Postoperative pathological complete response in a patient with PD-L1-negative stage IIIB lung squamous cell carcinoma following neoadjuvant tislelizumab treatment combined with chemotherapy: A case report and literature review

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Abstract. The utilization of immune checkpoint inhibitors in oncological treatment has increased in recent years. The therapeutic strategy of targeting the programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) pathway has altered the management of advanced non-small cell lung carcinoma (NSCLC). Tislelizumab, a novel anti-PD-1 monoclonal antibody developed in China, has demonstrated efficacy in treating advanced NSCLC. However, its potential role as a neoadjuvant therapy for locally advanced NSCLC has not been definitively established. Current guidelines do not specify which patient populations may gain the most benefit from neoadjuvant immunotherapy coupled with chemotherapy, nor do they indicate the optimal timing, dose or duration of adjuvant maintenance therapy post-NSCLC surgery. Similarly, data concerning the safety and practicability of surgical resection following neoadjuvant tislelizumab treatment for NSCLC remain limited. The present study describes the case of a patient diagnosed with stage IIIB NSCLC, which was initially deemed unresectable. A preoperative biopsy of the tumor mass revealed squamous cell carcinoma and a negative PD-L1 gene test. Notably, after two cycles of neoadjuvant tislelizumab treatment coupled with chemotherapy, the tumor exhibited marked shrinkage. This permitted the patient to undergo thoracoscopic radical lung cancer resection, which resulted in a pathological complete response. Postoperative pathology identified a large infiltration of lymphoplasmacytic cells and foamy histiocytes. The patient experienced grade 2 myelosuppression, a condition that was successfully addressed with the administration of recombinant human granulocyte colony-stimulating factor. The present case indicates the safety and feasibility of neoadjuvant immunotherapy integrated with chemotherapy for patients with locally advanced, PD-L1-negative NSCLC prior to surgical intervention. Moreover, the case suggests the potential of this therapeutic combination to alter the tumor microenvironment. However, the generalization of these findings necessitates further validation through randomized multicenter trials.

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Introduction

Globally, lung cancer ranks as the second most prevalent type of cancer and is the leading cause of cancer-related mortality. Non-small cell lung carcinoma (NSCLC) is responsible for ~85% of these cases, thus indicating its substantial contribution to the global cancer burden (1,2). In accordance with the Comprehensive Cancer Network guidelines, surgery is upheld as the primary and most effective therapeutic modality for resectable stage IA-IIIA NSCLC (3). However, enhancing overall survival duration and minimizing postoperative recurrence pose complex challenges in clinical practice. While perioperative management can marginally extend survival, the cumulative benefit remains restricted (4-6).

A number of studies have indicated that immunotherapy can markedly enhance the therapeutic outcome for patients with advanced NSCLC (7,8). The application of immunotherapy in advanced NSCLC provides a new therapeutic strategy for neoadjuvant treatment of resectable NSCLC. Additionally, a study on nivolumab (9) demonstrated that preoperative nivolumab induction therapy can lead to the expansion of T-cell clones, which may be an advantage of neoadjuvant immunotherapy in combating tumors. Currently, numerous clinical trials (10-12) are investigating neoadjuvant immune checkpoint inhibitor (ICI) therapy for stage IB-IIIA NSCLC. For patients with unresectable locally advanced lung cancer, the prevailing standard of care is concurrent chemoradiotherapy (13); however, a subset of patients still succumb due to disease progression or tumor metastasis (14). The demonstrated efficacy of immunotherapy in advanced NSCLC has generated renewed optimism for patients with unresectable

NSCLC. Furthermore, no definitive biomarkers predictive of the effectiveness of neoadjuvant immunotherapy have been identified. Research has proposed programmed death-ligand 1 (PD-L1) expression levels and tumor mutation burden as two concurrent and potentially predictive indicators of efficacy in neoadjuvant immunotherapy. However, the predictive value of these markers remains contentious, with different studies yielding disparate conclusions (9,15,16).

Tislelizumab is a novel humanized IgG4 monoclonal antibody that acts as an ICI targeting programmed death-1 (PD-1). It exhibits distinct binding epitopes from other PD-1 monoclonal antibodies to enhance its antitumor activity (17). Tislelizumab was approved by the National Medical Products Administration (NMPA) on December 27, 2019, for the treatment of relapsed or refractory classical Hodgkin lymphoma following at least second-line systemic therapy (18). Subsequently, in January and June 2021, it was approved for first-line treatment of metastatic NSCLC of both squamous and non-squamous histology (19,20).

The present case report suggested tislelizumab as neoadjuvant immunotherapy, which may provide significant benefits to patients with PD-L1-negative, potentially resectable stage IIIB NSCLC (21). Furthermore, neoadjuvant immunotherapy has the potential to modulate the immune microenvironment of the tumor without compromising surgical outcomes, thus providing a favorable immune microenvironment for subsequent immunotherapy.

