CASE REPORT

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# Adult Tracheobronchomalacia that Progressed Following Radiotherapy in an Advanced-stage Lung Cancer Patient: A Rare Case Report

## İleri Evre Akciğer Kanseri Hastasında Radyoterapi Sonrası İlerleyen Erişkin Trakeobronkomalazi: Nadir Bir Olgu

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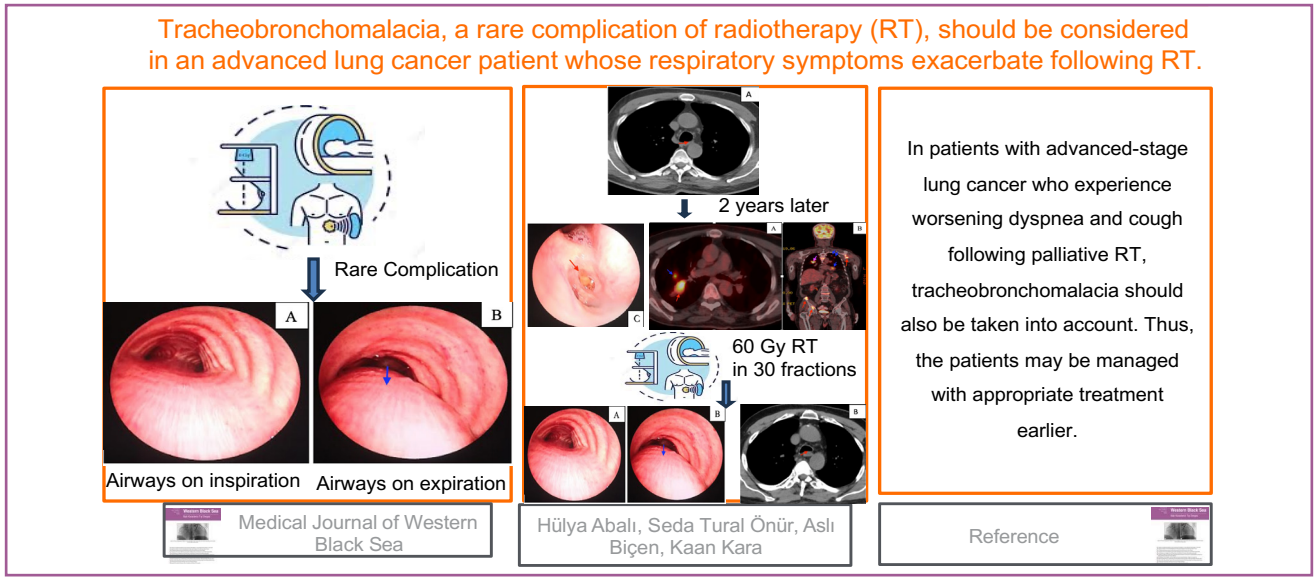
**GRAPHICAL ABSTRACT**




## ABSTRACT

**Background:** Tracheobronchomalacia (TBM) is the collapse of the trachea and bronchi, which leads to respiratory symptoms and complications, often on forced expiration. Radiotherapy (RT) is a rare cause of adult TBM. TBM developing after RT may worsen clinical findings in lung cancer patients. We intended to emphasize the rare potential damage of RT to tracheobronchial tree and review TBM caused by RT through this first case in the literature.

