Osimertinib as First-Line Therapy of Patients with Lung Adenocarcinoma EGFR TKI Mutation from Pleural Fluid Samples: A Case Report

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ABSTRACT

Introduction: Lung cancer is still a major contributor to cancer mortality worldwide. More than 80–85% of cases are constituted by Non-Small Cell Lung Cancer (NSCLC), consisting of approximately 40% adenocarcinomas. Molecular subtypes of Epidermal Growth Factor Receptor (EGFR) mutation are prevalent in up to half of NSCLC patients in the Asian population, making EGFR tyrosine kinase crucial treatment targets [1–3]. After 9–12 months of therapy, lung cancer with T790M mutation accounts for 30%–50% of resistance to first- and second-generation tyrosine kinase inhibitors (TKI) [2,3]. Osimertinib has been designated as a first-line target therapy of Pulmonary Adenocarcinoma with EGFR mutation. The administration of this therapy showed improvements in symptoms, survival rates, and a better prognosis in patients with the EGFR mutation [2,3]. Furthermore, lung cancer therapy has experienced significant progress, where chemotherapy and immunotherapy have their respective advantages. Targeted therapy yielded milder side effects, Pulmonary Vascular Scores (PVS), and improved survival rate compared to conventional chemotherapy. Although immunotherapy is still in the development stage, the method has become a guideline for adenocarcinoma-type lung cancer [4–6].

Case Presentation: This study presented a case of a 60-year-old woman with shortness of breath and cough accompanied by weight loss ± 10 kg in 3 months. Contrast chest MSCT (multislice computed tomography) scan showed a mass in the right lung accompanied by pleural and pericardial effusion. The results of the cytological examination of pleural fluid found a picture of adenocarcinoma. Furthermore, the diagnosis was continued by molecular examination of pleural fluid, and the results of the EGFR Exon 19 mutation were obtained. Based on the results of physical examination and several laboratory tests, a diagnosis of right pleural effusion and EGFR mutation lung adenocarcinoma was established.

Conclusions: In this case, there was a clinical improvement after 8 months of osimertinib administration, along with enhancement in the control CT-SCAN. Osimertinib also showed the potential to extend progression-free survival by approximately 18.9 months compared to other generations of tyrosine kinase inhibitor therapy. This result was supported by the improvement of the clinical and performance status of patients in this case during osimertinib administration.

INTRODUCTION

Lung cancer is still a major contributor to cancer mortality worldwide today. More than 80–85% of cases are constituted by Non-Small Cell Lung Cancer (NSCLC), consisting of approximately 40% adenocarcinomas. Molecular subtypes of Epidermal Growth Factor Receptor (EGFR) mutation are prevalent in up to half of NSCLC patients in the Asian population, making EGFR tyrosine kinase crucial treatment targets [1–3]. After 9–12 months of therapy, lung cancer with T790M mutation accounts for 30%–50% of resistance to first- and second-generation tyrosine kinase inhibitors (TKI). Osimertinib has been designated as a first-line target therapy of Pulmonary Adenocarcinoma with EGFR mutation. The administration of this therapy showed improvements in symptoms, survival rates, and a better prognosis in patients with the EGFR mutation [2,3]. Furthermore, lung cancer therapy has experienced significant progress, where chemotherapy and immunotherapy have their respective advantages. Targeted therapy yielded milder side effects, Pulmonary Vascular Scores (PVS), and improved survival rate compared to conventional chemotherapy. Although immunotherapy is still in the development stage, the method has become a guideline for adenocarcinoma-type lung cancer [4–6].
CASE PRESENTATION

This study presented a 60-year-old woman with shortness of breath and cough accompanied by weight loss ± 10 kg in 3 months. From the physical examination, it was found that the general condition appeared to be moderate pain, awareness with Glasgow coma scale (GCS) eye 4, verbal 5, motor 6 (E4V5M6), blood pressure 126/62 mmHg, pulse 100 times per minute, regular, breathing frequency 26 times per minute, regular, and axillary body temperature 36.0°C, Spo₂ 98% with nasal cannula 3 liters per minute. Furthermore, the conjunctiva was anemic and the sclera was not icteric. On chest examination, asymmetrical movement of the chest wall was obtained, the vocal fremitus decreased in the medial to basal right hemithorax, dimmed in the medial to basal right hemithorax, the breathing sound decreased, and there were rhonchi without wheezing. On abdominal examination, normal intestinal peristaltic was obtained, and there was no enlargement of the liver and spleen. Warm and acquired edema was palpable in the extremities palpable.

Laboratory examination results included a WBC (White Blood Cell) count of 22.6x10³/μL, Hemoglobin 10.4 gr/dL, Neutrophil 83%, Lymphocytes 8.4%, Platelets 365x 10³/μL, Albumin 2.5 g/dL, Sodium 110 mEq/L, Potassium 2.0 mEq/L, Chloride 63 mEq/L, Procalcitonin 0.19 ng/mL. Blood gas analysis examination obtained PH 7.59, SO₂ 95.6%, PO₂ 70 mmHg, PCO₂ 46 mmHg, HCO₃ 22 mEq/L, BE 33.3 mEq/L. Chest x-ray before therapy (Figure 1A) shows a homogeneous covering and chest x-ray after therapy (Figure 1B) has improved.