Case report

In August 2022, a 64-year-old Chinese male patient presented for a medical consultation at The Second Affiliated Hospital of Harbin Medical University (Harbin, China). The visit was prompted by the discovery of a pulmonary mass during a physical examination conducted 10 days prior. The patient was asymptomatic, demonstrating no symptoms such as sputum production, hemoptysis, chest pain, hot flushes or night sweats. Additionally, they had neither a history of smoking nor any prior medical issues, and there was no known familial history of cancer. An enhanced computed tomography (CT) scan of the chest and a positron emission tomography-CT (PET-CT) scan of the chest revealed a subpleural mass, measuring 70x59x56 mm, situated in the posterior lateral basal segment of the lower lobe of the right lung. Mediastinal lymph nodes (~20 mm in diameter) and right hilar lymph nodes (~23 mm in diameter) showed enlargement and increased radiological uptake, suggestive of metastases (Fig. 1). However, no notable metastases were detected elsewhere based on the brain magnetic resonance imaging and whole-body PET-CT scans.

A pathological biopsy from the right lung confirmed the presence of squamous cell carcinoma with necrosis in the lower lobe of the right lung (Fig. 2A and B). The patient's blood was analyzed for tumor markers using chemiluminescent immunoassay methods, and the results revealed elevated levels of squamous cell carcinoma antigen at 2.5 ng/ml, surpassing the reference value of ≤2.0 ng/ml. Notably, tests for cytokeratin (CK)19 fragment, neuron-specific enolase, serum carbohydrate antigen 125 and carcinoembryonic antigen returned negative results.

Immunohistochemical staining was also performed. Briefly, tissue was fixed in 4% paraformaldehyde solution at room temperature for 24 h. Subsequently, the tissue was dehydrated in a gradient alcohol series, embedded in paraffin and sectioned (4 μm). Paraffin-embedded sections were then dewaxed, and hydrated in xylene, anhydrous ethanol, gradient alcohol and distilled water. The tissue sections were then placed in citric acid antigen repair buffer (pH 6.0) for antigen repair in a water bath at 100˚C for 15 min; after cooling, the sections were washed three times with PBS (5 min/wash). Sections were blocked for endogenous peroxidase by placing them in 3% hydrogen peroxide solution for at 37˚C for 25 min, and then washed three times with PBS (5 min/wash). The sections were then blocked using 3% BSA (Beijing Coolaber Technology Co., Ltd.) for 30 min at 37˚C and incubated with the following primary antibodies (all antibodies were ready-to-use and supplied by Fuzhou Maixin Biotech Co., Ltd.) for 1 h at 37˚C: CK5/6 (cat. no. MAB-0744; clone no. MX040), P40 [cat. no. RMA-1006; clone no. MXR010], TTF-1 (cat. no. MAB-0599; clone no. SPT24), CD38 (cat. no. MAB-0755; clone no. MX044) and CD68 (cat. no. KIT-0026; clone no. KPI). The sections were washed three times with PBS (5 min/wash). Subsequently, the appropriate secondary antibody (Elivision plus mouse/rabbit; ready-to-use; cat. no. KIT-9902; Fuzhou Maixin Biotech Co., Ltd.) was added dropwise to the section and incubated for 20 min at room temperature. The sections were washed three times with PBS (5 min/wash) and were slowly rinsed with tap water to terminate the color development. Finally, the nuclei were stained with hematoxylin for 3 min, the sections were rinsed with running tap water, dehydrated and sealed. Images were captured under a light microscope.

PD-L1 expression was assessed by immunohistochemistry, as aforementioned. After antibody incubation, the sections were placed on a specific detection platform for 3 h to get the final results and the sections were then detected under a light microscope. Ready-to-use rabbit monoclonal anti-PD-L1 antibodies (cat. no. 8.17.0002; clone no. E1L3N; Amoy Diagnostics Co., Ltd.) were used. The testing platform was Leica Bond-MAx (supplied by Leica Microsystems GmbH). PD-LI protein expression was assessed according to the tumor proportion score (TPS), where TPS is the percentage of live tumor cells that are partially or completely membrane-stained at any intensity. TPS <1% indicates no PD-LI expression, TPS ≥1% indicates PD-L1 expression, and TPS ≥50% indicates high PD-L1 expression. Immunohistochemical staining demonstrated positive staining for CK5/6 and P40 (Fig. 2C and D), whereas TTF-1and PD-LI staining were negative (Fig. 3A and B). The patient's biopsy tissue was subjected to whole-genome sequencing, and the results revealed the absence of mutations in target genes, such as EGFR, ALK or ROS1. In light of the chest-enhanced CT, PET-CT and pathological findings, the patient was diagnosed with locally advanced NSCLC at TNM stage cT3N2M0, stage IIIB. Despite the patient's preference for surgical intervention, a thoracic surgery consultation determined that R0 resection was unfeasible using current surgical techniques. Following a multidisciplinary diagnosis and treatment (MDT) approach, the patient was advised to undertake two cycles of neoadjuvant therapy. Should the tumor decrease in size, the patient could