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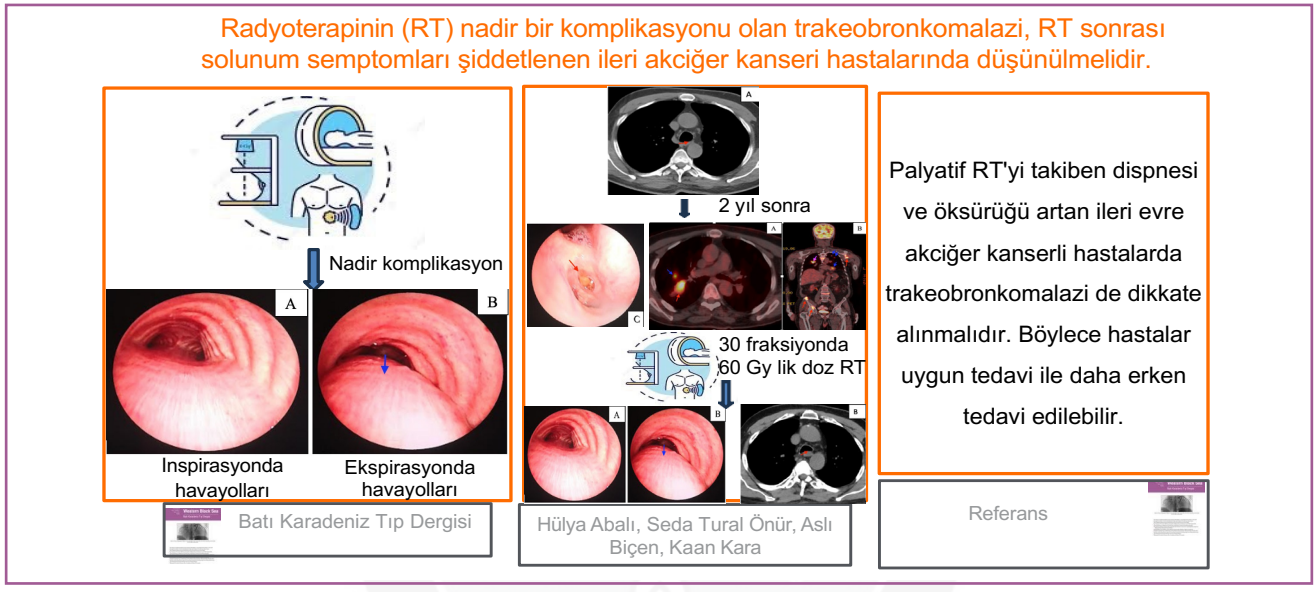
**Case report:** An 83-year-old male patient was referred to our pulmonology center to diagnose a lung mass detected on the thoracic computed tomography (CT) performed in an external hospital. TBM and a vegetating tumor was observed on bronchoscopy. Biopsy from the tumor was reported as a squamous cell carcinoma. The patient's dyspnea and cough had worsened two months after palliative RT. In the last thoracic CT scan, it was observed that the tracheal collapse two years ago had progressed. Inhaler bronchodilator and symptomatic treatment were initiated, and the patient was taken under intermittent outpatient clinic follow-up.

**Conclusion:** In patients with advanced-stage lung cancer who experience worsening dyspnea and cough following palliative RT, TBM should also be taken into account. Thus, the patients may be managed with appropriate treatment earlier.

**Keywords:** Tracheomalacia, bronchomalacia, radiotherapy, bronchoscopy, computed tomography

**GRAFİKSEL ÖZET**




## ÖZ

**Giriş:** Trakeobronkomalazi (TBM), sıklıkla zorlu ekspirasyon sırasında solunum semptomlarına ve komplikasyonlara yol açan trakea ve bronşların kollapsıdır. Radyoterapi (RT) erişkin TBM'nin nadir bir nedenidir. RT sonrası gelişen TBM, akciğer kanseri hastalarında klinik bulguları kötüleştirebilmektedir. Literatürdeki bu ilk olgu üzerinden RT'nin trakeobronşiyal ağaçta nadir görülen potansiyel hasarını vurgulamayı ve RT'nin neden olduğu TBM'yi gözden geçirmeyi amaçladık.

**Olgu sunumu:** 83 yaşında erkek hasta, dış hastanede çekilen toraks bilgisayarlı tomografisinde (BT) saptanan akciğer kitle tanısının konulması amaçlı göğüs hastalıkları merkezimize yönlendirildi. Bronkoskopide TBM ve vejetan tümör görüldü. Tümörden alınan biyopsiler skuamöz hücreli karsinom olarak rapor edildi. Hastanın dispnesi ve öksürüğü palyatif RT'den iki ay sonra şiddetlendi. Son toraks tomografisinde iki yıl önceki trakeal kollapsın ilerlemiş olduğu görüldü. İnhaler bronkodilatör ve semptomatik tedavisi başlanan hasta, aralıklı poliklinik takibine alındı.

**Sonuç:** Palyatif RT'yi takiben dispnesi ve öksürüğü artan ileri evre akciğer kanserli hastalarda TBM de dikkate alınmalıdır. Böylece hastalar uygun tedavi ile daha erken tedavi edilebilir.

**Anahtar Sözcükler:** Trakeomalazi, bronkomalazi, radyoterapi, bronkoskopi, bilgisayarlı tomografi

## INTRODUCTION

The weakness of any structure in the human anatomy is expressed by the term "malacia." Tracheobronchomalacia (TBM) is defined as tracheobronchial collapse brought on by the hypotonia of myoelastic fibers and loss of structural integrity of the tracheobronchial cartilage (1).

