CASE REPORT

Prolonged survival in advanced squamous cell lung carcinoma by rational and standardized treatment: A case report of long-term survival in a patient with NSCLC

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Abstract
Objective: To report the treatment of a long-term survival case of stage IV lung squamous cell carcinoma (LSCC) patient with multiorgan metastases, including intrapulmonary, brain, liver, bone, and multiple lymph nodes.

Methods and results: A 72-year-old male patient with stage IV LSCC achieved a total survival of 85 months with comprehensive treatment of chemotherapy, radiotherapy, targeted, and immunotherapy.

Conclusion: Full-course management, multidisciplinary diagnosis and treatment, and rational application of multiple treatment measures can improve the quality of life of the patient with advanced lung cancer and prolong their survival.

KEYWORDS
lung squamous cell carcinoma, MDT, NSCLC

1 | GENERAL INFORMATION

A 72-year-old male patient was admitted to our hospital on May 27, 2013 with chief complaint of “irritant dry cough for more than 2 months.” The patient had dry cough and mild chest tightness without any obvious reason from the end of March, 2013. Chest CT done on May 16, 2013 suggested right lung cancer (2.3 × 2.9 cm) with bilateral intrapulmonary metastases, possible mediastinal lymph node metastasis and space occupying lesion in the right lobe of the liver (metastasis could not be excluded). Brain MRI on May 20, 2013 (Figure 1) showed possible metastatic tumor. Fiberoptic bronchoscopy examination found there was a bronchial mucosa lump with a smooth surface in the right lower lobe. Cytopathological examination found malignant tumor cells and suggested nonsmall cell lung cancer with a high possibility of squamous cell carcinoma. Biopsy of mediastinal lymph node aspiration showed the presence of malignant tumor cells. The patient was diagnosed with LSCC by expert consultation. Bone ECT in May 2013 showed possible lesion in the right 12th posterior rib. Head MRI in May 2013 displayed multiple nodules in the brain parenchyma with obvious cerebral edema indicating multiple brain metastases. Chest and abdomen CT on May 27, 2013 (Figure 2) displayed a mass shadow in the right lower lobe of lung, and multiple nodules in the bilateral lungs.
which were considered to be lung cancer in the right lower lung with multiple intrapulmonary metastases. CT also showed multiple enlarged right supraclavicular, mediastinal and right hilar lymph nodes, and compressed trachea and esophagus. In addition, abdomen CT showed a nodular shadow in the right lower lobe of the liver, and the intrahepatic bile duct and common bile duct were dilated. Diagnosis at admission was “Right lung LSCC with multiple lymph node, intrapulmonary, liver, brain and bone metastases, T4N3M1, and stage IV”. ECOG was 2 points. The patient had no history of hypertension, diabetes, heart disease, hepatitis, tuberculosis, allergy, and drinking. However, the patient has had gallstone for 5 years and had not received any treatment. The patient had a 10-year smoking history (7-8 cigarettes/day) but had quit smoking for 30 years. The death reason of his parents was unknown; his siblings and children were healthy. Physical examination: temperature: 36.5°C, pulse: 76/min, respiratory rate: 18/min, blood pressure: 105/67 mmHg. The patient was in a good consciousness and spirit, had no dizziness, headache, hoarse voice, and difficult swallowing. Heart rate was 76 beats/min, and had no arrhythmia. The patient also had no chest pain and tightness, no obvious cough, sputum and dyspnea, and no obvious dry or wet rales in both lungs. The abdomen of the patient was soft and no tenderness as well as no nausea and vomiting. There were no petechiae on the skin and superficial lymph nodes were not enlarged. The physiological reflexes were present, and pathological reflexes were not induced.

2 | TREATMENT HISTORY

2.1 | First-line treatment (May 29, 2013 to August 5, 2013)

In June 2012, JCO published a phase III randomized controlled study, which compared the efficacy of albumin-bound paclitaxel combined with platinum and regular paclitaxel combined with platinum. The former showed significant clinical benefit. However, 2013 NCCN guideline updated the first-line treatment recommendation, that is, albumin-bound paclitaxel combined with cisplatin or carboplatin can be used in patients with performance status (PS) score of 2. Therefore, we chose the regimen of albumin-bound paclitaxel in combination with cisplatin as the first-line treatment for this patient. The patient received four cycles of the combination intravenous chemotherapy from May 29, 2013 to August 5, 2013. On May 29, 2013, the patient began the first cycle treatment of albumin-bound paclitaxel (d1) + cisplatin 120 mg (d1), and experienced headache on June 13, 2013. Numerical rating scale (NRS) score was 6. According to the guideline of lung cancer complicated with brain metastasis, as to the symptomatic NSCLC patients with brain metastases, surgical resection or whole brain + stereotactic radiotherapy can be used when the number of metastases is less than 3. If the number of metastases is more than