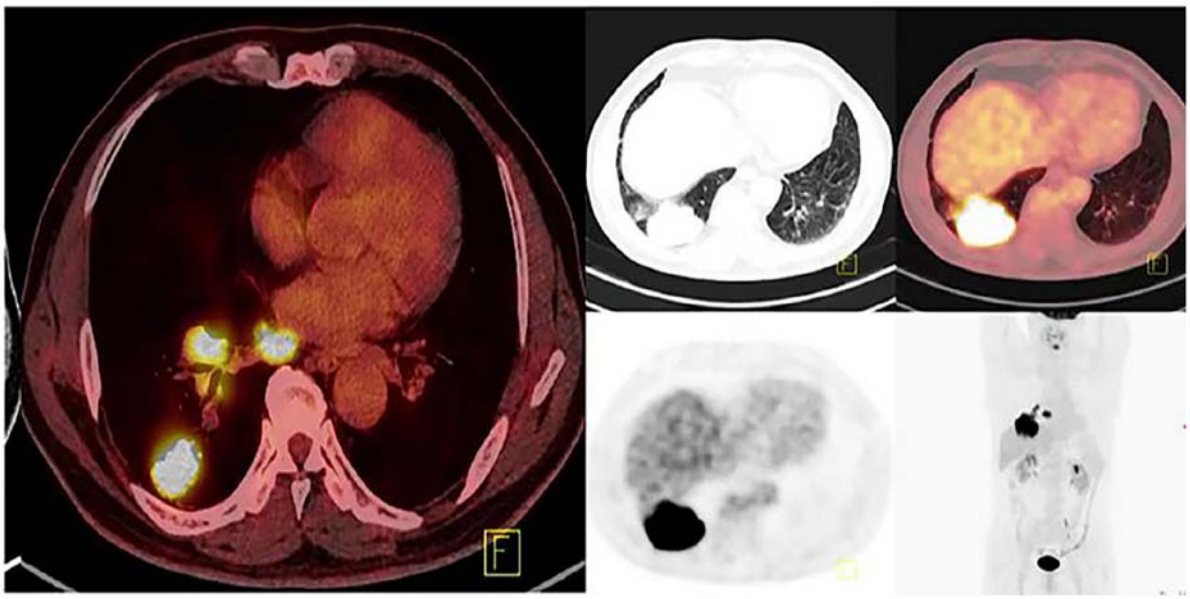

Figure 1. Positron emission tomography-computed tomography image of the patient showing a right lung mass (70x59x56 mm) and enlarged mediastinal lymph nodes before neoadjuvant therapy.

