Surgical Treatment of Initially Unresectable Locally Advanced Non-small Cell Lung Cancer Following Tislelizumab Plus Chemotherapy: A Case Report

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Case report

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Abstract

Background: Radical concurrent chemoradiotherapy is the preferred treatment for patients with stage IIIB non-small cell lung cancer (NSCLC), but the prognosis is poor. The emergence of immune checkpoint inhibitors has changed the treatment strategy for advanced NSCLC, providing new opportunities for therapy. However, neoadjuvant immunotherapy of locally advanced NSCLC is still in the exploratory stage.

Case presentation: A 47-year-old male with stage IIIB squamous cell lung cancer with invasion of the pulmonary artery, left superior pulmonary vein (LSPV), and left atrium (LA) at diagnosis. The patient's lesions were significantly reduced after four cycles of combined treatment with tislelizumab and carboplatin plus nab-paclitaxel, he then underwent successful left pneumonectomy with mediastinal lymph node dissection, and postoperative pathology showed a pathologic complete response (pCR).

Conclusions: The findings demonstrated that chemotherapy in combination with immunotherapy can provide an opportunity for radical surgery in some patients with locally advanced NSCLC.

Introduction

Lung cancer is the leading cause of cancer-related death worldwide[1]. Radical concurrent chemoradiotherapy is the preferred treatment for patients with stage IIIB lung cancer, but the five-year survival rate is only 24–26%[2]. Multiple studies have verified the value of surgery in multimodality treatment of stage IIIB non-small cell lung cancer (NSCLC)[3–5]. In recent years, the treatment of advanced NSCLC has transitioned to a new stage with the introduction of immune checkpoint inhibitors. Multiple clinical trials reported that chemotherapy combined with immunotherapy can provide more survival benefits than chemotherapy alone in patients with advanced NSCLC[6, 7]. In the era of immunotherapy, this new treatment strategy is expected to improve the prognosis of patients with unresectable stage T4 disease (invasion of the main bronchus or mediastinum). However, clinical experience with immunotherapy used as neoadjuvant therapy for locally advanced NSCLC[8, 9] is limited. Therefore, this study describes one patient with initially unresectable stage IIIB NSCLC who gained an opportunity for surgical treatment after chemotherapy combined with immunotherapy.

Case Presentation

A 47-year-old male with a smoking history of 30 years (30 cigarettes per day) was admitted into our hospital due to repeated cough and expectoration for the past three months. A chest computed tomography (CT) scan revealed irregular patchy high-attenuation patterns in the left hilar region with a size of approximately 6.1 cm × 5.2 cm and involvement of the left pulmonary artery (LPA), left pulmonary vein, and left atrium (LA) (Fig. 1A-C). The blood squamous cell carcinoma-associated antigen (SCC) level was 18.16 ng/mL, and neuron specific enolase (NSE) and carcinoembryonic antigen (CEA) levels were within normal ranges. Tracheoscopy suggested occlusion of the left upper lobe (Fig. 2A). Pathological biopsy of the opening of the upper left lobe confirmed the squamous cell carcinoma. Genetic testing

suggested the tumor was wild-type. The percentage of tumor cells with membranous programmed death-ligand 1 (PD-L1) staining (tumor proportion score) was 20% (Fig. 3A). A whole-body positron emission tomography-computed tomography (PET-CT) scan suggested hypermetabolism of the lymph nodes in stations 4L, 5, and 10L, indicating the possibility of tumor metastasis, and no metastatic lesions were observed in the rest of the body. The primary staging was unresectable cT4N2M0 (stage IIIB). The patient was treated with two cycles of carboplatin (area under the curve (AUC) 5 mg/mL/min) plus nab-paclitaxel (260 mg/m^2) and tislelizumab (200 mg) every 3 weeks. Repeat chest CT was performed two weeks after treatment, and a partial response (PR) was determined (Fig. 1D-F). So the patient received another two cycles treatment and a stable disease (SD) was determined by chest CT two weeks later (Fig. 1G-I). The patient developed fatigue and alopecia during treatment. The blood SCC level was reduced to the normal range. Tracheoscopy also showed a significantly improvement (Fig. 2B). The patient received left pneumonectomy and mediastinal lymph node dissection after preparation for cardiopulmonary bypass through femoral arteriovenous intubation. During the surgery, lymph nodes in station 4 were observed to surround the LPA, with the tumor invading the pericardium and the left superior pulmonary vein (LSPV) but not the LA. The LPA root was dislocated successfully without cardiopulmonary bypass, and intrapericardial cutoff of the LSPV was performed (Fig. 4). The patient had no postoperative complications and was successfully discharged from the hospital. Postoperative pathology revealed proliferation of fibrous tissue with inflammatory cell infiltration observed under a microscope, but no residual tumor cells were noted (Fig. 3B). Reactive hyperplasia was found in lymph nodes of stations 4–7 and 9. The patient was followed up for six months, and no tumor recurrence or metastasis was observed.