![Figure 1](image1.png)  
**Figure 1** Brain MRI on May 20, 2013 showed multiple brain metastases (red arrow shown)

![Figure 2](image2.png)  
**Figure 2** CT on May 27, 2013 showed a mass shadows in the right lower lobe of liver and multiple nodules in the bilateral lungs (red arrow shown)
3, stereotactic radiotherapy or whole brain radiotherapy can be used. The patient received whole brain radiotherapy with a transition dose of 30 Gy/10 F in our hospital from June 13, 2013 to June 25, 2013. The patient also received one cycle of chemotherapy of albumin paclitaxel 200 mg (d1, d8) + cisplatin 30 mg (d1-2, d7-8). Re-examination of chest CT on July 10, 2013 (Figure 3) showed: (a) The mass in the right lower lung was smaller than before; (b) The multiple nodules in both lungs, and liver metastases were all smaller than before (red arrow shown).

**FIGURE 3** After 2 cycle treatment, the maximum reduction rate was 41%. The lower right lung lesions, the multiple nodules in both lungs, and liver metastases were all smaller than before (red arrow shown).

**FIGURE 4** Before May 2013 radiotherapy (left) and after July 2013 radiotherapy (right), brain metastases were reduced (red arrow shown).

**FIGURE 5** After 4 cycle treatment, the right lower lung lesions, two lung metastases, and liver metastases were all smaller than before (red arrow shown).
showed brain metastases complicated with cerebral edema. Then the patient achieved partial response after 2 cycle treatment by efficacy evaluation and the maximum reduction rate was 41%. One cycle of chemotherapy of albumin paclitaxel 200 mg (d1, d5) + cisplatin 100 mg (d1) began from July 13, 2013, and another cycle of chemotherapy of albumin paclitaxel 200 mg (d1, d8) + cisplatin 100 mg (d1) was performed from August 5, 2013. Re-examination of chest CT on August 26, 2013 showed: (a) tumor in the right lower lung with bilateral lung metastases; mediastinal and right hilar, right supraclavicular lymph node metastases; liver metastasis had shrunken. (b) Gallbladder volume had increased significantly than before. Head MRI showed that metastatic lesions in the bilateral parietal lobes were smaller than before; peripheral cerebral edema reduced considerably than before. Evaluation of efficacy after 4 cycles was stable disease (SD) (Figure 5). Considering the patient could possibly not tolerate any further treatment after four cycles of chemotherapy and whole brain radiotherapy, the patient was recommended to follow up after discharge.

2.2 Second-line treatment (November 14, 2013 to October 20, 2014)

The patient was followed up after the first-line treatment. Re-examination of head MRI on October 31, 2013 found that brain metastases were further reduced than before, particularly, lesions in the right parietal lobe had basically retracted. Chest CT (Figure 6) showed: (a) The mass in the right lower lung was smaller than before; however, the number of nodules in both lungs increased and the size of the nodules also grew larger; (b) Lymph nodes in the mediastinum were smaller than before; (c) The nodule in the liver was not observed. To control disease progression, the patients received second-line targeted therapy from November 2013 to October 2014. From November 4, 2013, the patient voluntarily participated in a randomized, open-label phase III clinical trial which aimed at evaluating the efficacy of afatinib and erlotinib as second-line treatment in patients who had advanced LSCC and underwent first-line platinum-based chemotherapy. Pathological examination before enrollment diagnosed squamous cell carcinoma in the right middle lung. Then he was randomly assigned to the erlotinib group and started taking erlotinib (150 mg qd) from November 14, 2013. Re-examination of chest and abdomen CT on January 6, 2014 found the following signs: (a) The tumor in the right lower lung continued to shrink, the metastatic nodules in the bilateral lungs had also shrunken, and the mediastinal lymph nodes were slightly reduced in size; (b) Gallbladder was still enlarged but more improvement was observed. Efficacy evaluation was SD. Re-examination of chest and abdomen CT on February 7, 2014 showed that: (a) The tumor in the right lung and nodules in the bilateral lungs did not significantly
change compared with before; (b) Right supraclavicular, right hilar, and mediastinal lymph nodes did not show significant change than before; (c) Presence of a small amount of pericardial fluid was observed; (d) The gallbladder was still swollen. Head MRI (Figure 7) indicated the metastases in the brain further shrunk and some disappeared. Efficacy evaluation was SD. Chest CT on March 10, 2014 did not find obvious changes and head MRI showed significant regression of the lesions in the bilateral parietal lobes. Efficacy evaluation was SD. Chest CT and head MRI on May 4, 2014 showed the patient was still in SD. Chest CT on June 26, 2014 (Figure 8) found some intrapulmonary metastatic nodules enlarged slightly than before, and the patient was in SD. Re-examination of chest CT on August 21, 2014 did not show disease progression either. Chest CT on October 17, 2014 (Figure 9) demonstrated the enlargement of intrapulmonary nodules and supraclavicular and mediastinal lymph nodes. Other lesions were similar with before. The patient was judged to be progression disease (PD), and discontinued the administration of erlotinib after October 20, 2014. During the treatment of erlotinib, the greatest tumor regression rate was 17.1%. The progression-free survival was 11 months (from November 14, 2013 to October 20, 2014).

