Case Report

Both gefitinib and erlotinib induced drug-related interstitial lung disease in a patient with pulmonary adenocarcinoma

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Abstract

Treatment for non-small-cell lung cancer with gefitinib and erlotinib is efficacious. However, while many studies have reported on gefitinib-related interstitial lung disease (ILD), less published data are available regarding erlotinib-induced ILD. Here, we report a case of pulmonary adenocarcinoma who developed ILD due to gefitinib initially and erlotinib thereafter. The two episodes of ILD were treated successfully with the discontinuation of the tyrosine kinase inhibitors and high-dose intravenous corticosteroids.

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1. Introduction

Interstitial lung disease (ILD) is an infrequent but severe adverse effect of gefitinib treatment.1–3 For patients discontinuing gefitinib due to ILD the safety of a subsequent therapy with another small molecular epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI), erlotinib, remained uncertain.

2. Case report

A 44-year-old man was diagnosed with lung adenocarcinoma with right pleural seeding. He received cisplatin and docetaxel every 3 weeks as an initial anticancer treatment. After two cycles of chemotherapy, chest computed tomography (CT) revealed a new onset of right loculated pleural effusion (Fig. 1), and disease progression was documented. Gefitinib (250 mg/d) was administered as a second-line treatment. However, the patient suffered from exertional dyspnea 3 weeks after the administration of gefitinib. A plain chest radiograph (Fig. 2) revealed right loculated pleural effusion and extensive interstitial infiltration in the left lung. High-resolution CT (Fig. 3) showed ground-glass opacities in both lungs. Gefitinib-induced interstitial pneumonitis was impressed. Immediate withdrawal of gefitinib and administration of methylprednisolone 2 mg/kg/d was prescribed. The patient’s dyspnea improved 6 days later. A follow-up plain chest radiograph revealed improvement in ILD (Fig. 4). Subsequent treatment with other cytotoxic chemotherapies was suggested, but the patient requested treatment with another EGFR-TKI, erlotinib. The patient was carefully informed of high-fatality complications of erlotinib before its administration. After informed consent was received, erlotinib (75 mg/d) combined with steroids was introduced 10 days later. Two weeks later, dyspnea with hypoxemia occurred again, and another chest CT (Fig. 5) showed the recurrence of ILD.
Therefore, erlotinib treatment was withheld and systemic steroid (methylprednisolone 2 mg/kg/d) was readministered. The patient’s condition improved after treatment, and he was discharged 1 week later.

3. Discussion

Gefitinib and erlotinib are both small-molecule EGFR-TKIs, and they are both second- and third-line treatments for advanced or metastatic non-small-cell lung cancer in Asia. There is the potential risk of drug-induced ILD by using these two target therapy agents, especially gefitinib.\(^1\)\(^-\)\(^5\) The worldwide reported incidence of ILD following gefitinib administration is estimated at 1% (approximately 2% in Japan and 0.3% in the United States).\(^4\) However, few case reports have revealed successful treatment with erlotinib after gefitinib-induced interstitial pneumonitis\(^5\)\(^,\)\(^6\) Another case report showed that one patient who previously tolerated gefitinib developed ILD after receiving erlotinib treatment.\(^7\) The risk factors for gefitinib-induced ILD include a smoking history, male gender, and the coincidence of interstitial pneumonia.\(^8\) One study compared the two TKIs for the incidence of ILD, and the results showed that poor performance status and prior pulmonary fibrosis were significantly correlated with the occurrence of ILD, but not with the type of TKI.\(^9\) The etiology

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Fig. 1. Chest computed tomography before gefitinib administration revealed right loculated malignant pleural effusion and no pre-existing interstitial lung disease.

Fig. 2. Chest X-ray showed diffuse ground-glass zones in the left lung (thin arrows) and right loculated malignant pleural effusion (thick arrow) on the 3rd week of gefitinib therapy.

Fig. 3. Chest computed tomography showed diffuse interstitial infiltrates over left lung (thin arrows) and right loculated pleural effusion (thick arrows) on the 3rd week of gefitinib therapy.

Fig. 4. A follow-up chest X-ray revealed improvement with regard to interstitial lung disease (thin arrows) and right loculated pleural effusion (thick arrows) 6 days after discontinuation of gefitinib and steroid treatment.
and molecular mechanism of TKI-induced ILD are not clearly understood. One study suggested that gefitinib therapy may augment any underlying pulmonary fibrosis via a decrease in EGFR phosphorylation, based on a coincident decrease in regenerative epithelial proliferation in a murine model.10 Successful treatment of gefitinib-induced ILD with high-dose intravenous corticosteroids has been reported in many cases,11,12 but only one report reveals that intravenous corticosteroids may be beneficial in cases of erlotinib-induced ILD.13 Therefore, carefully evaluating a patient’s new onset of respiratory symptoms (e.g., dyspnea, dry cough) after TKI administration is very important and early discontinuation of such agents is beneficial to patients. The role of corticosteroids for TKI-induced ILD may need more trials to support the notion of perceived benefits. In our report, both gefitinib and erlotinib have the potential of inducing ILD in one patient. This case reminds us that substitution with another EGFR-TKI still has the risk of developing a similar pulmonary toxicity.

References