Discussion

In recent years, immune checkpoint inhibitors have changed treatment options for patients with locally advanced NSCLC. In the NADIM trial, 46 patients with resectable locally advanced stage IIIA (N2 or T4N0) NSCLC received surgical treatment after three cycles paclitaxel plus carboplatin and nivolumab, 34 (83%) of whom achieved a major pathological response (MPR), while 24 (71%) patients achieved a pCR [10]. Tislelizumab (BGB-A317) is an anti-PD-1 monoclonal antibody. Due to the optimized antibody variable regions binding to the PD-1 target, the affinity of tislelizumab is approximately 50- and 100-times higher than those of nivolumab and pembrolizumab, respectively[11]. No studies have investigated tislelizumab combined with chemotherapy for neoadjuvant therapy of locally advanced NSCLC. The RATIONALE307 trial showed that carboplatin plus paclitaxel/nab-paclitaxel combined with tislelizumab significantly improved the progression-free survival (PFS) of patients with advanced squamous NSCLC compared with chemotherapy alone. More importantly, no relationships were found between clinical response rates and PFS and PD-L1 expression[12]. In this case, the patient with initially unresectable tumor achieved a pCR and received surgical treatment finally, which implied neoadjuvant chemotheraphy combined with tislelizumab may provide an opportunity of radical resection for such patient.

According to previous study, significant response to induction chemotheraphy, both in form of mediastinal downstaging and pCR, has been associatied with improverd survival in such patients

undergoing trimodality therapy[4]. In this case, lesions were significantly reduced after four cycles of chemotherapy combined with immunotherapy, providing an opportunity for radical resection. The experience from this case provides new perspectives for patients with stage T4 NSCLC, especially those with invasion of the mediastinum. Establishing cardiopulmonary bypass before surgery allows surgeons to appropriately manage possible massive hemorrhage during treatment of the lung hilum[13]. Disassociation of the LPA root from enlarged lymph nodes in station 4 with the arterial ligament (AL) as a marker is the key to successful surgery.

This study had 2 problems. First, in this case, clinical efficacy was evaluated as a PR after treatment but as a pCR by postoperative pathology, indicating that differences existed between the imaging and pathological evaluation results for the treatment response. Studies have shown that PET-CT can more accurately evaluate the response of patients with NSCLC to immunotherapy according to metabolic changes in tumor tissues[14]. Developing a better method to evaluate the response to immunotherapy and thus select suitable cases for surgical treatment remains an urgent task. Second, the patients in the NADIM trial received three cycles of immunotherapy combined with chemotherapy before surgical treatment and were still treated with sequential nivolumab therapy postoperatively for one year. However, in this case, the patient received four cycles of immunotherapy combined with chemotherapy before surgery and achieved a pCR. Is sequential immunotherapy necessary? Further studies are needed to answer this question.

Conclusions

In conclusion, this study describes a patient with initially unresectable stage T4N2M0 IIIB squamous cell carcinoma who achieved a pCR through chemotherapy in combination with immunotherapy and successfully underwent surgical resection. Although a long-term follow-up is needed to confirm the efficacy of multimodality treatment, this case reveals that multimodality therapy is important for the treatment of locally advanced NSCLC, and we believe that chemotherapy combined with immunotherapy may offer new hope to some patients with such situation.

Abbreviations

CT: computed tomography; AL: arterial ligament; AA: aortic arch; LPA: left pulmonary artery; LA: left atrium; LSPV: left superior pulmonary vein; LUL: left upper lobe; RPA: right pulmonary artery. NSCLC: non-small cell lung cancer; pCR: pathologic complete response; SCC: squamous cell carcinoma-associated antigen.

Declarations

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Availability of data and materials

All available data are presented in the case.