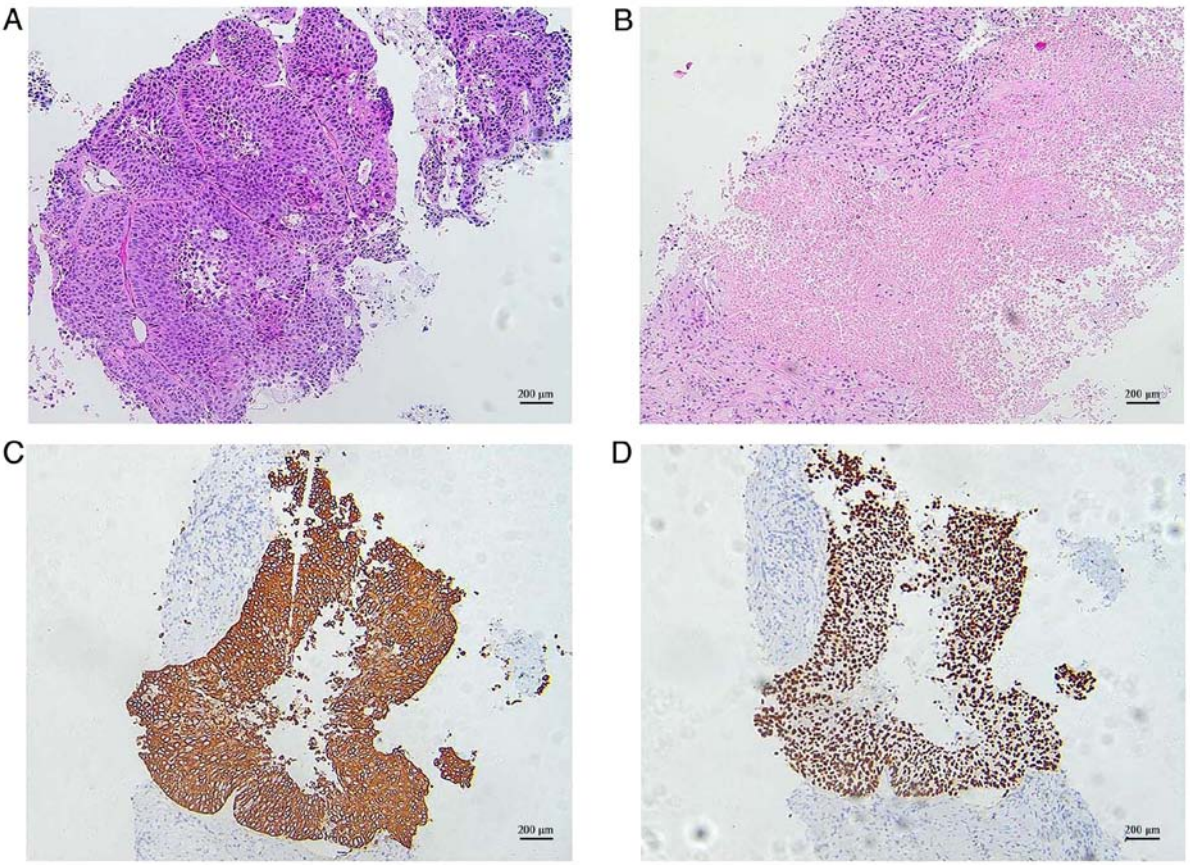

Figure 2. Histological and immunohistochemical findings of preoperative puncture biopsy of the right mass. (A) Microscopic pattern of squamous cell carcinoma in the right side of the lung mass(hematoxylin and eosin; magnification, x100). (B) Necrotic tissue in the lung lesion (hematoxylin and eosin; magnification, x100). (C) Positive immunohistochemical CK5/6 staining (magnification, x100). (D) Positive immunohistochemical P40 staining (magnification, x100) CK, cytokeratin.

be considered suitable for NSCLC resection. Conversely, if the tumor and lymph nodes remained unchanged, radical chemoradiotherapy would be the recommended course.

From August to October 2022, the patient underwent two cycles of neoadjuvant chemotherapy [carboplatin 500 mg (area under the curve, 5) and albumin-bound paclitaxel 300 mg]

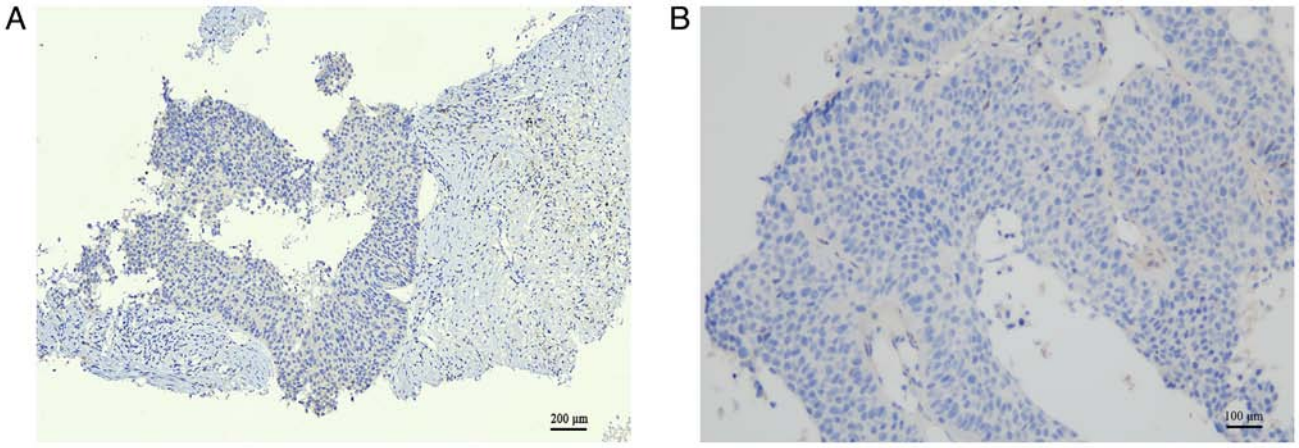

Figure 3. Preoperative pathological microscopic immunohistochemical staining. (A) Negative immunohistochemical TTF-1 staining (magnification, x100). (B) Tissue section staining showed a tumor proportion score of <1%, indicating negative PD-L1 expression (magnification, x200). PD-L1, programmed death-ligand 1.

