

Case Report

A case of methylprednisolone treatment for interstitial pneumonia induced by gefitinibin

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Abstract: In this case, an old man was diagnosed as lung cancer, clinical stage IV. In order to alleviate cancer, this patient was treated with gefitinib. Three months later, symptoms such as a significant weakness, chest tightness and shortness of breath after sports arised and intensifying. Implosive therapy with high dose methylprednisolone is used to control the weakness caused by gefitinib. Eight days after treatment, patient's condition significantly improved. The use of methylprednisolone can effectively treat interstitial pneumonia induced by gefitinibin, help patients get better from critical condition such as type I respiratory failure. This new discovery is a good guidance for clinical treatment of gefitinibin caused interstitial pneumonia.

Keywords: Methylprednisolone, gefitinibin, interstitial pneumonia

Introduction

Lung cancer is one of the most common malignant tumor in the world today. In addition to traditional approaches such as chemotherapy for lung cancer treatment, method of molecular targets can also be used now. As a selective epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors, gefitinibin has been widely used in clinical treatment of lung cancer. However, the inhibition of gefitinibin on EGFR tyrosine kinase increases lung damage. In inhibiting tumor tissue EGFR activity, gefitinibin restrains growth and damage repair of the tracheal epithelial cells and disorders its immune inflammatory response, which may be one of the causes of acute interstitial pneumonia. In this case, we firstly reported the use of high dose methylprednisolone can effectively treat interstitial pneumonia induced by gefitinibin, help patients get better from critical condition such as type I respiratory failure. This new discovery is a good guidance for clinical treatment of gefitinibin caused interstitial pneumonia.

Clinical data

The patient was a 75-year-old man who attacked migratory arthralgias since 2012 and had

gone to his local doctor. To remedy the osteoarthritis, he was given total glycosides of paeony (TGP) and artodar treatment. He stopped taking these medications when the joint becomes obviously painful. He suffered from high blood pressure for 20 years and joint pain over and over again. He took pills of felodipine and kept good control over blood pressure. However, he lost 10 kg weight with no clear trigger since 2012, but neither did he take it seriously nor did he hospitalize. This patient began to paroxysmal frequent cough in early 2014, and felt obvious chest pain when coughing severely. Chest computed tomography (CT) detected in April of the same year suggested there were multiple infectious diseases in lungs, pleural effusion in both sides, bone damaged in multiple thoracic vertebrae (**Figure 1**).

Thoracentesis and pleural fluid drainage on the right side suggested pleural fluid containing cancer cells (**Figure 2**). Epidermal growth factor receptor (EGFR) gene testing on pleural effusion found arginine substituted 858th leucine in the 21th exon. Therefore, he was diagnosed as lung cancer, clinical stage IV. He was given molecular target therapy of 250 mg gefitinib once a day since May 2014 combined with azole phosphonic acid sodium to prevent bone

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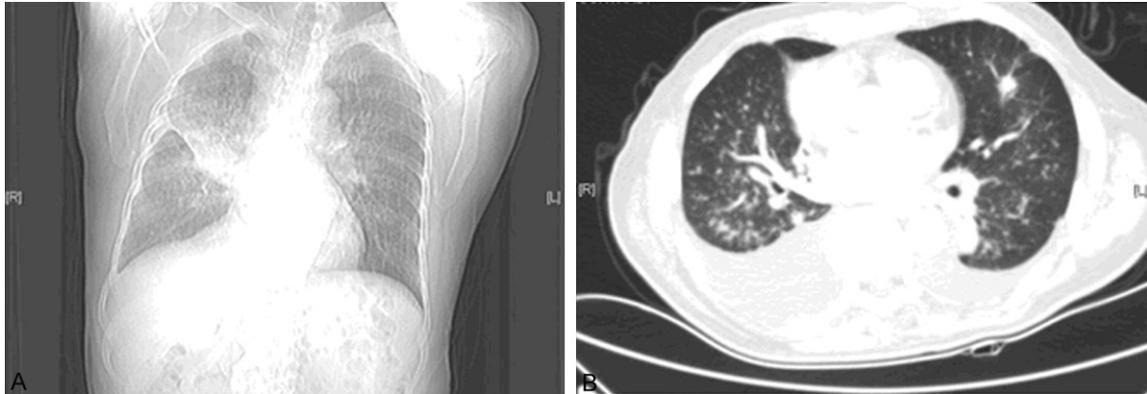


Figure 1. Multiple infectious diseases in lungs detected by CT. A. Surview image; B. Helix image.