Authors' contributions

C.H.—Conceptualization, writing original draft. Y.D.—Writing review & editing, supervision. Q.C.—Case collection. F.L.—Writing original draft. X.X.—Conceptualization, case analysis and editing. All authors have read and agreed to the published version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Written informed consent was obtained from the patient for publication of

this case report and accompanying images. A copy of the written consent is

available for review by the Editor-in-Chief of the journal.

Ethics approval and consent to participate

We performed this case report in accordance with the Declaration of Helsinki

and the Ethics Committee of Fujian Provincial Hospital.

New software

The authors declare that no new software has been used.

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Figures

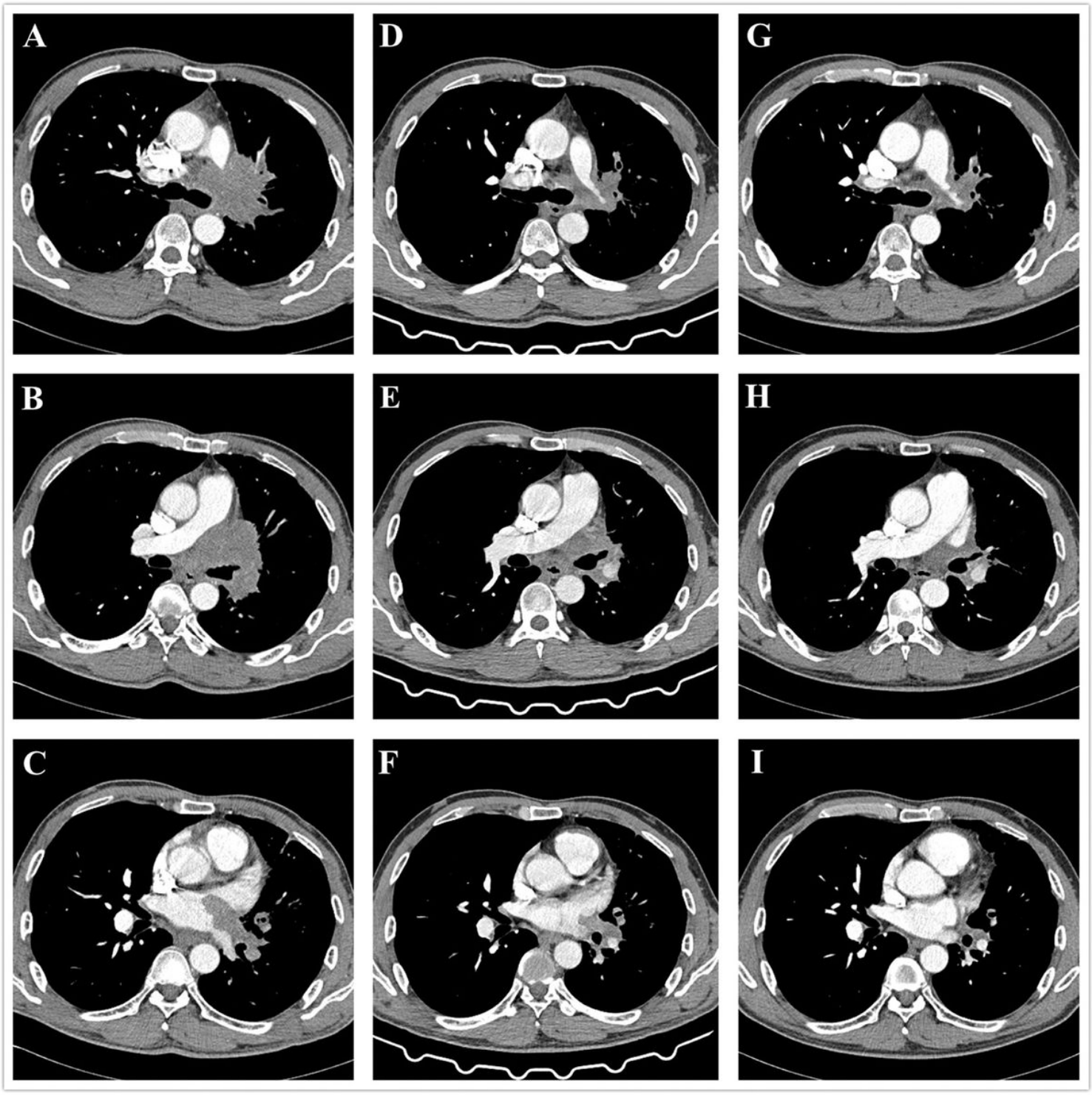

Figure 1

Changes on enhanced chest CT images during treatment. (A-C) Before treatment. (D-F) After two cycles of chemotherapy combined with immunotherapy. (G-I) After four cycles of chemotherapy combined with immunotherapy.

