



Case Report

Long-term survival of non-small-cell lung cancer patients with EGFR inhibitor treatment

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ABSTRACT. The epidermal growth factor receptor (EGFR) inhibitors gefitinib and erlotinib are effective in the treatment of advanced non-small-cell lung cancer (NSCLC), but the median survival of patients is short. Here, we describe 2 patients with NSCLC receiving conventional chemotherapy and alternative treatment with gefitinib or erlotinib as second-line therapy. The first patient was alive at 8 years with alternative conventional chemotherapy and gefitinib, and the second patient was alive at long-term follow-up with conventional chemotherapy and gefitinib or erlotinib. Gefitinib, erlotinib, and conventional chemotherapy can be combined for satisfactory therapy for NSCLC.

Key words: Non-small-cell lung cancer; Long-term survival; Epidermal growth factor receptor inhibitor

INTRODUCTION

Standard platinum-doublet chemotherapy is usually used for non-small-cell lung cancer (NSCLC) in phase I trials, but patients cannot tolerate the side effects of traditional chemotherapy. Epidermal growth factor receptor (EGFR) is important in advanced NSCLC and is involved in tumor growth, development, metastasis, and progression (Fontanini et al., 1995). As inhibitors of EGFR, gefitinib and erlotinib are effective in treating advanced NSCLC (Kim et al., 2008; Kamiya et al., 2011). The side effects of EGFR inhibitors, such as skin rash and mild diarrhea, are acceptable. EGFR inhibitors are effective in patients with EGFR mutation. Tumor markers may be used to evaluate their effect. The level of carcinoembryonic antigen (CEA) predicts tumor response well in patients with advanced NSCLC treated with gefitinib or erlotinib (Parra et al., 2004; Okada et al., 2004; Mok et al., 2009). Here, we describe 2 Chinese patients with advanced NSCLC treated with gefitinib or erlotinib in terms of long-term survival.

CASE REPORTS

Case 1

A 73-year-old woman received a diagnosis of left lower lung cancer with upper left lung metastasis, lymph gland metastasis and hydrothorax by lung CT (Figure 1A; April, 2005); the classification was stage IV adenocarcinoma, and serum CEA level was 20 ng/mL (normally 0.0-6.0 ng/mL). The patient underwent 6 pulses of standard platinum-doublet chemotherapy; serum CEA level was reduced to 10 ng/mL, and the primary tumor size was decreased (Figure 1B). After 12 weeks, the serum CEA level increased to 36.2 ng/mL, and the primary tumor volume was the same as in Figure 1A. The patient was positive for EGFR mutation. She received oral gefitinib, 250 mg daily. After 4 weeks, the serum CEA level decreased to 18.0 ng/mL, but the primary tumor volume did not change from the size in Figure 1B. The CEA level remained stable for 12 weeks. The primary tumor size then changed (Figure 1C), where the CEA level increased to 40 ng/mL with the increase in tumor size after gefitinib treatment for 20 weeks. With 3 pulses of alternative chemotherapy, the serum CEA level was reduced to 25 ng/mL, and the tumor volume changed (Figure 1D). With gefitinib treatment for about 8 weeks, the serum CEA level increased to 60 ng/mL, but the primary tumor volume did not change from the size in Figure 1D. The patient was still alive at the last follow-up and received conventional chemotherapy and gefitinib as an alternative to neoadjuvant therapy to stabilize her condition.

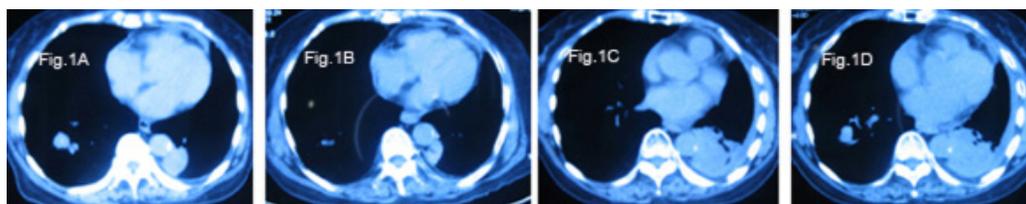


Figure 1. Chest CT scans of the primary tumor. Case 1: **A.** first chest CT on admission, **B.** after conventional chemotherapy, **C.** after 12 weeks of gefitinib therapy, **D.** after secondary conventional chemotherapy.

