CASE REPORT

Successful afatinib treatment through nasogastric tube in a ventilated patient with non-small cell lung cancer

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Abstract: The majority of lung cancer patients are discovered at advanced stages and some of them may often have complex medical problems in addition to the diagnosis of cancer, such as oncologic emergency requiring assistance in an intensive care unit (ICU). In the last decade, epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors have been recognized as key drugs for non-small cell lung cancer (NSCLC) harboring sensitive EGFR mutation. We report a case of stage IV NSCLC with EGFR mutation (exon 19 deletion). He was in a life-threatening stage due to a massive intrathoracic hemorrhage. After chest tube drainage and mechanical ventilation, afatinib was administered through nasogastric tube. Consequently, a dramatic response was obtained and he was able to be discharged from our hospital 11 weeks after the initiation of afatinib. This approach may be of benefit to rescue from life-threatening condition for selected patients.

Keywords: afatinib; non-small cell lung cancer; EGFR mutation; intensive care unit; mechanical ventilation; water-dispersion type


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Introduction

The increased use of intensive care unit (ICU) for the management of oncologic emergencies such as intrathoracic hemorrhage, superior vena cava syndrome, cardiac tamponade, or major airway obstruction results in significant advantages in patients with lung cancer[1]. However, current studies suggest that advanced refractory cancer, poor performance status (PS), the need for mechanical ventilation and multiple organ failure are factors associated with worse ICU outcome[2,3]. Therefore, ICU support of lung cancer patients remains to be controversial and not all patients will be candidates for such aggressive care. Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), such as gefitinib, erlotinib, or afatinib, block EGFR signaling pathway and the treatment with TKIs provides higher response rates, longer progression free survival, and better quality of life compared with conventional platinum-based chemotherapy in the cohort of patients harboring sensitive EGFR mutation[4–6]. Here we report a case of a non-small cell lung cancer (NSCLC) in a fetal state successfully treated with afatinib of a water-dispersion type through a nasogastric tube.

Case report

A 59-year-old man presented to a community hospital with a persistent cough. He had a history of heavy smoking (60 pack year), with no family or past history of disease. A chest computed tomography (CT) scan revealed a solid tumor in the middle lobe of the right lung with enlarged lymph nodes in the right supraclavicular fossae, mediastinum, and right lung hilum (Figure 1A). A bronchoscopy was
performed with transbronchial biopsy. Histological examination indicated NSCLC with adenocarcinoma of the right lung. Brain magnetic resonance imaging (MRI) revealed three metastatic tumors (right frontal lobe, left parietal lobe, and left cerebellar hemisphere) (Figure 2A). The finding of the abdominal CT was normal. Serum levels of carcinoembryonic antigen (CEA), CYFRA, and ProGRP were 19.5 ng/mL (normal range: <5.0 ng/mL), 39 U/mL (normal range: <3.5 U/mL) and 37.2 pg/mL (normal range: <80.0 pg/mL), respectively. He was diagnosed with stage cT3N3M1b lung adenocarcinoma, and was transferred to our hospital for chemotherapy in September 2014. His physical condition was an Eastern Cooperative Oncology Group (ECOG) PS of 0 and his respiratory function was not disturbed; therefore, we decided to apply gamma knife radiotherapy to the brain metastasis prior to systemic chemotherapy. He was immediately referred to an institute related to our hospital for gamma knife treatment. However, after the gamma knife treatment to the right frontal lobe tumor, his condition suddenly worsened due to the onset of massive bleeding (Figure 1B). He underwent thoracic drainage, tracheal intubation, and mechanical ventilation for respiratory support. He was urgently transferred to the ICU at our hospital. At that time, an EGFR exon 19 deletion was identified. His family had hoped for any treatment. Treatment options were discussed with the Oncology Board. We explained to the family that afatinib, having the superior clinical effect, is administered as a water-dispersion type and there is little evidence of safety in this type of treatment. After getting informed consent, we administered afatinib (40mg/body) through a nasogastric tube. This led to an improvement of respiratory status. A dramatic response to the primary tumor of the lung was observed on a chest CT scan after one month and he was extubated (Figure 3). In addition, a follow-up brain MRI on day 87 showed a marked shrinkage of metastatic brain tumors—especially, the metastatic tumor in left cerebellar hemisphere disappeared (Figure 2B). He experienced a grade 1 diarrhea in line with the National Cancer Institute Common Toxicity Criteria (version 4), but it could be controlled with loperamide. No skin and liver toxicity were observed during the treatment. He subsequently recovered well and was discharged from the hospital 11 weeks after the initiation of afatinib. He continued receiving afatinib, maintaining a partial remission.