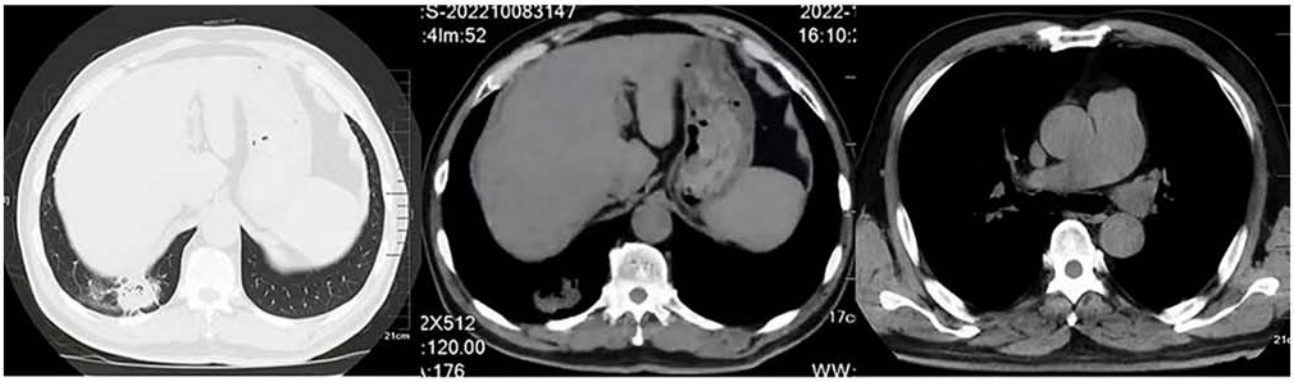

Figure 4. Computed tomography scan of the patient after two cycles of neoadjuvant therapy with immune combination chemotherapy showed a significant reduction in the right lung mass and mediastinal lymph nodes compared with the pre-treatment period.

combined with immunotherapy (tislelizumab 200 mg). After two cycles of neoadjuvant chemotherapy combined with immunotherapy, the patient underwent a follow-up chest contrast-enhanced CT scan in October 2022. The results showed a significant therapeutic effect. In comparison to before the treatment, the tumor in the lower lobe of the right lung was reduced to ~31x27 mm, and there was also a noticeable decrease in the size of the mediastinal lymph nodes (Fig. 4). Following an MDT discussion, surgical intervention was recommended. A total of 6 days after treatment was completed, after ruling out contraindications, the patient underwent radical thoracoscopic lung cancer surgery. Intraoperative cryopathology revealed no metastasis in the lymph nodes of the 7th group (the lymph nodes situated below the tracheal prominence). Postoperative pathology revealed the following: Resected specimen of squamous cell carcinoma of the right lower lobe (below the tracheal prominence) of the lung after chemotherapy; no residual cancer observed in the tumor bed area. Patchy necrosis, fibrosis, and extensive lymphoplasmacytic and foamy histiocytic infiltration were noted. The localized presence of cholesterol crystals and a multinucleated giant cell reaction (~4x2.5 cm) were observed. Bronchial stumps (-) and visceral pleura (-) were unaffected. Lymph nodes in groups 2, 4, 7, 9, 10 and 11 were uninvolved (0/1, 0/2, 0/12, 0/1, 0/3 and 0/6, respectively). Immunohistochemistry results of the postoperative tissue showed CD38 (+) and CD68 (+) expression, predominantly in plasma cells and histiocytes, respectively. CD38 is a surface molecule expressed on plasma cells, whereas CD68 is a reliable marker for macrophages. These findings indicated the infiltration of plasma cells and macrophages in the surgical tissue of the patient (Fig. 5). The patient had an uneventful recovery and was discharged on postoperative day 7. In November 2022, 1 month post-surgery, the patient underwent two further cycles of the pre-surgery chemotherapy and immunotherapy regimen. Subsequently, the patient received maintenance therapy of tislelizumab 200 mg every 21 days. The patient had grade II myelosuppression during tislelizumab treatment, which was controlled by subcutaneous administration of recombinant human granulocyte growth factor and did not prevent the use of tislelizumab. Initial follow-up results were encouraging; however, long-term outcomes are yet to be assessed.

Discussion

Lung cancer is the second most prevalent type of cancer and the leading cause of cancer-related mortality worldwide. In 2020, ~1.8 million fatalities were attributed to lung cancer, with NSCLC responsible for ~85% of these deaths (1,22). Squamous lung cancer represents the most prevalent subtype