Changes in the morphology of the bronchi and/or central trachea are characteristic of TBM. The regular C-shape of the trachea and bronchi that appeared on cross-sectional imaging or bronchoscopy is displaced by narrowing to the anteroposterior dimension of the trachea and/or bronchi with concurrent widening of the lateral dimension or expansion of the airway. With either tidal breathing or forceful

exhalation, this shape change results in a crescent-shaped trachea, referred to as a "frown" (2-4). This disorder leads to immoderate airway narrowing that is induced by increased mediastinal pressure by forced expiration, cough, and Valsalva (5).

TBM may be misdiagnosed with chronic diseases such as chronic obstructive pulmonary disease (COPD) and asthma, which have common symptoms such as cough, dyspnea, and recurrent infections. The pulmonary function test is a diagnostic and severity metric for COPD and asthma but not for TBM. Because patients with TBM have standard flow loops frequently (6).

TBM is categorized into two types: congenital and acquired etiologically. Most adult TBMs are of the acquired type. Radiotherapy (RT) may develop TBM by causing cartilage damage and airway collapse rarely (7). Herein, an advanced lung cancer case with progressed TBM secondary to RT is presented in the literature for the first time.

## CASE REPORT

An 83-year-old male patient had dyspnea, wheezing, barking cough, and right chest pain on admission to our pulmonology outpatient clinic two months after completing RT lasting for one month. When the patient's complaints were questioned in detail, he stated that exertion dyspnea occurred three weeks after, and dyspnea at rest occurred two months after receiving RT. Sixty-pocket-year smoker patient was using acetylsalicylate for coronary arterial disease (CAD) and dexamethasone for localized enteritis. He was operated on for a sigmoid colon tumor in 2014.

Bilateral hypermetabolic lung masses had been detected on the positron emission computed tomography (PET-CT) performed in a cardiology outpatient clinic where he had applied for CAD 2 years ago. However, the masses could not be examined due to the neglect of the patient during the pandemic period. He had presented to an external center for the right arm pain lasting for three months. The PET-CT ordered to examine the previous lung masses revealed bilateral hypermetabolic lung masses, the largest of which was 5 cm in the upper lobe of the right lung (RUL) (Figure 1A), and skeletal metastases (Figure 1B). The patient had undergone the transthoracic fine needle aspiration biopsy from the nodule in the left lower lobe, and the histopathology of the sample was non-diagnostic. The patient had applied 60 Gy RT in 30 fractions. Two months after completion of palliative RT, the patient was admitted to an external emergency department for the exacerbation of dyspnea and barking cough and was referred to our reference center for chest diseases and lung cancer for a histopathological diagnosis and further evaluation upon worsening of symptoms. The patient demonstrated respiratory physical examination with rhonchi on auscultation and tachypnea. The saturation of $O_2$ was 95%, and the pulse/min was 134. The lab was in the standard range (Table 1). Paralytic left vocal cord, tracheomalacia (Figure 2A, Figure 2B), bronchomalacia, and a yellowish vegetating tumor obliterating the posterior segment of the RUL were observed (Figure 2C) on fiberoptic bronchoscopy. Histopathology of the biopsies from the tumor was reported as a squamous cell carcinoma. The tracheal collapse was observed at approximately 50%. Previous computed tomography (CT) scans were checked for the etiology of TBM. The mildly collapsed distal tracheal lumen was detected on the thoracic CT scan two years ago (Figure 3A). In contrast, the CT scan in the emergency department, where he presented with exacerbation of dyspnea, revealed a progressed collapse in the distal tracheal lumen (Figure 3B). The patient was recommended to quit

