

Case Report

Low-Dose Radiotherapy Combined with Tislelizumab in Operable Non-Small Cell Lung Cancer, With New Postoperative Pulmonary Lesions: Diagnosed with Tuberculosis. A Case Report

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Received: April 04, 2026

Accepted: April 23, 2026

Published: April 30, 2026

Abstract

Radiotherapy combined with immunotherapy can be a treatment option for Non-small cell lung cancer. However, distinguishing tumor recurrence from other post-treatment complications, can be diagnostically challenging, especially when clinical and radiological features are ambiguous. We report a patient with respectable NSCLC who received neoadjuvant tislelizumab plus low-dose radiotherapy, achieved MPR after surgery, and later developed multiple new pulmonary nodules. A systematic differential diagnosis ultimately ruled out recurrence and confirmed pulmonary tuberculosis. This case highlights the significant diagnostic value of ctDNA-based MRD technology in precisely identifying the etiology of suspicious lesions in post-NSCLC treatment patients. It demonstrates that ctDNA analysis can be a tool to differentiate tumor recurrence from infectious complications like tuberculosis, thereby guiding appropriate clinical management and preventing misdiagnosis and overtreatment.

Keywords: Low-dose radiotherapy (LDR); Immunotherapy; Tislelizumab; Non-small cell lung cancer; Minimal residual disease (MRD); Tuberculosis.

Introduction

Neoadjuvant immunotherapy has become an important strategy for resectable Non-Small Cell Lung Cancer (NSCLC). Emerging evidence suggests that integrating radiotherapy with immune checkpoint inhibition may further enhance antitumor immune responses. In resectable NSCLC, neoadjuvant durvalumab combined with radiotherapy followed by surgery has been reported to be feasible and safe [1]. Nevertheless, clinical data on neoadjuvant radioimmunotherapy remain limited, and most reported regimens employ conventional or high-dose radiotherapy fields and doses.

In addition, not all patients benefit from immunotherapy, and accurately identifying therapeutic responders and detecting early recurrence remain the major challenges. Circulating Tumor DNA (ctDNA)-based Minimal Residual Disease (MRD) assessment provides a sensitive, dynamic method to evaluate residual tumor burden and relapse risk in early-stage cancers.

Immune Checkpoint Inhibitors (ICIs) can also lead to Immune-Related Adverse Events (irAEs). Although less commonly recognized, tuberculosis reactivation has been increasingly reported during PD-1/PD-L1 blockade. Here, we describe a resectable NSCLC patient treated with neoadjuvant tislelizumab plus low-dose radiotherapy who achieved Major Pathological Response (MPR) but developed new postoperative pulmonary lesions that were ultimately diagnosed as tuberculosis rather than tumor recurrence. We also discuss the clinical value of MRD in recurrence surveillance and the potential association between ICIs and tuberculosis.

Case Presentation

On September 6, 2024, a 70-year-old man presented with intermittent hemoptysis lasting more than 20 days. Baseline PET-CT revealed a soft-tissue mass in the anterior segment of the right upper lobe with increased FDG uptake, accompanied by FDG-avid mediastinal and bilateral hilar lymph nodes (Figure 1A). Additional FDG-avid findings were noted in the intestinal tract and a patchy, mildly hyperdense lesion in the right iliac bone. Subsequent gastroscopy and sacroiliac joint MRI did not support metastatic disease. On September 9, 2024, a lung biopsy confirmed adenocarcinoma (Figure 1B). Molecular testing did not identify actionable driver alterations. The patient then received three cycles of tislelizumab, tislelizumab is 2 pills per cycle, a total of 200mg, as neoadjuvant immunotherapy, combined with LDR which targeted the lung lesion with a prescribed dose of 40 Gy in 20 fractions. Repeat PET-CT demonstrated a reduction in tumor size and decreased FDG uptake compared with baseline (Figure 1C).

