This is an Open Access article licensed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 License (www.karger.com/OA-license), applicable to the online version of the article only. Distribution for non-commercial purposes only.

Erlotinib Achieved Partial Response in a Non-Small Cell Lung Cancer Patient with Gefitinib-Induced Interstitial Lung Disease

Qing Tian Liang-an Chen

Department of Respiratory Diseases, PLA General Hospital, Beijing, China

Key Words

Non-small cell lung cancer · Epidermal growth factor receptor tyrosine kinase inhibitors · Interstitial lung disease

Abstract

Interstitial lung disease (ILD) induced by epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), such as gefitinib and erlotinib, is a rare but fatal complication of TKI treatment. Transfer to chemotherapy or continuation with TKI of reduced dose are alternative treatment strategies. We report a case of severe ILD in a non-small cell lung cancer patient treated with gefitinib. She experienced partial response with restarted low-dose EGFR-TKI erlotinib and corticosteroid treatment.

Introduction

The epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), such as gefitinib and erlotinib, have been shown to have significant antitumor activity in non-small cell lung cancer (NSCLC) patients with EGFR mutations. Although the common side effects of EGFR-TKIs (including skin rash, diarrhea, asthenia and anorexia) are mild and controllable, interstitial lung disease (ILD) remains a rare but always fatal complication. The disease will relapse after EGFR-TKI suspension which is mandatory to rescue the patients who contracted the ILD. We report a case of severe ILD in a NSCLC patient treated with gefitinib. She experienced partial response with restarted low-dose EGFR-TKI erlotinib and corticosteroid treatment.

Case Report

A 41-year-old woman who complained of non-productive cough and breathlessness was diagnosed with lung adenocarcinoma stage IV (T_{2a}N₃M_{1a}) in November 2009. Chest computed tomography (CT) revealed a 3.0 × 2.6-cm mass in the left lower lobe and left pleural effusion (fig. 1a). EGFR mutation status was not evaluated. Because first-line chemotherapy with paclitaxel plus cisplatin cannot be tolerated for grade 3 gastrointestinal side effects, she received gefitinib 250 mg/day as second-line treatment. Only 7 days after the start of gefitinib, the symptoms disappeared. However after 20 days' treatment of gefitinib, the patient reported high fever and severe respiratory distress on effort. Despite high-flow supplemental oxygen delivered via nasal cannula, hypoxemia developed with a PaO₂ of less than 45 mm Hg. A chest CT revealed bilateral pulmonary infiltrates, patchy airspace consolidation, and air bronchograms despite decreased size of the primary tumor (fig. 1b). The diagnosis of EGFR-TKI-induced interstitial lung disease was made, and gefitinib therapy was stopped. Mechanical ventilation and corticosteroid treatment (120 mg/day of intravenous methylprednisolone) were started immediately. The patient experienced improvement and weaned from the ventilator after 8 days of treatment. Repeated CT scan showed complete resolution of infiltrates. The corticosteroid was tapered over 1 month.

In June 2010, the patient developed progressive disease after 4 cycles of docetaxel-cisplatin chemotherapy (fig. 1c). From July 2010, erlotinib (75 mg/day) was prescribed with oral prednisolone (20 mg/day). She achieved a partial response after 1 month's treatment of erlotinib (fig. 1d). The prednisolone was withdrawn after 3 months without recurrence of EGFR-TKI-induced ILD. She is still alive 1 year after the restart of EGFR-TKI therapy.

Discussion

The worldwide incidence of ILD is about 1% in both gefitinib- or erlotinib-treated patients; ILD was reported to have a prevalence of 3.5% and mortality of 1.6% in gefitinib-treated patients in Japan [1]. For the patients who had partial or complete response to gefitinib and experienced gefitinib-induced ILD, obligatory suspension of EGFR-TKI treatment will cause progression of disease. After recovery from ILD, most of the patients received chemotherapy, which is not as effective as EGFR-TKI. Although a case with recurrent gefitinib-induced ILD was reported [2], a reduced dose of gefitinib might induce a response without recurrent gefitinib-induced ILD [3]. Several cases of NSCLC successfully rechallenged with erlotinib after developing gefitinib-induced ILD were also described [4, 5]. We add another case report which shows that a reduced dose of erlotinib in combination with steroid therapy achieved partial response in a patient recovered from gefitinib-induced ILD. So a reduced dose of erlotinib seems to be a potential therapeutic option for the treatment of NSCLC patients who develop gefitinib-induced ILD, although it is required to pay attention to the possibility of the development of recurrent ILD. The underlying mechanisms of ILD and strategies to overcome TKI resistance are warranted further investigation.

Fig. 1. **a** CT scan shows a mass in the left lower lobe at the diagnosis of lung adenocarcinoma. **b** Chest CT after gefitinib treatment revealed patchy airspace consolidation and air bronchograms despite decreased size of the primary tumor. **c** Chest CT revealed progress of disease after 4 cycles of chemotherapy. **d** After one month of treatment of erlotinib, a partial response was seen.

References

- 1 Ando M, Okamoto I, Yamamoto N, et al: Predictive factors for interstitial lung disease, antitumor response, and survival in non-small-cell lung cancer patients treated with gefitinib. *J Clin Oncol* 2006;24:2549–2556.
- 2 Suzuki M, Asahina H, Konishi J, et al: Recurrent gefitinib-induced interstitial lung disease. *Intern Med* 2008;47:533–536.
- 3 Takamochi K, Suzuki K, Bashar AH, et al: Readministration of gefitinib in a responder after treatment discontinuation due to gefitinib-related interstitial lung disease: a case report. *J Med Case Reports* 2007;17:138.
- 4 Fukui T, Otani S, Hataishi R, et al: Successful rechallenge with erlotinib in a patient with EGFR-mutant lung adenocarcinoma who developed gefitinib-related interstitial lung disease. *Cancer Chemother Pharmacol* 2010;65:803–806.
- 5 Chang S-C, Chang C-Y, Chen C-Y, et al: Successful erlotinib rechallenge after gefitinib-induced acute interstitial pneumonia. *J Thorac Oncol* 2010;5:1105–1106.