



Treatment of stage IIIA–N2 *EGFR*-mutant non-small cell lung adenocarcinoma

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Introduction

Lung cancer remains the leading cause of death worldwide and is the most common cancer both in incidence and mortality (1.35 million deaths annually). Lobectomy, along with hilar and mediastinal lymph node dissection, is the standard surgical treatment for lung cancer. Roughly 20–25% of patients diagnosed with non-small cell lung cancer (NSCLC) are suitable for surgical resection with curative intent (1).

In patients with advanced-stage *EGFR*-mutant NSCLC (2,3), 60–75% of those treated with *EGFR* tyrosine kinase inhibitors achieve a response, with a median progression-free survival of 10–11 months. On the other hand, 15–30% of individuals achieve a response to platinum-based chemotherapy with a progression-free survival of 5–6 months.

Zhong *et al.* showed that adjuvant gefitinib led to significantly longer disease-free survival than vinorelbine plus cisplatin treatment in patients with completely resected stage II–IIIA (N1–N2) *EGFR*-mutant NSCLC (median 28.7 *vs.* 18.0 months, respectively, $P=0.0054$). Based on this superior disease-free survival, as well as the reduced toxicity of this regimen and the resulting improved quality of life, adjuvant gefitinib could be a potential treatment option compared with adjuvant chemotherapy in these patients (4).

Clinical vignette

A 51-year-old female presented at our institution with a pulmonary peripheral lesion. Chest computed tomography revealed a circular shadow with high density in the inferior lobe of the right lung of approximately 2.4 cm × 2.0 cm

in size, which showed uneven density, vacuole sign, and pleural indentation around the border. No obvious swelling was detected in the lymph nodes of the mediastinum. Resection of the right inferior lobe and mediastinal lymph node dissection were performed under general anesthesia through single-hole video-assisted thoracoscopic surgery in November 2017. Postoperative pathological findings included an adenocarcinoma (3.0 cm × 2.2 cm), invasion of the visceral pleural membrane, and cancer cells in group 7 and 11 lymph nodes. The patient was diagnosed with pT1cN2M0 stage IIIa NSCLC (TNM staging of lung cancer, version 8) and the tumor showed an exon-21-L858R mutation in *EGFR*. Two weeks after surgery, gefitinib was orally administered at 250 mg once a day for 24 months.

Operative techniques

Anatomic lobectomy plus mediastinal lymph node dissection was performed through single-hole video-assisted thoracoscopic surgery (*Figure 1*). The patient was lying on their left side for the surgery. The incision for observation was approximately 1 cm from the 7th intercostal space of the right midaxillary line. The incision for the operation was at the 4th intercostal space between the midaxillary line and the front axillary line, and the length was approximately 3 cm.

Exploration

The adhesion of the lung and chest wall and the presence of effusion in the chest cavity were examined. The position of the tumor and the degree of invasion of the pleural membrane and the surrounding tissue by the tumor was analyzed to determine whether radical resection could be



Figure 1 Anatomical resection of the right inferior lobe and lymphadenectomy with a single operating hole under thoracoscopy (5).

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achieved.

Opening of the anterior and posterior mediastinal pleura to address the hypoplastic lung crack

The pulmonary ligament was released and group 8 and 9 lymph nodes were obtained. Next, the anterior and posterior mediastinal pleura were opened and the mediastinum group 7 and 11 lymph nodes were dissected. The lung branch and esophagus branch of the vagus nerve should be protected when dissecting the subcarinal lymph nodes; protection of the vagus nerve is useful to reduce postoperative cough and promote expectoration drainage and gastric emptying. Next, the sheath of the visceral pleura and pulmonary arteries at the junction of horizontal and oblique fissures in the lungs was opened and group 11 lymph nodes were removed. The tunnelings between the anterior and posterior mediastinal pleura and the vessel sheath were opened. To reduce postoperative pulmonary air leakage, the hypoplastic lung crack should be sewn up and cut off using linear cut staplers.

Management of blood vessels and bronchi

It is easy to free blood vessels after fully opening the vascular sheath of the right inferior pulmonary artery and vein. Free blood vessels were then sewn up and cut off with linear cutting staplers. After thorough dissection of the lymph nodes around the bronchus of the inferior lobe of the right lung, the right inferior lobar bronchus was clipped with a linear cutting stapler and severed after ensuring that the middle and upper lobe of the right lung

could swell. The inferior lobe of right lung was placed in a glove and removed; this specimen was sent for quick pathology.

Before cutting off the vessels and bronchi, the surrounding nodules were cleaned to ensure that no lymph nodes were pinned to the vessels and bronchus stump to avoid leaving any tumor cells.

Lymph node dissection, hemostasis, and closure of the incision

After rapid pathological confirmation of lung adenocarcinoma, the lymph nodes of mediastinal groups 2R, 4R, 10 and 11 were dissected. Warm saline was used to flush the chest and to thoroughly stop the bleeding. To reduce postoperative rebleeding, lymphatic leakage, and postoperative intractable cough, gelatinous sponges were placed in the dissected lymph node beds. These can help block hemostasis and prevent lymphatic leakage and can reduce the occurrence of postoperative cough by reducing postoperative tracheal activity.

Comments

(I) We first cut off the pulmonary artery and then the pulmonary vein (*Figure 1*). The main purpose was to reduce the amount of blood remaining in the lung. This strategy can reduce blood loss; however, it can also reduce the volume of the resected lung. This allows easy removal of the resected lung through the surgical incision.

Expert opinion: in principle, the pulmonary vein should be cut first, followed by the pulmonary artery. Evidence has already shown that tumor thrombus can be found in the blood vessels of a resected lung, and thus cutting off the pulmonary vein first can minimize the possibility of tumor thrombus disseminating into the blood circulation.

(II) This patient had no evidence of lung infection. Computer tomography (CT) of the lung showed that the right lung mass had lobulation, cavitation, and pleural depression, all of which strongly suggested the possibility of lung cancer. Therefore, we directly performed lobectomy through a single hole.

Expert opinion: direct lobectomy is not advisable without definitive pathology. Moreover, as the patient's lung placeholder was peripheral, we could confirm the pathological diagnosis by percutaneous lung puncture

before surgery or by intraoperative frozen pathology. The decision to undertake a lobectomy was made according to the pathology. Pulmonary lobectomy is more formal and more reasonable after definitive pathology.

Discussion

NSCLC accounts for approximately 80% of all lung cancers, and approximately 20% of NSCLC cases are stage IIIA–N2 (6,7). The overall survival rate of patients with stage IIIA–N2 NSCLC administered a single treatment regimen (surgery alone or radiotherapy alone) is poor. *The Guidelines for Lung Cancer in 2015: Consensus and Controversy* (8) indicated that surgery and postoperative chemotherapy should be the first choice for some stages of NSCLC (such as T3N1 or T1–2N2) that can be surgically resected. Complete surgical resection has an important role in the treatment of stage IIIA–N2 NSCLC. Zhong and colleagues reported that adjuvant gefitinib led to significantly longer disease-free survival compared with vinorelbine plus cisplatin in patients with completely resected stage II–IIIA (N1–N2) *EGFR*-mutant NSCLC (4). Based on superior disease-free survival, reduced toxicity, and improved quality of life, adjuvant gefitinib could be a potential treatment option compared with adjuvant chemotherapy in these patients. Therefore, for stage IIIA–N2 *EGFR*-mutant NSCLC, our hospital performs radical surgical resection first, oral targeted drug treatment is started two weeks after surgery and lasts 24 months if the patient can tolerate the side effects of targeted drug.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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