CT scan thorax showed the presence of a mass in the right lung accompanied by right pleural and pericardial effusions (Figure 2A before treatment; Figure 2B after treatment). A cytological examination of pleural fluid confirmed an image of adenocarcinoma (Figure 3). The diagnosis was followed by an examination of the molecular pleural fluid, which identified the EGFR Exon 19 mutation. Based on anamnesis, physical examination, laboratory, and other supporting examinations, a diagnosis of right pleural effusion caused by lung adenocarcinoma with EGFR mutation was established.

The administration of osimertinib therapy 80 mg/24 hours/day for 2 weeks yielded significant improvements in respiratory symptoms and performance status. Patient vital signs showed improvement as the respiratory rate decreased from 26 to 24 times/minute, accompanied by a performance status from 3 to 2, enabling engagement in various activities. After giving therapy for 3 months, the respiratory rate showed 22 times/minute with performance status from PS 2 to PS 1, where patients carried out daily activities independently. Subsequently, after 8 months of therapy, the CT scan thorax showed improvement with a reduction of mass size accompanied by minimal pleural effusion.

Figure 1. (A) Thorax photo at the beginning of the diagnosis of a pulmonary tumor; (B) Thorax photo after administration of osimertinib therapy.

Figure 2. (A) CT scan of thorax of a patient before treatment; (B) CT scan of thorax of a patient after treatment osimertinib of 8 month.
DISCUSSION

The diagnosis of right pleural effusion due to EGFR mutation lung adenocarcinoma was confirmed based on anamnesis, physical examination, laboratory, and other supporting examinations. EGFR mutation in lung adenocarcinoma is a frequent class of driver mutation. Although a single EGFR tyrosine kinase inhibitor (TKI) offers significant clinical benefit, complete radiographic responses are rare [6–8]. Despite patients invariably progress, post-treatment therapy, such as EGFR TKIs, chemotherapy, or other procedures can extend survival for several years [9].

According to the National Comprehensive Cancer Network (NCCN) 2022, one of the first-line therapies for pulmonary adenocarcinoma EGFR mutation is osimertinib. In this study, the administration of osimertinib showed an extension of progression-free survival up to 18.9 months and reduced the risk of aggravation by approximately 54%. The T790M mutation structurally inhibited the binding of first-generation EGFR-TKI to the ATP binding site. When the T790M mutation was added to the EGFR activation mutation, the affinity of EGFR for ATP increased, and the binding properties of EGFR-TKI were relatively decreased. Therefore, downstream signals were not inhibited and cancer was tolerated. Based on a previous study, a small number of cancer cells that had a secondary T790M mutation other than the active EGFR mutation existed before treatment with EGFR-TKI and gradually became dominant during treatment with first-generation EGFR-TKI, such as gefitinib and erlotinib [10].

EGFR mutation had mainly been found in adenocarcinoma, associated with a response rate of 70% to EGFR-TKI therapy. Therefore, EGFR mutation analysis served as the best predictive marker for the use of EGFR-TKI therapy in KPKBSK with adenocarcinoma components. EGFR-TKI therapy including gefitinib, erlotinib, afatinib, and osimertinib was recommended as a first-line treatment for patients with positive EGFR mutation.

In this case, the EGFR mutation examination showed positive results in pleural fluid samples. The provision of therapy immediately given by the third generation of TKI, namely osimertinib, exhibited a good effect on patients in the form of clinical improvement and changes in performance status. This aligned with an existing study on osimertinib, which responded to pulmonary adenocarcinoma passing through EGFR mutation. In this patient, the clinical manifestations were shortness of breath and a slimy cough for 3 months. After a 2-week administration of osimertinib, significant clinical improvements were observed. These included improved performance status from 3 to 1,
accompanied by complaints of tightness and reduced cough, enabling patients to independently carry out daily activities.

Osimertinib was the first third-generation EGFR TKI to receive FDA and EMA approval for metastatic EGFR-mutant NSCLC patients who had acquired the EGFR T790M resistance mutation [10]. Furthermore, osimertinib was a mono-aniline-pyrimidine compound that specifically binds to the EGFR kinase domain irreversibly by targeting the cysteine-797 residue in the ATP binding site via covalent bond formation. In the cell line, osimertinib potently inhibited the phosphorylation of EGFR in PC-9 (Del19) and H3255 (L858R) cell lines with mean IC50 values ranging from 13 to 54 nmol/l [11].

Shortness of breath in adenocarcinoma-type lung tumors occurs due to the infiltration of the tumor into the pleura. This resulted in increased capillary permeability, leading to the leakage of intracellular fluid into the pleural cavum for effusion to occur. The effusion contributed to lung compression, often called compression atelectasis. This phenomenon was observed in patients, with a weight loss of 10 kg in 3 months due to the release of various kinds of cytokines such as TNFα mediator. The release of TNFα caused a decrease in appetite, resulting in weight loss. Osimertinib, an irreversible group of TKI, specifically targeted both EGFR and EGFR T790M mutation, making it a promising potential therapy in these patients. Osimertinib administration has also been observed in other cases in terms of prolongation of free life compared to other therapies [12].

CONCLUSIONS

This study showed that there was a clinical improvement after 8 months of osimertinib administration, along with enhancement in the control CT-SCAN.

DECLARATIONS

Competing of Interest
The authors declare no competing interest in this study.

Acknowledgment
Not applicable

REFERENCES