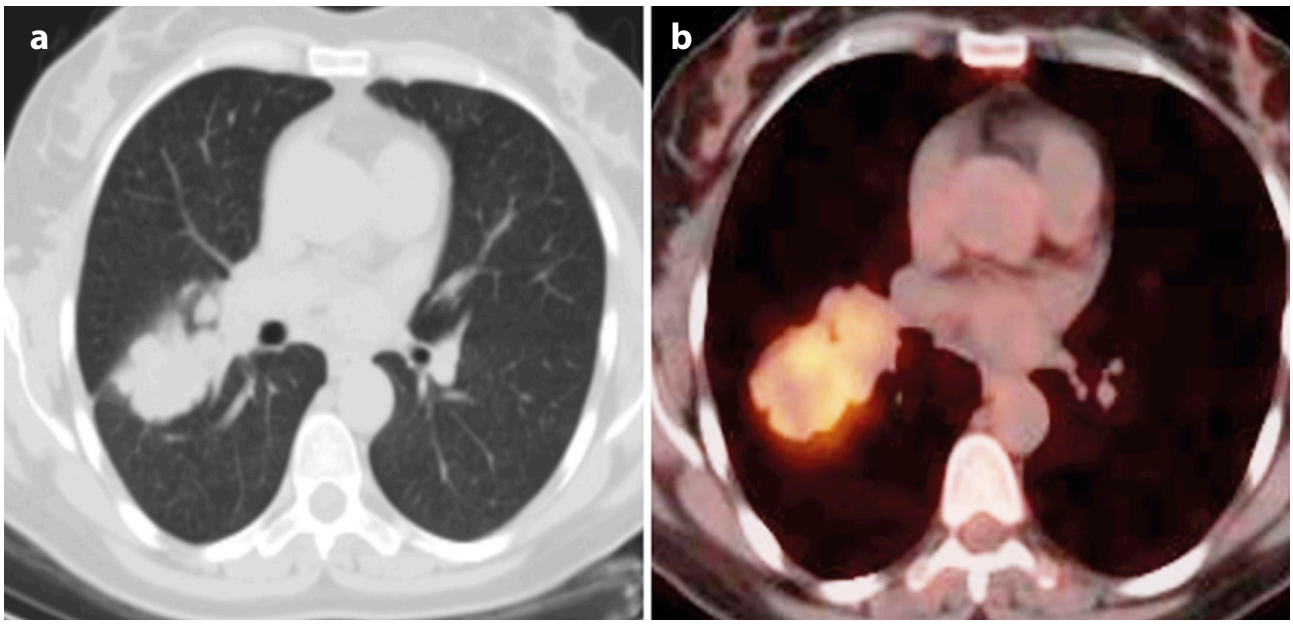

Figure 4. a, b. *Axial thoracic CT scan showing a cavitary mass lesion in the right lower lobe* ***(a)****. PET-CT scan demonstrating increased FDG uptake in the right lower lobe mass, consistent with malignancy* ***(b)****.*

right upper lobe (T2aN0M0) and squamous carcinoma in situ (Tis) in the right lower lobe bronchus. The patient underwent right upper lobectomy; additional surgical intervention was not deemed necessary. No adjuvant therapy was administered, and the patient remained recurrence-free after 10 months of follow-up.

The fourth patient was a 73-year-old female with a 55 pack-year smoking history and a past occupational history in agriculture, without documented asbestos exposure. Radiologic evaluation revealed a mass lesion in the right lower lobe and bronchiectatic changes in the adjacent right middle lobe (Fig. 4). Due to the proximity of the lower lobe mass to the middle lobe and the presence of bronchiectatic changes, a VATS right lower and middle bilobectomy was performed. Histopathological examination confirmed squamous cell carcinoma in the right lower lobe (T2bN0M0), while adenocarcinoma in situ was incidentally detected in the bronchiectatic middle lobe. Postoperative recovery was uneventful, and the patient remained disease-free at the six-month follow-up.

These four cases demonstrate the heterogeneity of synchronous primary lung tumors in terms of histologic subtypes, anatomical distribution, and treatment strategies, emphasizing the importance of a multidisciplinary and individualized approach.

Discussion

The management of synchronous primary lung tumors remains a clinical challenge, mainly due to the lack of standardized diagnostic criteria and treatment algorithms. Although the Martini-Melamed criteria and subsequent refinements have provided some guidance in differentiating MPLCs from intrapulmonary metastases, overlap in radiological, histopathological, and even molecular features continues to pose significant diagnostic uncertainty[6,7]. This distinction is crucial, as it directly influences staging, prognosis, and therapeutic decision-making.

In our series, except for the case of carcinoma in situ, all patients presented with combined histological subtypes, most commonly adenocarcinoma and squamous cell carcinoma, supporting the likelihood of distinct primary origins. Surgical intervention was feasible in three of the four cases, whereas one patient required definitive concurrent chemoradiotherapy due to poor pulmonary reserve. The incidence of synchronous primary lung tumors in our cohort was 1.6% (4/250 patients), which is consistent with the reported range of 0.5–2% in the literature. Early postoperative outcomes were favorable, with no recurrence observed during a median follow-up of 10.5 months. These findings emphasize the importance of individualized, multidisciplinary decision-making to achieve satisfactory oncological outcomes in this rare but clinically significant entity.