On December 18, 2024, the patient underwent video-assisted thoracoscopic right upper lobectomy under general anesthesia. Postoperative pathology (Figure 1D) indicated treatment response consistent with MPR after neoadjuvant therapy. The post-neoadjuvant pathological stage was ypT1aN0Mx. Postoperatively, ctDNA-based MRD testing was negative. The patient was followed regularly as an outpatient. On March 30, 2025, he developed cough, sputum production, and recurrent hemoptysis. Chest CT showed multiple bilateral pulmonary nodules, increased in number and size compared with prior imaging (Figure 2A). Tumor recurrence

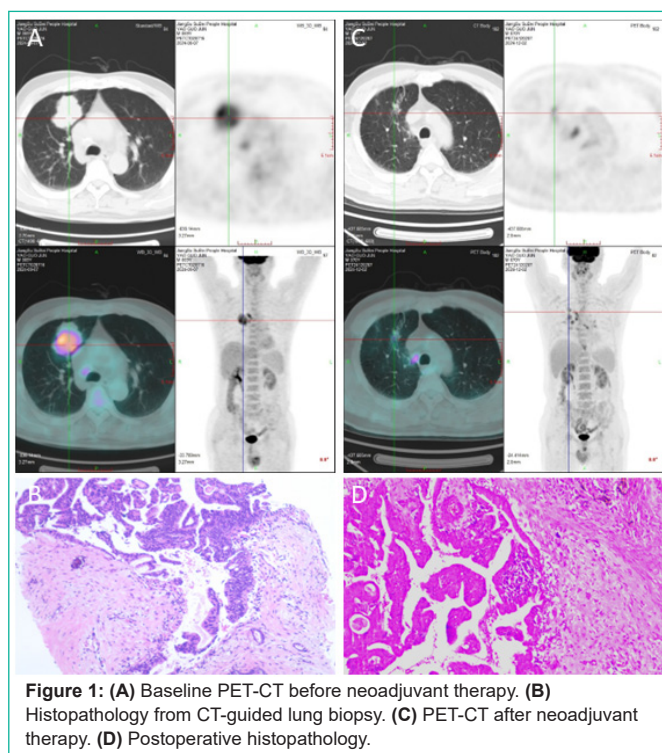


Figure 1: (A) Baseline PET-CT before neoadjuvant therapy. (B) Histopathology from CT-guided lung biopsy. (C) PET-CT after neoadjuvant therapy. (D) Postoperative histopathology.

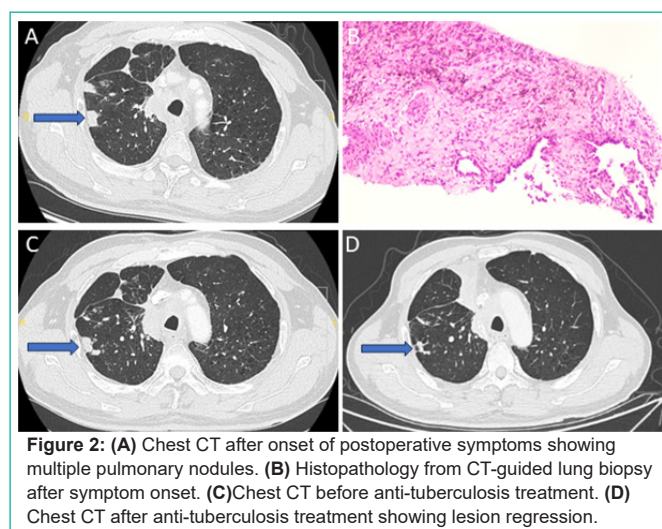


Figure 2: (A) Chest CT after onset of postoperative symptoms showing multiple pulmonary nodules. (B) Histopathology from CT-guided lung biopsy after symptom onset. (C) Chest CT before anti-tuberculosis treatment. (D) Chest CT after anti-tuberculosis treatment showing lesion regression.

was initially suspected. The patient underwent bronchoscopy with bronchoalveolar lavage on April 7, 2025, which did not reveal malignant cells. A repeat MRD test remained negative. After symptomatic management, the patient's symptoms partially improved.