2.3 | Third-line treatment (October 22, 2014 to March 31, 2015)

After being resistant to second-line TKI treatment, the patient voluntarily participated in a phase I clinical trial which was used to evaluate the tolerance and pharmacokinetics of paclitaxel micellar for injection from October 20, 2014. The first cycle treatment (paclitaxel micellar 720 mg[430 mg/m2] d1) began from October 22, 2014. Blood routine test showed grade IV bone marrow suppression, the dose was then reduced to 540 mg, d1 from November 12, 2014 and severe bone marrow suppression was relieved and did not occur again. Re-examination of chest and abdomen CT on December 1, 2014 showed that the nodules in the bilateral lower lungs were slightly smaller than before, and other signs did not change much. Head MRI did not find significant changes either. Six cycles of paclitaxel micellar chemotherapy (540 mg, d1) were performed on December 2, 2014, December 23, 2014, January 14, 2015, February 10, 2015, March 10, 2015, and March 31, 2015. After finishing the fourth cycle, chest CT showed the nodules in the right lower lung regressed and the small nodules in the left lower lung shrunk more than before. The maximum shrinking rate
was 18.5% and efficacy evaluation was SD. After 6 cycles, re-examination of the chest CT on March 6, 2015 showed that the nodule in the left lower lung further reduced and other signs were similar with before. The patient was in SD and was followed up regularly. Chest CT on June 12, 2015 showed the nodule in the left lower lung was slightly smaller than before and head MRI did not find obvious brain space occupying lesions. Chest CT on December 14, 2015 showed the lesion in the left lower lung enlarged than before. Furthermore, chest CT on April 27, 2016 (Figure 10) demonstrated the nodule in the left lung enlarged and the left hilar lymph nodes also enlarged, suggesting disease progression. The patient obtained an 18-month progression-free survival from October 22, 2014 to April 27, 2016.

2.4 | Post-third-line treatment (May 4, 2016 to July 10, 2016)

The patient self-administered icotinib (125 mg, qd) from May 4, 2016. Chest CT on May 26, 2016 showed (Figure 11, left) that the nodule in the left lower lung enlarged slightly compared with the CT image on April 27, 2016. Then he discontinued icotinib from July 10, 2016. Chest CT on July 28, 2016 (Figure 11, right) showed that the nodule in the left lower lung enlarged compared with the former image. Head MRI obtained similar results with the examination on June 13, 2015 that obvious space occupying lesion was not observed. Imaging examination indicated disease progression. Progression-free survival was more than 2 months by taking icotinib.

2.5 | Post-third-line treatment (August 29, 2016 to July 11, 2018)

After progression in July 2016, the patient voluntarily participated in an international multicenter phase III clinical study aiming at comparing the efficacy and safety of atezolizumab (anti-PD-L1) and docetaxel in NSCLC patients who failed platinum-based chemotherapy. From August 29, 2016, the patient received MPDL3280A (1200 mg, q3w) for a total of 32 doses. Chest and abdomen CT on July 20, 2018 (Figure 12) demonstrated that compared with the image on May
18, 2018, the nodules in the left lower lung enlarged. The nodules in the right lower lung did not change much. The intrahepatic bile duct and common bile duct were slightly dilated which was similar with before. Other signs, including thickened gallbladder wall and small amount of pelvic effusion, did not show obvious change. Head MRI did not find new lesions either. The patient took chest and abdomen CT again on August 31, 2018 (Figure 13). Compared with the image last time, the nodule in the left lower lung was slightly larger. The patient achieved partial response (PR) with the treatment of MPDL3280A and the maximum shrinking rate was 74.1% (Figure 14). Progression-free survival was 24 months.

2.6 | Post-third-line treatment (September 17, 2018 to April 26, 2019)

After disease progression on July 2018, the patient underwent stereotactic body radiation therapy (SBRT) to control the metastatic tumor in the left lower lung (Figure 15) suggested by a multiple disciplinary team (MDT). The transition dose was 50 Gy/10 F. Chest and abdomen CT on October 11, 2018 showed: compared with the image on August 31, 2018, the lesion in the left lower lung had reduced; the flake-like shadow in the posterior segment of the right upper lung enlarged significantly than before; other signs were similar with before. Genetic test on January 30, 2019 showed mutation of TP53, MMR, TMB, and MSI, and no actionable mutations were identified. Radiotherapy was given to control the lesion in the right lung (PTV 48 Gy/8 F) from April 17, 2019 to April 26, 2019. Re-examination of chest and abdomen CT on May 28, 2019 found there was a large consolidation shadow in the left lower lung which could not be clearly differentiated from the tumor, which was considered to be radiotherapy-associated adverse effect; the inflammatory changes in the right lung were more obvious. There were also newly occurred inflammatory changes under the left upper lung pleura. Metastasis in the right adrenal gland could not be excluded. Due to low physical performance score, the patient was intermittently treated with multitargeted anrotinib. Efficacy evaluation was SD.