Surgical resection is generally considered the mainstay of treatment for patients with synchronous lung tumors when anatomically and functionally feasible. However, the extent of resection remains a topic of ongoing debate[1,4,8]. In cases where tumors are localized and resectable, lobectomy or even pneumonectomy may be required to achieve oncologic control. Yet, in select patients –particularly those with limited cardiopulmonary reserve or multifocal disease– sublobar resection (e.g., segmentectomy or wedge resection) may offer an acceptable compromise between oncologic efficacy and preservation of lung function. Several studies have suggested that sublobar resections can provide comparable outcomes to lobectomy in carefully selected patients, particularly when lesions are small, peripheral, and biologically indolent.

For patients who are poor surgical candidates or present with bilateral or centrally located lesions, definitive chemoradiotherapy serves as a viable alternative[9–11]. The use of advanced imaging modalities, bronchoscopic techniques, and multidisciplinary evaluation is essential in treatment planning, especially when deciding between surgical and non-surgical approaches.

An additional layer of complexity arises when different histological subtypes are present in the same patient, as seen in our series, where combinations of squamous cell carcinoma, adenocarcinoma, and carcinoma in situ coexisted. These cases underscore the heterogeneity of synchronous tumors and highlight the importance of individualized treatment strategies based on histopathological characteristics, anatomical distribution, and functional assessment.

Moreover, the evolving role of molecular and genomic profiling may further enhance our ability to distinguish synchronous primaries from metastases. Recent studies have demonstrated that next-generation sequencing (NGS) can reveal distinct mutational profiles in anatomically separate lesions, supporting the diagnosis of multiple primaries[12,13]. Incorporating such technologies into routine diagnostic workflows may improve staging accuracy and enable more tailored therapeutic decisions in the near future.

In summary, the management of synchronous lung tumors requires a personalized, multidisciplinary approach. These cases emphasize the necessity of integrating clinical judgment, pathological confirmation, and, where available, molecular diagnostics to guide treatment. Further prospective studies with larger patient cohorts and molecular analyses are needed to refine diagnostic criteria and optimize therapeutic strategies for this complex patient population.

References

1. Niu N, Zhou L, Zhao J, Ma X, Yang F, Qi W. Sublobar resection versus lobectomy in the treatment of synchronous multiple primary lung cancer. World Journal of Surgical Oncology. 2023;21(1):135.
2. Gazdar AF, Minna J D. Multifocal lung cancers--clonality vs field cancerization and does it matter?. Journal of the National Cancer Institute. 2009;101(8):541–543.
3. Rostad H, Strand TE, Naalsund A, Norstein J. Resected synchronous primary malignant lung tumors: a population-based study. The Annals of Thoracic Surgery. 2008;85(1):204–209.
4. Watanabe T, Tanahashi M, Suzuki E, Yoshii N, Tsuchida H, Yobita S, et al. Surgical treatment for synchronous multiple primary lung cancer: Is it possible to achieve both curability and preservation of the pulmonary function?. Thoracic Cancer. 2021;12(22):2996–3004.
5. Raju SC, Peters GW, Decker RH, Park HS. Clinical Outcomes and Safety Profile in the Treatment of Synchronous Nonmetastatic Lung Tumors With Stereotactic Body Radiation Therapy. Practical Radiation Oncology. 2022;12(2):e110–e116.
6. Martini N, Melamed MR. Multiple primary lung cancers. J Thorac Cardiovasc Surg. 1975;70:606–612.
7. Stiles BM. Say goodbye to Martini and Melamed: genomic classification of multiple synchronous lung cancers. Journal of Thoracic Disease. 2017;9(1):E87-E88.
8. Ishikawa Y, Nakayama H, Ito H, Yokose T, Tsuboi M, Nishii T, et al. Surgical treatment for synchronous primary lung adenocarcinomas. The Annals of Thoracic Surgery. 2014;98(6):1983–1988.
9. Shen KR, Meyers BF, Larner JM, Jones DR. Special treatment issues in lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition) . Chest. 2007;132:290S-305S.
10. Chen C, Huang X, Peng M, Liu W, Yu F, Wang X. Multiple primary lung cancer: a rising challenge. J Thorac Dis. 2019;11(Suppl 4):523–36.
11. Brunelli A, Kim AW, Berger KI, Addrizzo-Harris DJ. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143:166–90.
12. Wu X, Huang W, Geng T, Wei Y. Next-Generation Sequencing of Synchronous Multiple Primary Lung Cancers in a Patient with Squamous Cell Carcinoma and Small Cell Lung Cancer. OncoTargets and therapy. 2020;13:11621–11626.
13. Yang DS, Huang K, Su M, Wang TT, Liu SS, Xu Y, et al. Next-generation sequencing revealed synchronous double primary lung squamous carcinoma: a case report. The Journal of International Medical Research. 2021;49(5):3000605211018575.