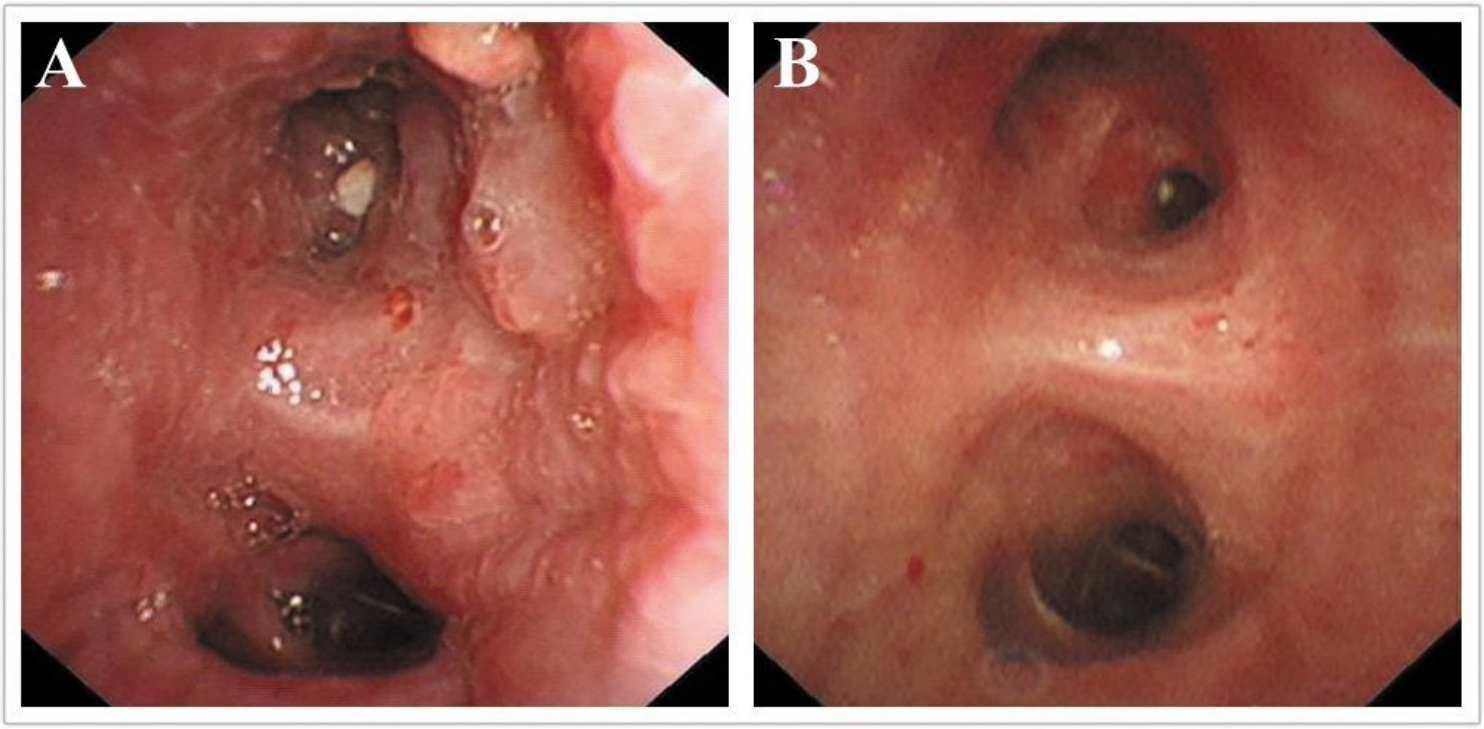

Figure 2

Changes in bronchoscopy findings before and after treatment. Above is the opening of the left superior lobar bronchus, and below is the opening of the left inferior lobar bronchus. (A) Before treatment. (B) After four cycles of treatment.