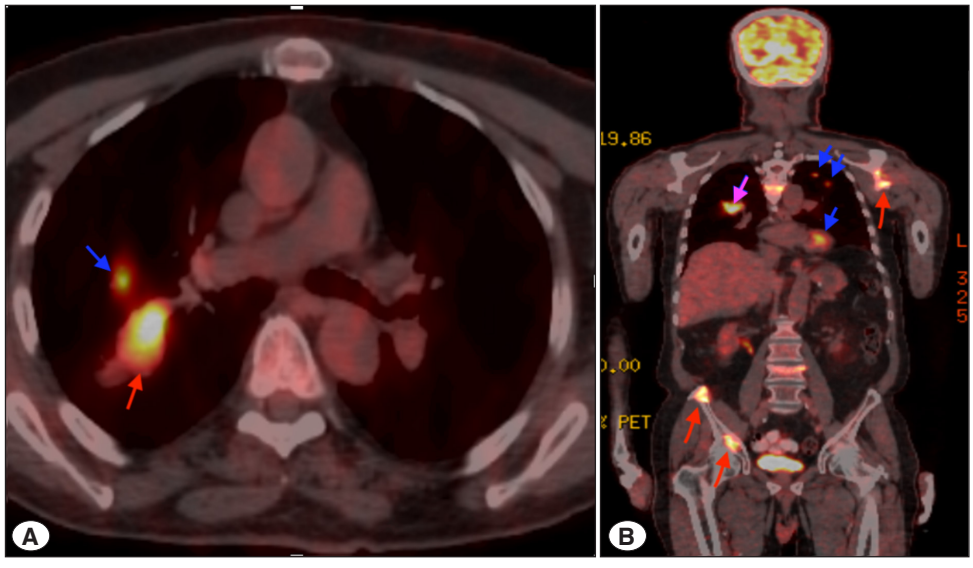



**Figure 1: A)** A 5-cm mass (signed with red arrow) and 1.5-cm nodule (signed with blue arrow) in the posterior segment of the right upper lobe of lung, **B)** A 5-cm mass (signed with pink arrow) in the right upper lobe of lung and metastatic lung nodules (signed with blue arrows) and multiple skeletal metastases (signed with red arrows).

**Table 1:** Laboratory results of the patient on admission to the outpatient clinic

| | Patient values | Standard values |
|---|---|---|
| Fasting blood glucose (mg/dl) | 96 | 74-109 |
| Urea (mg/dl) | 35 | 10-50 |
| Creatinine (mg/dl) | 1.23 | 0.6-1.2 |
| AST (U/L) | 12 | <40 |
| ALT (U/L) | 9 | <41 |
| Total protein (g/L) | 73 | 66-87 |
| Albumin (g/L) | 44.3 | 35-52 |
| Sodium (mmol/L) | 138 | 136-145 |
| Calcium (mg/dl) | 10 | 8.6-10.6 |
| CRP (mg/L) | 8 | <5 |
| Sedimentation (mm/saat) | 138 | 136-145 |
| WBC (10e3/ul) | 8.33 | 4-10 |
| Hemoglobin (g/dl) | 14.3 | 11-16 |
| Hematocrit (%) | 43.1 | 37-54 |
| PLT (10e3/ul) | 250 | 150-450 |
| Lymphocyte (10e3/ul) | 2.27 | 0.8-4 |

**AST:** Aspartate transaminase, **ALT:** Alanine transaminase, **CRP:** C-reactive protein, **WBC:** White blood cell, **PLT:** Platelet

smoking, and antitussives and inhaler bronchodilator treatment were initiated. Afterward, the patient was advised to have an intermittent follow-up from our pulmonology outpatient clinic, and he was referred to an oncology outpatient clinic.

## DISCUSSION

An extreme increase in tracheal compliance, defined as tracheomalacia, makes the airway more vulnerable to dynamic and/or static collapse. Tracheomalacia, which may be localized or diffuse, is termed TBM with the involvement of the mainstem bronchi. TBM can progress and cause significant morbidity and infrequent mortality. A study demonstrated that 59.5% of patients were alive and 38% were suffering from lung disease in a follow-up period of 5.2 years (1).

Airway malacia may occur due to congenital causes that predispose to the collapse of airway cartilage or due to acquired malformations. Adult TBM is frequent in smokers, middle-aged, and older men (2) and is found incidentally in 1% of patients undergoing bronchoscopy for any indication (8). The main symptoms are dyspnea, cough, sputum production, and rarely hemoptysis due to narrowing of the airways (9). The demographic features and clinical findings