However, on May 12, 2025, the respiratory symptoms recurred. CT-guided lung biopsy was performed, and pathology showed no evidence of malignancy (Figure 2B). Repeated sputum testing eventually yielded acid-fast bacilli on sputum culture. After multidisciplinary consultation (Third People's Hospital of Yangzhou), the diagnosis of pulmonary tuberculosis was favored. The patient was transferred to an infectious disease hospital and started on anti-tuberculosis therapy (Figure 2C). Follow-up CT after treatment demonstrated marked reduction of pulmonary lesions (Figure 2D).

Discussion

Immune checkpoint inhibitors enhance antitumor immunity by restoring T-cell-mediated cytotoxicity. Pivotal trials (KEYNOTE-010, -024, -189, -407) established the efficacy of pembrolizumab as monotherapy or in combination regimens for advanced EGFR wild-type NSCLC [2–5]. In resectable NSCLC, the RATIONALE-315 study demonstrated improved Event-Free Survival (EFS) and Overall Survival (OS) with tislelizumab [6], supporting the clinical relevance of perioperative immunotherapy.

Radiotherapy also exerts immunomodulatory effects. It can increase tumor antigen release, enhance antigen presentation, and upregulate PD-L1 expression on tumor cells, potentially creating synergy with PD-1/PD-L1 blockade [7–9]. High-dose radiation may activate antitumor CD8⁺ T-cell responses but can also contribute to immunosuppressive remodeling in certain contexts [10,11]. In contrast, low-dose radiotherapy has been reported to reshape the tumor microenvironment by preserving lymphocytes, attenuating suppressive stromal/immune components, promoting effector immune-cell infiltration, and modulating chemokine expression [12–14]. In this case, neoadjuvant tislelizumab plus low-dose radiotherapy was followed by radiographic response and MPR at resection, suggesting potential feasibility of this strategy in selected operable NSCLC patients.

Despite advances, identifying responders and detecting early relapse remain challenging. MRD monitoring using ctDNA has emerged as a sensitive approach for detecting residual disease and predicting recurrence, often earlier than imaging. In CheckMate 816, ctDNA clearance correlated strongly with pCR, suggesting ctDNA dynamics may serve as a biomarker for deep response and potentially long-term benefit [15]. In our patient, MRD was negative both perioperatively and at the time new pulmonary lesions emerged, which supported consideration of non-malignant etiologies, prompting further diagnostic work-up.

An increasing number of evidence suggests that tuberculosis can occur during PD-1/PD-L1 blockade, possibly via reactivation of latent infection. Barber et al. described tuberculosis developing after PD-1 inhibition [16], and additional case reports have linked nivolumab to reactivation or dissemination of tuberculosis [17]. A nationwide observational study also indicated that the risk of tuberculosis among cancer patients treated with immune checkpoint inhibitors may be higher than that in the general population [18]. Importantly, cancer itself and prior therapies may contribute to immune dysregulation, complicating causal attribution. In the present case, the patient had unknown history of tuberculosis; however, latent infection could not be excluded. The identification of acid-fast bacilli and lesion regression after anti-tuberculosis therapy supported tuberculosis as the primary cause of postoperative pulmonary nodules. Clinically, this case underscores two practical messages: (1) MRD can provide valuable supportive evidence when imaging suggests recurrence but pathology and cytology are negative; and (2) clinicians should maintain vigilance for infectious complications, including tuberculosis, in patients receiving immune checkpoint inhibitors—particularly in regions with higher background prevalence. Consideration of baseline LTBI screening in selected patients may be warranted, although optimal strategies require further evidence.

Conclusion

Dynamic ctDNA-based MRD monitoring may help distinguish recurrence from non-malignant causes when postoperative imaging shows new pulmonary lesions in NSCLC. Tuberculosis is a potential complication during immune checkpoint inhibitor therapy, possibly through reactivation of latent infection. While immunotherapy enhances antitumor immunity, clinicians should also consider the risk of infection reactivation and pursue timely evaluation when new pulmonary findings emerge.

Author declarations

Declaration of interest

The authors declare that they have no conflicts of interest relevant to the content of this manuscript. No financial, personal, or other relationships have influenced the outcomes or interpretations of the study. All authors certify that the manuscript submitted is original, has not been published before, and is not under consideration for publication elsewhere.

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