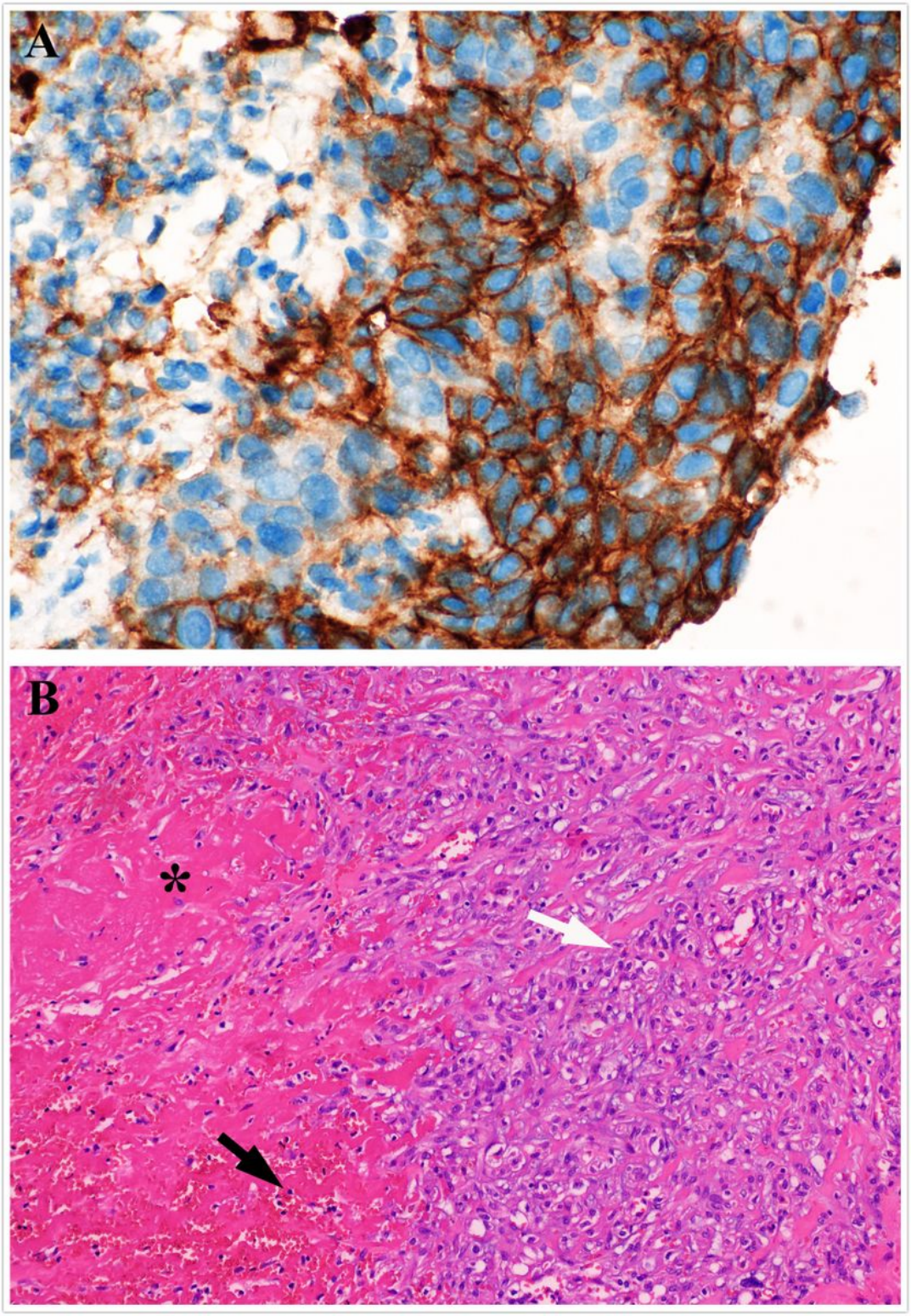

Figure 3

Pathological images (A) Tracheoscopic biopsy specimen before treatment. The tumor cell membrane appears brown after PD-L1 immunohistochemistry staining (22C3). Magnification: 400x. (B) Hematoxylin-eosin (HE) staining of the surgical specimen shows no residual living tumor cells in the tumor bed, and local necrosis (*), inflammatory cell infiltration (black arrow), and fibroplasia (white arrow) are noted. Magnification: 100x.