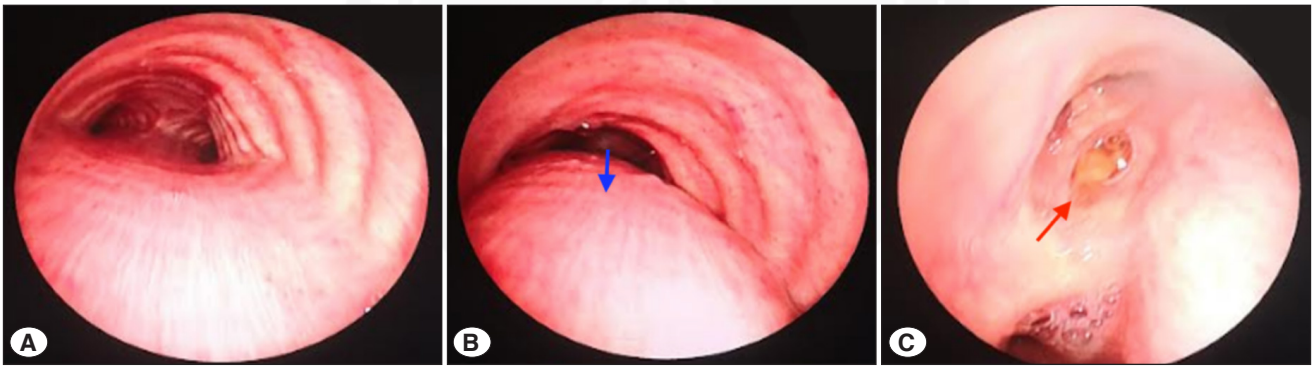



**Figure 2: A)** Tracheal image in inspiration. **B)** Tracheal image in expiration showing the collapse of the posterior membrane by approximately 50% leading to symptomatic large airway obstruction (signed with blue arrow). **C)** Fiberoptic bronchoscopy image of bronchomalacia and a vegetative tumor obliterating right upper lobe entrance (signed with red arrow).

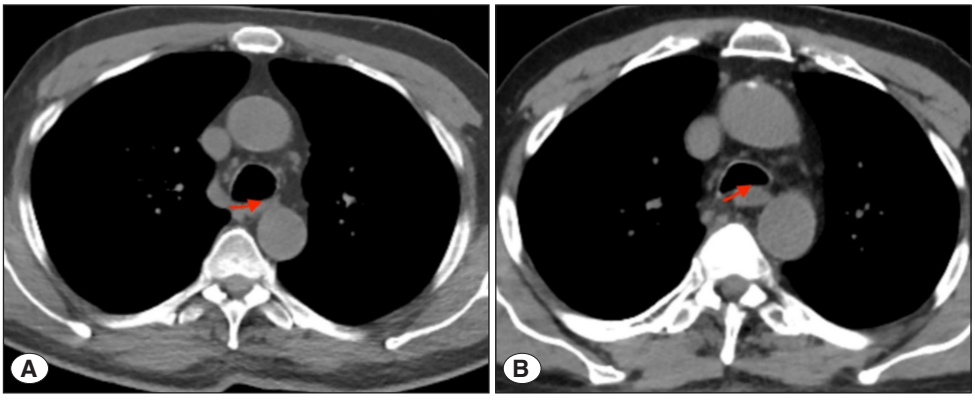



**Figure 3: A)** A mild collapse in the distal tracheal lumen on the thoracic CT scan performed 2 years ago (signed with red arrow). **B)** Progressed collapse in the distal tracheal lumen on the thoracic CT scan taken after radiotherapy (signed with red arrow).

of this case were in line with the literature. We consider that the smoking of the 60-pocket/year current smoker patient caused the development of his pre-existing TBM.

TBM is among the rare complications caused by RT, such as bronchial stenosis, mediastinal fibrosis, and associated recurrent laryngeal nerve injury (10,11). Edematous thickening and softening of the tracheal mucosa and obscuration of the tracheal cartilages were observed in a postmortem TBM case similar to this patient. Histopathologically, selective destruction of the cartilage with Ki-67 stainability from the trachea to the segmental bronchi with inflammatory infiltrations of predominant T lymphocytes (UCHL 1-positive) and activated macrophages (CD68-positive with marked HLA class II antigen) and replacement by collagen fibers through the affected lesion were examined. Every tissue was intact, even the membranous part, with the exception of the cartilage in the airway. Other than the airway, the cartilage of the organs remained unaltered (7). COPD represents the leading etiology for adult TBM (12). A significant fraction of patients suffering from severe emphysema exhibit some degree of central airway malacia. The tracheal wall weakening could be a result of recurrent lung damage from cigarettes, which causes emphysema, or it could just be an extension of the airways' peripheral hypermobility (13). The other etiological factors for adult TBM include post-intubation, post-pneumonectomy, chest trauma, post-lung transplantation, post-tracheostomy, relapsing polychondritis, causes of tracheal compression (goiter, larynx tumor, abscesses, an aortic aneurysm, cysts), undiagnosed vascular rings in children, and severe scoliosis (2,14). We eliminated these factors and considered that the present patient's TBM progressed due to the palliative RT and long-term smoking contributed to this progression.