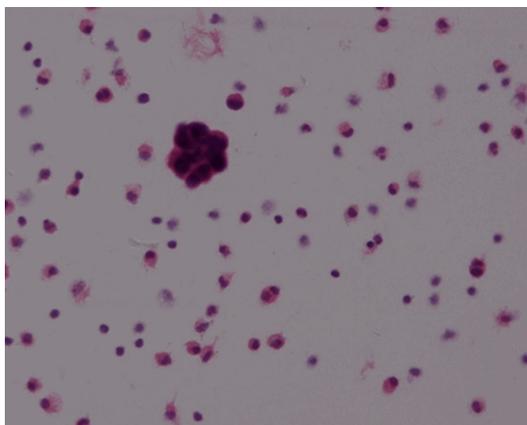


Figure 2. Cancer cells in pleural fluid (200 \times).

adverse reactions. He was treated with cisplatin intrathoracic injection in July, the chemotherapy process is smooth, without any discomfort for patient after chemotherapy. The gefitinib treatment for this patient lasted until October in the same year when symptoms such as a significant weakness, chest tightness and shortness of breath after sports arised and intensifying. Blood oxygen saturation of him was only 75%. Breast enhancement CT suggested there is extensive diffuse disease in both two lungs, accompanied by interstitial lesions (**Figure 3**). Combining with the history records, it is possible to induce interstitial pneumonia after treatment of gefitinib, and this conformed to the duration between drug usage and pneumonia (appeared as early as a month, an average of 4-6 months). Then the patient was terminally ill as both lungs appear dry and wet rale, and type I respiratory failure. Implosive therapy with methylprednisolone (40 mg every 8 h by injection), stop taking gefitinib, celebrex (0.2 g every

12 h take orally) is used to control the pain, use the oxygen mask (oxygen flow rate by 4 L/min at first and later changed to 5 L/min). Eight days after treatment, patient's condition significantly improved that he can get out of bed for activity, and he was conscious again, shortness of breath is not obvious, dry and wet rale not appeared in both lungs. 11 days after treatment, he was up and about. Treatment after 15 days, due to the improvement, methylprednisolone reduction to 10 mg, and take orally instead, other analgesic drugs remains the same. 19 days after CT treatment showed inflammation relief, beside hilum of right lung obstructive atelectasis in nodules (**Figure 4**). Hospital discharge, continue to use the drug after discharge, methylprednisolone (8 mg every day take orally), celebrex (0.2 g every 12 h take orally), felodipine (5 mg every 12 h take orally), valsartan (40 mg every day take orally), omeprazole (20 mg every day take orally).

Discussion

According to the statistics of USA in 2008, the incidence of lung cancer accounts for 15% of all male and 14% of all female malignant tumor onset, both rank second. But because of lung cancer deaths in men and women accounted for 31% and 26% of all deaths from malignant tumor death, lung cancer is the first reason for cancer death. Gefitinib (also called Ziressa) is developed by AstraZenica company. It is a selective epidermal growth factor receptor tyrosine kinase inhibitor used in the treatment of late non-small cell lung cancer (NSCLC). It combines with EGFR tyrosine kinase competitively, inhibits its the activity, thus blocking EGFR mediated tumor cell signal transduction, inhib-

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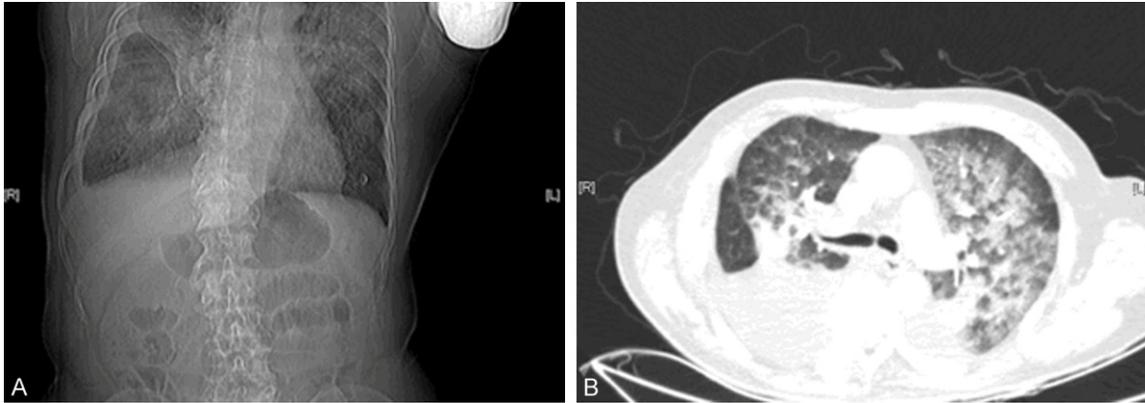


Figure 3. Interstitial lesions and extensive diffuse disease in lungs. A. Surview image; B. Helix image.