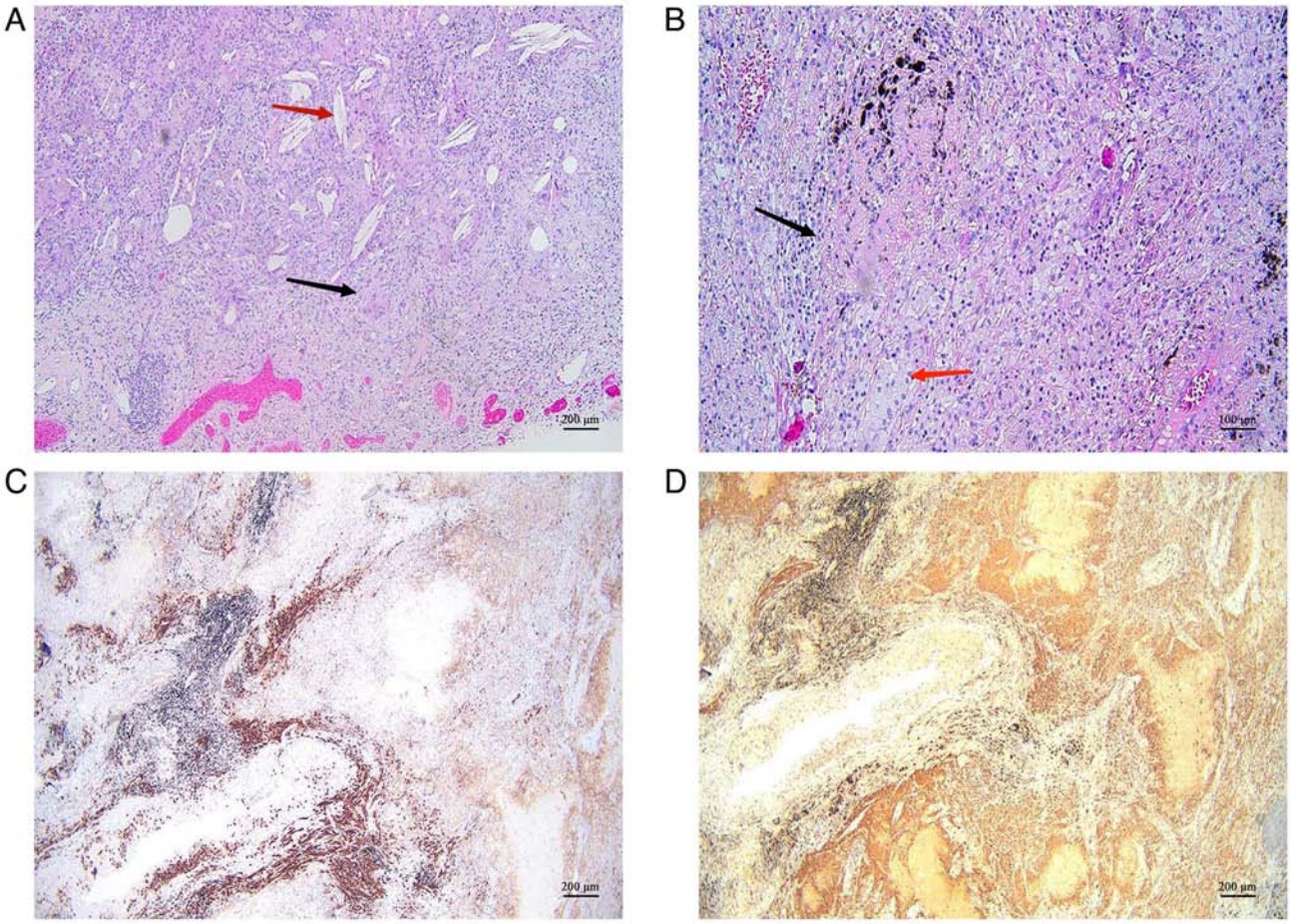

Figure 5. Histological and immunohistochemical findings of postoperative tissues. (A) Red arrows show cholesterol crystals in postoperative tissues and black arrows show multinucleated giant cell infiltration (magnification, x100). (B) Black arrows show plasma cell and lymphocyte infiltration in postoperative tissues and red arrows show foam-like cell infiltration (magnification, x200). (C) Immunohistochemical CD38 positivity in postoperative tissues (magnification, x100). (D) Postoperative tissue immunohistochemical CD68 staining (positive for histiocytes) (magnification, x100).

of NSCLC. The occurrence rate of common driver gene mutations, such as EGFR mutations and ALK gene rearrangements, in lung squamous cell carcinoma is generally low, ~2.7 and 1.5-2.5%, respectively (23-25). Therefore, only a small proportion of patients with squamous cell carcinoma have the opportunity to receive treatment with EGFR-tyrosine kinase inhibitors or ALK inhibitors. Chemotherapy continues to be the main treatment of advanced lung squamous cell carcinoma. Furthermore, several trials on the development of new targets for lung squamous cancer have been terminated due to a lack of efficacy of the drugs or drug toxicity (26,27), thus hampering the advancement of targeted therapies for this disease (28). Immunotherapy has successfully altered the clinical guidelines for advanced lung cancer, including squamous lung cancer. Neoadjuvant immunotherapy, albeit still in the early stages of development, may allow for enhanced activation of antigenic immune activity, control of distant metastases and reduction of disease recurrence, dependent on the preoperative antigens of the patient, an intact lymphatic system and a robust physical condition (29). Previous research has demonstrated that during the initial phase of ICI treatment, patients with NSCLC exhibit a substantial increase in tumor-specific cytotoxic T cells in their blood; this is accompanied by a significant increase in regulatory T cells, and a decrease in natural killer cells and dendritic cells (30,31). Initial findings from prior phase I/II studies have suggested that the combination of immunotherapy and neoadjuvant chemotherapy can yield major pathological response rates ranging from 50-80% in resectable NSCLC (32). Table I provides a summary of several neoadjuvant immunotherapy trials, for which data are currently available.

In recent years, the adverse impacts of coronavirus disease 2019 have limited patient access to care, and subsequently, the diagnosis and treatment of lung cancer. This has led to an increase in patients presenting with unresectable NSCLC and advanced lung cancer (33). NSCLC is a complex disease with diverse clinical treatment modalities, including surgery, chemotherapy, radiation therapy, targeted therapy and immunotherapy. The selection of treatment strategies is closely related to tumor staging. For patients with stage IIIA or IIIB NSCLC without N2 lymph node metastasis, surgical intervention is the preferred approach; however, for patients with positive N2 lymph node metastasis, surgical resection can still be considered following chemotherapy or radiation therapy (34); however, complete microsurgical resection (R0) combined with adjuvant chemotherapy only enhances survival by ~5% (35). Given the demonstrated benefits of immunotherapy in lung cancer, the preferred treatment for temporarily unresectable but potentially

Table I. Trials and results of several neoadjuvant immunotherapies for which data are available.

