



Radical surgical resection after neoadjuvant targeted therapy in non-small cell lung cancer: a single-center retrospective study of 6 cases

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Introduction

With the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) recurrence, gefitinib is the first targeted drug to be approved for advanced non-small cell lung cancer (NSCLC) that failed to respond to chemotherapy (1). A great quantity studies show that gefitinib has fairly active anti-tumor activity, especially for tumors with mutations or a copy number gain of *EGFR* gene (2). However, there have been few data about the preoperative gefitinib treatment in NSCLC patients (3). At present, the first line treatment of patients with locally advanced NSCLC still mainly rely on neoadjuvant chemotherapy (4). While the effect of gefitinib as a neoadjuvant or preoperative therapy remains unclear (5). Preoperative neoadjuvant targeted treatment is a new departure (6).

To explore the efficacy of preoperative targeted adjuvant therapy, we describe one case of radical surgical resection of residual disease after dramatic response to gefitinib in patients with locally advanced lung adenocarcinoma harboring *EGFR* gene mutation in this report.

Methods

Patient

We retrospective collected 6 cases, clinical staging IIIA-IIIB from March 2017 to September 2018 (Table 1). This typical patient was a 43-year-old woman. She accepted the EBUS-TBNA first because complete resection of the tumor would not have been technically feasible. The pathological result of the 7th lymph node (LN) is adenocarcinoma while the

L858R harbored a detectable mutation by the directed polymerase chain reaction-based sequencing analysis method. The patient accepted neoadjuvant gefitinib therapy for 8 weeks as the first-line therapy. The subsequent chest computed tomography (CT) examination had revealed that the lump located on the inferior left lobe and the mediastinal lymph nodes rebound significantly. The carcinoembryonic antigen (CEA) also descend from 20 to 7.2 ng/mL (6). Therefore, preoperative gefitinib treatment made it possible to perform radical resection in this case. Due to the patient have the indications for surgery, the lobectomy and mediastinal lymphadenectomy were performed.

Operative technique

The surgery was performed under general anesthesia with double lumen tubes which ensure that the operated thoracic cavity had good visual field, along with contralateral one-lung ventilation. The patient was placed in a vertical lateral position, with a sponge mat under the right side of the chest. The left upper limbs were elevated to form a 90-degree angle with the trunk.

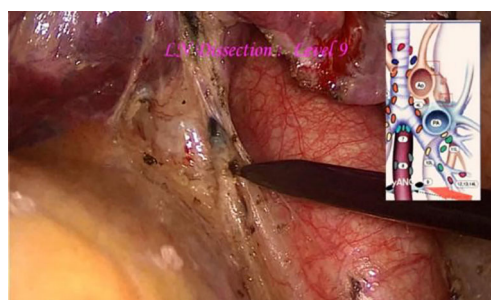
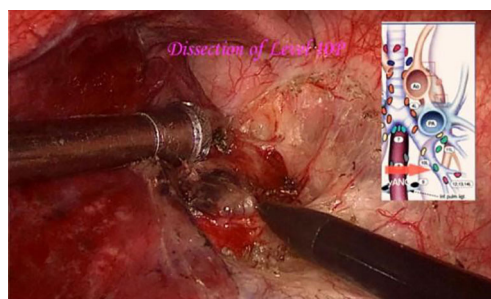
Three operating ports were used during the single-direction video-assisted thoracoscopic lobectomy. The three operating ports were located as follows: a 1.5-cm observation port was created in the 7th intercostal space at the left middle auxiliary line, a 3-cm incision was made in the 4th intercostal space at the left anterior line, and a 2-cm auxiliary port was made at the 7th intercostal space at the left posterior line. The operator stood at the abdominal side of the patient, and the assistants stood at the back side.

Table 1 Patient characteristics

Clinical parameters	Total
Age, range	42–62
Sex, male/female	2/4
ECOG	
0 or 1	6
2	0
Smoking status, yes/no	2/4
Preoperative staging	
IIIA	5
IIIB	1
Histological type	
Adenocarcinoma	6
Squamous-cell carcinoma	0
Gene mutation site	
L858R	3
19-del	3
EGFR TKI	
Gefitinib	6
Others	0
Operation time	170–230 min
Operative blood loss	50–200 mL
Postoperative staging	
IA	1
IIA	0
IIB	2
IIIA	3
IIIB	0

ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

At first, the thoracoscope was inserted along the observation port, and the position of the tumor and the pleural cavity should be observed (1). With a thoracic exploration, the assistant inserted a forester forcep into the auxiliary port to track the left lower lobe towards the head side, to expose the left inferior pulmonary ligament (2). The metastatic mediastinal lymph node was dissected firstly before the lobectomy because the pathological result was confirmed by EBUS-TBNA before the neoadjuvant targeted therapy (4).

**Figure 1** Dissection the 9th LN. LN, lymph node.**Figure 2** Dissection the 10thP LN. LN, lymph node.

The single-direction video-assisted thoracoscopic lobectomy was performed due to the fused oblique fissure (7). For traditional left lobectomy, the following structures are operated in the order: pulmonary vein—oblique fissure—pulmonary artery—poorly developed fissure—bronchus (3). In this case, the following structures are operated in this order: pulmonary vein—bronchus—pulmonary artery—fused oblique fissure.