Discussion

To our knowledge, this is the first report of an NSCLC patient under the support of mechanical ventilation who was successfully treated with afatinib of a water-dispersion type. Afatinib is usually administered as a tablet taken orally every day; however, in this case, it was used as a preparation of a water-dispersion type in hot water at 55°C because of the state of mechanical ventilation. The same alternative approach of administration was reported, resulting in better outcomes in the case of gefitinib or crizotinib[7,8]. Cantarini et al. indicated that there are no apparent differences in the absorption, elimination, and plasma concentration-time

Figure 1. Radiological findings of the right lung. (A) Computed tomography (CT) images at the time of diagnosis showed a solid tumor in the middle lobe of the right lung. (B) CT image showed massive bleeding from the tumor in the right chest cavity and thoracic drainage was undergone.
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Figure 2. Radiological findings of the brain. (A) Pre-treatment. (B) Day 87 after an initiation of afatinib. Brain magnetic resonance imaging (MRI) on day 87 showed a marked shrinkage of metastatic brain tumors. Metastatic tumor in left cerebellar hemisphere, especially, disappeared only with afatinib.

Figure 3. Clinical course. (A) Day 1. (B) Day 30. (C) Day 107. Dramatic response was obtained after treatment with afatinib. The patient was discharged from the hospital 11 weeks after the initiation of afatinib.
profiles among three gefitinib-preparation types (tablet, dispersion via drink, and dispersion via nasogastric tube) [9]. However, drug formulation and administration approach would affect pharmacokinetics. Therefore, clinical research on the bioavailability of afatinib among these preparation types should be conducted.

Solid tumors including lung cancer are usually less sensitive to chemotherapy, therefore a PS 3 or 4 is considered to be contraindication for chemotherapy. However, in the last decade, TKIs have yielded clinical benefits for poor PS patients with mutated tumors, and ESMO guideline states that patients with PS 3–4 also may be offered an EGFR TKI[10,11]. Thus, we decided to administer EGFR TKI to our patient. Nowadays, we have three TKIs (gefitinib, erlotinib, and afatinib) available for patients with NSCLC harboring EGFR mutations. In the same ICU setting, Suzumura et al. and Bosch-Barrera et al. indicated the efficacy of gefitinib and erlotinib, respectively[7,12]. Among these TKIs, afatinib is an irreversible multiple-target TKI. Preclinical studies have shown superior activity of afatinib over gefitinib or erlotinib due to irreversible binding and its ability to circumvent the resistance mechanism to first-generation TKI[13]. Moreover, Banno et al. and Yang et al. suggested that afatinib is especially effective against NSCLC carrying an EGFR exon 19 deletion[14,15] and Hoffknecht et al. indicated superior clinical effect of afatinib on the central nervous system metastasis[16]. Afatinib has toxicities that are similar to gefitinib or erlotinib, such as diarrhea, skin rash, stomatitis and interstitial pneumonia. Overall, diarrhea is the most common adverse event and the incidence of grade 3 diarrhea is higher than that reported with gefitinib or erlotinib. However, it is important to point out that, in spite of these toxicities, only 6%–8% of patients discontinued afatinib[6,17,18]. Thus, we chose afatinib and fortunately our patient experienced only a grade 1 diarrhea with clinical benefit.

**Conclusion**

ICU admission of patients with advanced lung cancer should be decided on a case-by-case basis. In our case report, transitory mechanical ventilation plus afatinib treatment successfully help the patient make through the life-threatening condition back to ambulatory care. Recent improvements in pathogenic oncogenes for tumor progression have become a novel therapeutic target for the treatment of NSCLC. Many kinase inhibitors such as EGFR kinase inhibitors and anaplastic lymphoma kinase inhibitors have presented a possibility of individualized treatment[4–6,19,20]. Our patient gained a considerable survival benefit through the administration of afatinib of water-dispersion type via nasogastric tube in the ICU. Previous reports and our case may indicate that the ICU support can be of benefit to selected patients with tumors harboring activating gene mutations.

**Conflict of interest**

The authors declare no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

**References**

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