A, Immunotherapy

Trial	Phase	Patient population	N	Treatment regimen	Initial findings	R0 resection		(Refs.)
						N	Rate, %	
CheckMate159	II	Stage I-IIIA NSCLC	22	Nivolumab	MPR 45% (9/20)	20	100	(9)
LCMC3	II	Stage IB-IIIB (T3N2) NSCLC	181	Atezolizumab	MPR 21% (30/144); pCR 7% (10/144)	145	80.1	(45)
ChiCTR-OIC-17013726	I	Stage IA-IIIB NSCLC	49	Sintilimab	MPR 40.5% (15/37); pCR 16.2% (6/37)	37	92.5	(46)

B, Immunotherapy + ChT

Trial	Phase	Patient population	N	Treatment regimen	Initial findings	R0 resection		(Refs.)
						N	Rate, %	
NCT02987998	I	Stage IIIA NSCLC	9	ChT + pembrolizumab	pCR 67% (4/6)	6	66.7	(31)
NCT04326153	II	Stage IIIA/IIIB NSCLC	20	Sintilimab + ChT	MPR 62.5% (10/16); pCR 31.25% (5/16)	16	80	(47)
NADIM	II	Stage IIIA (N2) NSCL	46	ChT + nivolumab	MPR 83%; pCR 63%	41	89.1	(48)
NCT02716038	II	Stage IB-IIIA NSCLC	14	ChT + atezolizumab	MPR 50% (7/14); pCR 21% (3/14)	11	78.6	(49)
CheckMate 816	III	Stage IB-IIIA NSCLC	358	Arm A: ChT + nivolumab Arm B: ChT	Arm A: MPR 36.9%; pCR 24% Arm B: MPR 8.9%; pCR 2.2%	Arm A: 124 Arm B: 105	Arm A: 83 Arm B: 75	(32)
SAKK16/14	II	Stage IIIIA NSCLC	67	Docetaxel combined with cisplatin + durvalumab	MPR 62%; pCR 18%	55	82	(50)

Table I. Continued.

Trial	Phase	Patient population	N	Treatment regimen	Initial findings	R0 resection		(Refs.)
						N	Rate, %	
C, Double Immunotherapy								
NEOSTAR	II	Stage I-IIIA NSCLC	44	Arm A: Nivolumab arm Arm B: Nivolumab+ ipilimumab	Arm A: MPR 22%; pCR 9% Arm B: MPR 38%; pCR 29%	Arm A: 21 Arm B: 16	Arm A: 24 Arm B: 50	(15)

ChT, chemotherapy treatment; NSCLC, non-small cell lung cancer; MPR, major pathological response; pCR, pathological complete response.

resectable patients now lies in surgical intervention following tumor load reduction via neoadjuvant immunotherapy. However, current trials of neoadjuvant immunotherapy combined with chemotherapy for NSCLC have included only a limited number of patients with stage IIIB cancer.

The present case details a patient with stage IIIB squamous cell carcinoma of the lung, characterized by considerable hilar lymph node enlargement. In this scenario, complete microsurgical resection (R0) may not be feasible and a direct surgical approach might not yield optimal long-term survival benefits. After MDT discussions, and considering the successful application and good accessibility of tislelizumab, the present case employed a neoadjuvant regimen of tislelizumab in combination with liposomal paclitaxel and carboplatin in a patient with stage IIIB squamous cell NSCLC. Despite preoperative genetic testing yielding negative results for PD-L1 expression, the patient achieved a favorable outcome. The procedure was successful and pathological complete response was attained postoperatively. Tislelizumab is an innovative anti-programmed death-1 (PD-1) antibody independently developed by BeiGene (17). The Fc segment of tislelizumab has been engineered to diminish antibody-dependent cellular phagocytosis, T-cell depletion and the potential risk associated with resistance to anti-PD-1 therapy. The RATIONALE307 study (36), which was announced at the 2020 American Society of Clinical Oncology conference, confirmed the effectiveness and safety of tislelizumab in combination with either paclitaxel + carboplatin or albumin-bound paclitaxel + carboplatin, compared with paclitaxel + carboplatin alone, as first-line treatment for advanced squamous NSCLC. Based on the excellent data from the RATIONALE307 study, tislelizumab officially received approval from the NMPA on January 12, 2021, for use as first-line treatment for advanced squamous NSCLC (20); this treatment was revealed to significantly prolong progression-free survival in patients. Relevant investigations regarding the perioperative use of tislelizumab in NSCLC are currently in progress. The RATIONALE 315 (NCT04379635) study (37), which holds the distinction of being the largest perioperative phase III clinical study involving a predominantly Chinese NSCLC patient population, is actively comparing tislelizumab (or placebo) in tandem with platinum-based doublet chemotherapy. This is employed as a neoadjuvant therapy in patients exhibiting resectable stage II or IIIA NSCLC. In May 2023, it was officially announced that the study yielded positive results, with specific data yet to be released. However, it is noteworthy that patients with stage IIIB lung squamous carcinoma were not included in the study.