The gold standard for confirming the diagnosis, severity, and extent of TBM is dynamic bronchoscopy (15). TBM is diagnosed by dynamic bronchoscopy when a reduction of 50% in airway diameter is observed on expiration (16). Real-time visualization of the airways and narrowing is provided by this intervention, and up to 97% of patients have demonstrated concordance between dynamic bronchoscopy and dynamic CT imaging (17). Approximately 50% narrowing of the tracheal and central bronchial lumen was seen on expiration by bronchoscopic evaluation of the patient. Furthermore, the lumen of the trachea, with a mild collapse on the CT scan two years ago, was observed to progress on the CT scan taken after RT.

A fiberoptic bronchoscope should be preferred over large-lumen bronchoscopes that may damage the airways to examine airway collapse. In particular, the middle and distal of the trachea and the proximal of the mainstem bronchi should be evaluated. Patients should be instructed to inspire deeply and expire quickly. The tracheobronchial tree should also be examined on standard tidal respiration. Then, the degree of present collapse can be assessed using images and measurements (18).

To determine the degree of the tracheobronchial collapse, CT scans have been employed. In a previous study (19), the degree of decrease in cross-sectional area (CSA) that would cause symptoms has been detected via end-inspiratory – end-expiratory CT scan. Aquino et al. have proved that the likelihood of tracheomalacia is 89–100% if a patient has a higher than 18% change in CSA in the proximal trachea and a higher than 28% change in CSA in the middle trachea between inspiration and end-expiration. The diagnosis of tracheomalacia can be ruled out at the rate of 95–100% if the change in CSA is less.

Although there are some suggestions for the management of TBM, there is still no guideline. Smoking cessation is an essential supportive treatment as it improves respiratory functional parameters, including obstruction parameters and symptoms, in a short time (20). Patients with clinical findings should be treated. Once many quality metrics (dyspnea, functional status, performance status, and quality of life ratings) have been assessed, medical interventions and noninvasive positive pressure ventilation should be the primary therapies. Interventional bronchoscopy is performed if symptoms persist. It provides malacic airway stenting, the control of complications associated with stents (obstruction, plugging, migrating granuloma), and thermo-ablative therapeutics (electrocautery, argon-plasma coagulation, radio-frequency ablation, laser ablation) (21). Severe patients may be offered a stent trial to see if surgical repair of the obstruction is a feasible option if primary therapies are unable to alleviate significant symptoms. A tracheobronchoplasty may be recommended as the last resort for treatment if the stent trial improves the patient's symptoms and they are judged fit for surgery (15).

The most important limitation was the collection of the patient's data from the hospital's electronic registration system retrospectively. Since the patient received RT at a previous external center and the follow-up doctor did not request an imaging scan before the procedure, the retrospective imagings were scanned, and the last CT scan taken two years ago was compared with the post-radiotherapy CT scan.

In conclusion, TBM should also be considered in the etiology of exacerbated dyspnea and cough in patients with advanced lung cancer after palliative RT. Fiberoptic bronchoscopy and thoracic CT scans are practical tools to diagnose TBM. However, the worsening in the patient's clinical findings, such as dyspnea and cough two months after palliative RT and diagnostic bronchoscopy and thoracic CT findings, confirmed that TBM was progressing.

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## Author Contributions

Concept: **Hülya Abalı,** Design: **Hülya Abalı,** Data collection or processing: **Hülya Abalı, Seda Tural Önür, Aslı Biçen, Kaan Kara,** Analysis or Interpretation: **Hülya Abalı, Seda Tural Önür, Aslı Biçen, Kaan Kara,** Literature search: **Hülya Abalı,** Writing: **Hülya Abalı,** Approval: **Hülya Abalı, Seda Tural Önür, Aslı Biçen, Kaan Kara.**

## Conflicts of Interest

The authors have no conflict of interest to declare.

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The authors declare that this study has received no financial support.

## Ethical Approval

Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

## Review Process

Externally peer-reviewed.

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