3 | DISCUSSION

For patients with early stage LSCC, radical surgery is still the most effective treatment. However, the patient in this case had progressed to stage IV when diagnosis was made, and brain metastases had also developed. Currently, there are few effective treatment measures for advanced patients, and the overall survival of LSCC was lower than that of lung adenocarcinoma. Lung cancer has the highest incidence of brain metastasis. In primary NSCLC, the incidence of brain metastasis at initial diagnosis is 10% and increases to 40%-50% during treatment. The risk of brain metastasis in lung adenocarcinoma,
Squamous-cell carcinoma and large cell carcinoma are 11%, 6%, and 12%. The median overall survival (mOS) of untreated patients with brain metastasis is about 1-3 months, the 1-year survival rate is about 10%-20%. Brain metastasis not only seriously threatens the lives of patients and reduces the quality of life, but also an important factor leading to poor prognosis. Therefore, for patients with advanced LSCC and multiple brain metastases, it is very important to choose the appropriate high-efficiency and low-toxic treatment plan at the first diagnosis. In addition, according to our experience from this case, paying close attention to patient’s symptoms and signs, as well as adopting a full-course management strategy is also vital for their long-term survival.

Treatments of NSCLC brain metastasis include systemic chemotherapy, whole brain radiotherapy (WBRT), stereotactic radiotherapy (SRT), stereotactic radiosurgery (SRS), surgical resection, and molecular targeted therapy. Traditional opinion is that the ability of chemotherapeutic drugs which have a large molecular mass to penetrate blood-brain barrier is low; therefore, the efficacy of chemotherapy in treating brain metastasis is limited. Platinum-based combinational chemotherapy is still the standard treatment for late NSCLC, but the 5-year survival of patients with late NSCLC is less than 5%. Recent studies found that the blood-brain barrier may be destroyed and chemotherapeutic drugs will pass through when the diameter of brain metastatic tumor is greater than 0.25 mm. In this case, brain radiotherapy is still an indispensable measure for the treatment of brain metastasis, and also the standard treatment recommended by the NCCN guideline. The treatment is effective for alleviating symptoms of intracranial hypertension and control of local lesions. The overall effective rate of WBRT achieves to 80% and patient’s median survival can extend to 3-6 months. Surgical treatment of NSCLC brain metastasis is associated with a high risk of recurrence and complication, and patient’s quality of life may reduce after surgery. The treatment of lung cancer has entered into an era of precision medicine and full-course management. Molecular targeted therapy has been widely used in the treatment of lung cancer and significantly improves patient’s prognosis.

This case showed that those LSCC patients with brain metastasis, full-course management is vital for their long-term survival. In addition, emerging novel therapies and treatment regimens will continue to improve patient’s survival. The patient in this case was treated with new medicines and investigated treatment plan through participating in multiple clinical trials, which prolonged the patient’s survival to a certain extent. Through MDT cooperation, the patient was given local radiotherapy intervention in an appropriate timing, which resulted in him not only obtaining better local control but also increased the quality of life and survival. MDT model can maximize the expertise of various clinical departments, strengthen the collaboration between different disciplines, and promote standardized and personalized treatment. Retrospective studies have indicated that patient’s overall survival is improved through MDT cooperation. For patients who have been resistant to first-generation TKI, it is also highly possible to be resistant to other first-generation TKIs. For these patients, combinational treatment including immunotherapy plus multisite radiotherapy, chemotherapy or anti-angiogenesis therapy may bring more benefits.

In conclusion, the treatment mode for advanced lung cancer is becoming more and more diversified. The long-term survival of the reported patient who had multiorgan metastases was benefited from MDT cooperation, comprehensive and personalized treatment, and precise full-course management.
CONFLICT OF INTEREST
The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS
Min Ji, Yue Shi, Renrui Zou: Manuscript preparation and literature review.
Yingying Jiang: Data collection. Li Wang, Rong Ma, Meiqi Shi: Survey design; data collection. Xiuming Zhang, Xiangzhi Zhu, Cheng Chen: Data collection and analysis. Xiaohua Wang: Survey design; data analysis; manuscript preparation and review. Jifeng Feng: Manuscript review.

ETHICS STATEMENT
The study was approved by the Jiangsu Cancer Hospital Ethics Committee and the patient gave written informed consent.

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