It is widely acknowledged that the expression level of PD-L1 serves as a critical biomarker for predicting the effectiveness of PD-1 inhibitors. Generally, enhanced PD-L1 expression is considered to correspond to greater efficacy of PD-1 inhibitors; however, emerging evidence in recent years has suggested that the association between the effectiveness of immunotherapy and PD-L1 expression in patients with lung squamous carcinoma is not as robust as in those with non-squamous carcinoma (38). The following potential reasons have been suggested: i) The inherent bias of the assay may be a factor, owing to the absence of a uniform standard for the detection of PD-L1 expression; ii) biological attributes of PD-L1 itself could contribute, such as the non-uniform distribution of PD-L1 within the tumor; iii) the instability of

PD-L1 expression in tumor tissues may serve a role. PD-L1 expression can be influenced by various molecular signals and may change dynamically. Consequently, the PD-L1 expression level determined during a particular sampling may not accurately represent the overall PD-L1 expression level within tumor tissues. Additionally, the efficacy of immunotherapy is deeply intertwined with the molecular pathological characteristics of tumors. Lung squamous cell carcinoma, being a highly mutated and immunogenic type of cancer, tends to exhibit a reduced dependency on PD-L1 expression (39). In the present case report, a pathological assessment of the patient's postoperative specimen revealed that the tissue, after neoadjuvant immunotherapy combined with chemotherapy treatment, exhibited patchy necrosis, fibrosis, and significant lymphoplasmacytic and foamy histiocytic infiltration. Furthermore, local observations of cholesterol crystals and multinucleated giant cell reactions were noted. These findings are consistent with the immune-related pathological response characteristics reported in a previous study (40). The emergence of this response is primarily related to the mechanism of action of immunotherapeutic drugs (41). Neoadjuvant immunotherapy kills tumor cells indirectly by activating tumor-specific T cells, and the stroma that provides nutrients to tumor cells is destroyed, thus leading to the sudden death of the entire tumor cell nest; subsequently, tumor cell debris is rapidly phagocytosed by macrophages to form granulomas, and consequently, a lower proportion of necrosis is pathologically evaluated after neoadjuvant chemotherapy alone (29).

With the continuous emergence of immunotherapy resistance, determining the interaction between immunotherapy and the tumor microenvironment may represent a critical breakthrough to address tumor resistance to immunotherapy. Recently, Hu *et al* (42) performed single-cell sequencing of primary tumor samples from 15 patients with stage IIIA NSCLC, taken before and after neoadjuvant immunotherapy, in order to characterize alterations in the tumor microenvironment during the course of immunotherapy. The study suggested that the presence of $FCRL4^+$ $FCRL5^+$ B cells, $CD16^+$ $CX3CR1^+$ monocytes and alterations in plasma estrogen signatures could serve as novel biomarkers. These findings were further corroborated through validation with independent and publicly available transcriptome data, providing valuable insights for subsequent studies focusing on the interaction between immunotherapy and the tumor microenvironment. According to the imaging assessment, the patient still had lesions after two cycles of neoadjuvant therapy. However, postoperative pathological findings showed complete remission of the tumor and lymph nodes. These results suggested that the conventional criteria (The Response Evaluation Criteria In Solid Tumors) used to evaluate the efficacy of cytotoxic chemotherapy might not be applicable to ICIs (43). Previous research has suggested that pronounced fibrosis, which is typically induced by an effective immunotherapy response, may potentially complicate surgical procedures (44). This can, in some instances, necessitate a transition from thoracoscopy to a more invasive thoracotomy (44); however, such a scenario did not transpire in the current case report. It is important to note that the follow-up period for this case has been relatively brief, necessitating an extended follow-up duration to accurately evaluate long-term efficacy. This finding presents a contrast to previous studies that have suggested PD-L1 positivity as a potential predictor of a favorable response to immunotherapy. Therefore, it is necessary to continue to identify specific predictors of response to neoadjuvant immunotherapy.

In conclusion, the present case report indicated that using tislelizumab in tandem with chemotherapy as a neoadjuvant treatment may serve as an effective therapeutic strategy for patients with stage IIIB lung squamous cell carcinoma who are PD-L1-negative. However, this conclusion warrants further validation through an expanded study with a larger sample size to provide more robust evidence.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

GHC and DQ are the primary physicians who performed the diagnosis and treatment of the patient. GHC, YB, XKS and YJL collected and analyzed clinical data. YJL collected and processed the images. GHC and YY wrote the manuscript. DQ and YY conceived and designed the study. GHC, DQ and YY confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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