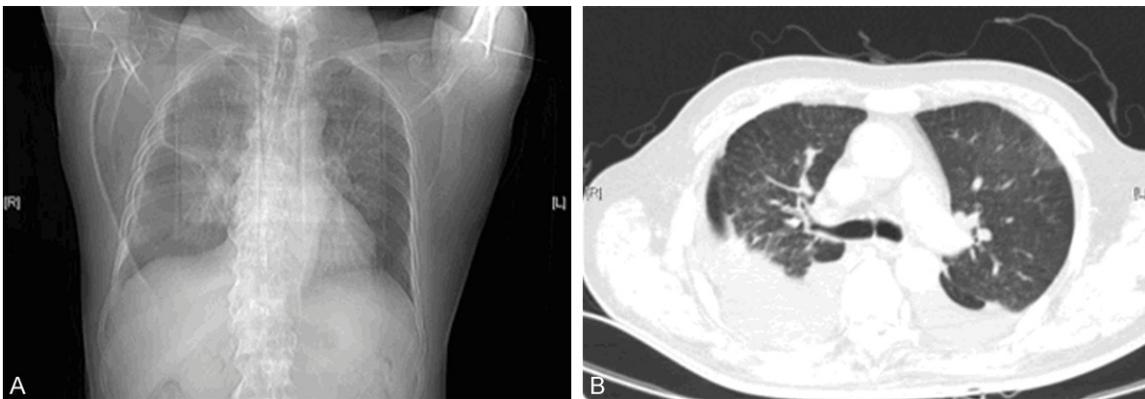


Figure 4. Inflammation relief in lung. A. Surview image; B. Helix image.

iting proliferation and metastasis of tumor cells, promoting the apoptosis of tumor cells [1]. The drug came into the market in Japan in July 2002, and in May 2003 the United States food and drug administration (FDA) approved the drug for the treatment of NSCLC. It is permitted to be used to treat locally advanced or metastatic NSCLC ever received or not suitable for chemotherapy, and to cure advanced NSCLC with EGFR gene specific locus mutation. Listed on the global clinical research and applications, interstitial lung disease caused by gefitinib is a rare but deadly serious adverse reaction [2].

Interstitial Pneumonia is a set of diffuse parenchymal lung disease major involves pulmonary interstitial alveolar and bronchioles. Main clinical manifestations of interstitial pneumonia were exertional dyspnea, restrictive ventilatory disorder and dispersion function reduction in pulmonary function tests, with hypoxemia and symptoms such as chest tightness dry cough.

Imaging examination revealed bilateral pulmonary diffuse infiltrative shadow and cellular interstitial shadow, mainly exudative change, distribution of the solid lesions and ground glass shadows scattered in bilateral lower lung peripheral. Then exudative lesions progress quickly, extends from a peripheral to the central axis of the lungs, and from middle and lower pulmonary lung upwards, and obvious changes in the pulmonary interstitial systems, thickening can seen interlobular septa, the interval inside flocculus, and axial interstitial. Chest high-resolution computed tomography (HRCT), alveolar lavage cytology and surgical lung biopsy are three important inspection methods for diagnosis of acute interstitial pneumonia [3]. After the patients take gefitinib, rule out other factors, such as heart failure, lung infection, tumor progression, especially lymphangitic spread of carcinoma, etc., interstitial pneumonia can be diagnosed to have been induced by gefitinib with the help of imaging examination.

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At present, the use of steroid medicines in the treatment of interstitial pneumonia has been reported [4, 5]. Methylprednisolone belongs to the hormone drugs, high dose methylprednisolone can inhibit the cell-mediated immune response [6, 7]. The effect of high dose pulse therapy is attributed to nonreceptor dependent steroid activities [8, 9]. Steroid pulse therapy has been used in a number of inflammatory, especially autoimmune states, and has also proved effective in bronchiolitis obliterans organizing pneumonia (BOOP) in connection with graft versus host disease after allogeneic bone marrow transplantation [10].

However, dosage and duration of steroids should be modified according to disease severity and chronicity. The dosage that we used was high, and has generally been applied in cases of severe lung disease with life-threatening events [11, 12]. Therefore, the efficacy and clinical outcome of different steroid regimens should be carefully determined in a well-designed comparative study.

It is concluded that increasing dose of methylprednisolone pulse therapy can be used to treat interstitial pneumonia resulted from gefitinib. In this case the patient is older, his disease is severe, but using of high doses of the hormone drugs works well, suggesting this treatment is safe, is of good curative effect and can shorten treatment time, can be widely used in clinic.

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Disclosure of conflict of interest

None.

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