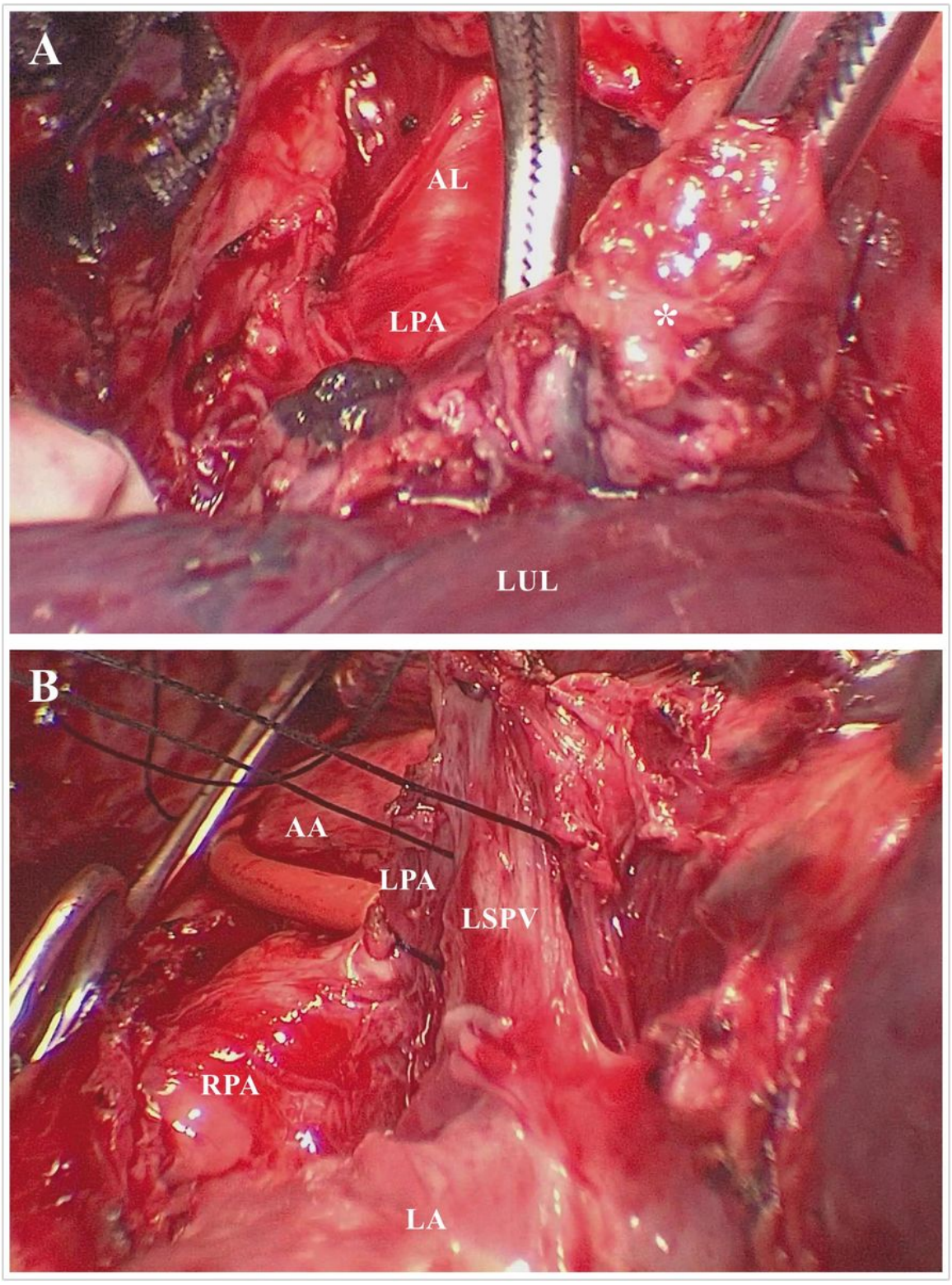

Figure 4

Findings during surgery. (A) Dissociation of the LPA with AL as a marker. (B) Intrapericardial treatment of LSPV. AL: arterial ligament; AA: aortic arch; LPA: left pulmonary artery; LA: left atrium; LSPV: left superior pulmonary vein; LUL: left upper lobe; RPA: right pulmonary artery. *, Station 4 lymph node.