The primary surgical procedure about the mediastinal lymph node dissection was illustrated below (*Figures 1–8*). The primary surgical procedure about lobectomy was illustrated below (*Figures 9–11*). The left inferior pulmonary vein was first isolated (*Figure 9*). The bronchus was isolated and dissected without flipping the lobe in the single-direction method (*Figure 10*). The inferior pulmonary artery was resected at last by endo straight cutting stapler (*Figure 11*). The fused pulmonary fissure was resected finally, and the specimen was removed.

Comments

Clinic result

The resected tumor exhibited components of adenocarcinoma. No metastasis was found in all the 11 resected lymph nodes



Figure 3 Dissection of the 7th LN. LN, lymph node.



Figure 7 Dissection the 6th LN. LN, lymph node.

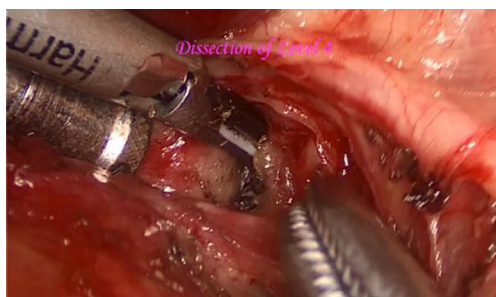


Figure 4 Dissection of the 4th LN. LN, lymph node.

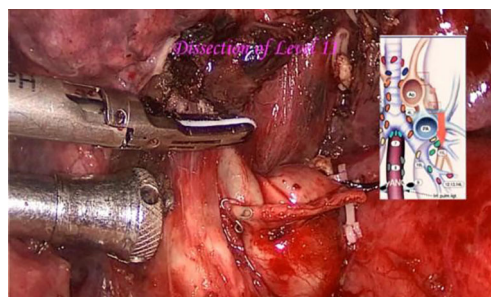


Figure 8 Dissection 11th LN. LN, lymph node.

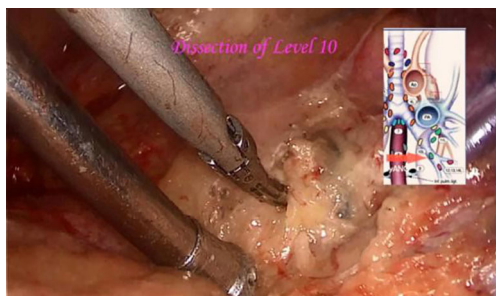


Figure 5 Dissection of the 10th LN. LN, lymph node.



Figure 9 Dissection of left inferior pulmonary vein.

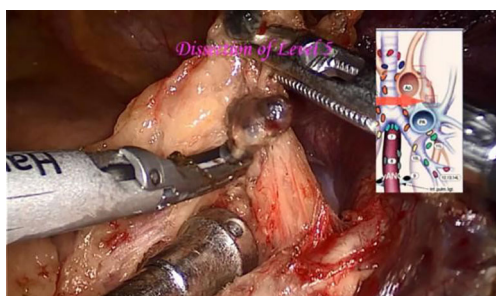


Figure 6 Dissection of the 5th LN. LN, lymph node.

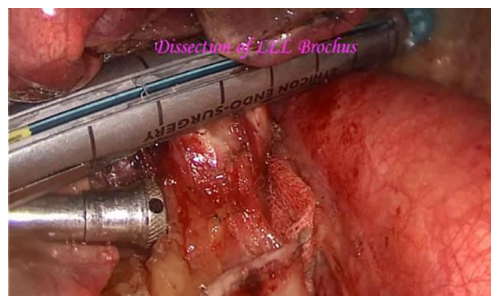


Figure 10 Dissection of the bronchus.

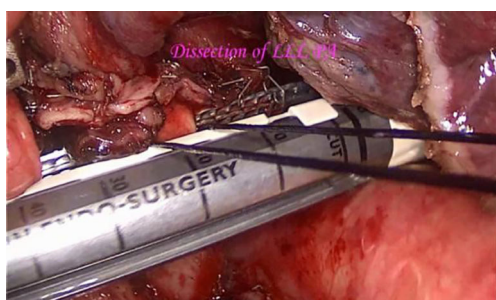


Figure 11 Dissection of the inferior pulmonary artery: pull the artery with silk suture, tense the suture probe endoscopic linear stapler in and cut the artery off.

in this case while the postoperative pathological result was ypT1N0M0, stage I. The patient was discharged without complications at the 5th postoperative days. The patient received targeted adjuvant therapy in 2 weeks after operation. The patient is still alive, without recurrence or metastasis for 12 months after the operation.

In our medical center, all the six patients with neoadjuvant targeted therapy were performed complete video-assisted thoracic surgery (cVATS) since Jan 2017. There is no conversion to hybrid VATS or thoracotomy. Neoadjuvant targeted therapy does not reduce the patient's physical strength, allowing the patient to undergo surgery. Different from the cases who accepted neoadjuvant chemotherapy, no additional tissue adhesions, indistinct interface and increased fragility of the blood vessels were observed during the operation in these neoadjuvant targeted cases. The neoadjuvant targeted therapy eventually improves tumor resectability.

In conclusion, TKI therapy provided an alternative approach for neoadjuvant or preoperative treatment in patients with locally advanced NSCLC with EGFR mutations.

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Footnote

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

Informed Consent: Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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