Case 2

A 70-year-old woman with a serum CEA level of 28 ng/mL received a diagnosis of right lower lung cancer with upper-left lung metastasis by lung CT (Figure 2A; March, 2011); the classification was stage IV adenocarcinoma. The patient received 2 pulses of standard platinum-doublet chemotherapy. The serum CEA level was reduced to 19.7 ng/mL, and the size of the primary tumor was decreased (Figure 2B). After the third chemotherapy pulse, the patient rested for 12 weeks; serum CEA level increased to 34.4 ng/mL, and the primary tumor volume increased to the size in Figure 2A. The patient received gefitinib as second-line therapy but was not evaluated for EGFR mutation. After 12 weeks, the serum CEA level was reduced to 15.1 ng/mL, and the primary cancer volume decreased to the size in Figure 2B (Figure 2C). Gefitinib was maintained, and serum CEA level slowly increased. With gefitinib treatment for 28 weeks, serum CEA level increased to 27.5 ng/mL, and the primary tumor volume increased to the size in Figure 2A (Figure 2D). The patient received 3 pulses of alternative conventional chemotherapy; the serum CEA level decreased to 20.9 ng/mL, and the primary tumor volume did not change. With gefitinib treatment for about 8 weeks, the serum CEA level slowly increased to 54.5 ng/mL, the primary tumor volume did not change, but broad metastasis was revealed in the left lung. With 6 pulses of alternative conventional chemotherapy, the serum CEA level slowly increased to 122.4 ng/mL, but the primary tumor volume and metastasis did not change. By alternating days of treatment with erlotinib, 150 mg daily, for 2 weeks, the serum CEA level decreased to 80.0 ng/mL, then slowly increased to 135 ng/mL. At 12 weeks, the primary tumor volume and metastasis had not changed. The patient alternated conventional chemotherapy and gefitinib or erlotinib and was still alive at the last follow-up.

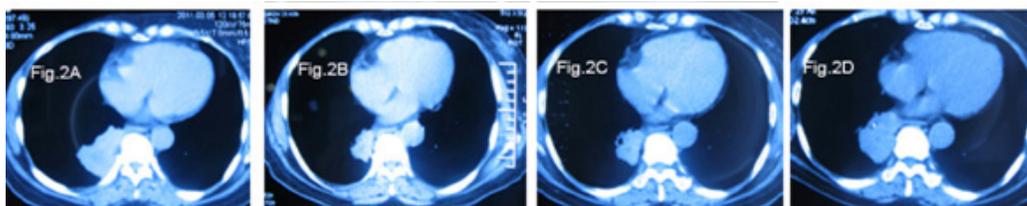


Figure 2. Case 2: **A.** first chest CT on admission, **B.** after 2 pulses of conventional chemotherapy, **C.** after 12 weeks of gefitinib therapy, **D.** after secondary conventional chemotherapy.

DISCUSSION

Most lung tumor patients have NSCLC and receive treatment with only standard platinum-doublet chemotherapy in phase I trials and often do not experience side effects. EGFR plays an important role in advanced NSCLC. As inhibitors of EGFR, gefitinib and erlotinib are considered phase II trial drugs. However, the median survival is 4 months and the 1-year survival only 18% (Shepherd et al., 2005).

NSCLC patients with a high serum CEA level should be carefully followed up and might represent a suitable population for neoadjuvant clinical trials (Chiu et al., 2007). To evaluate the curative effect, we monitored serum CEA level in 2 patients. The serum CEA level changed with effective standard platinum-doublet chemotherapy.

EGFR gene mutation is a strong predictor of better outcome with EGFR inhibitor treatment (Kappers et al., 2010). The first patient was positive for EGFR mutation and showed stable disease with gefitinib treatment for 12 weeks. With gefitinib treatment for 20 weeks, alternative traditional chemotherapy for 3 pulses, then gefitinib treatment for 8 weeks, the effect was poorer than for the first time with gefitinib, but the primary tumor size did not change. With the second patient receiving gefitinib, without EGFR mutation analysis, the effect of gefitinib was as for the first patient. Erlotinib treatment after failure of gefitinib has been satisfactory in a patient with meningeal carcinomatosis secondary to NSCLC (Fujikura et al., 2010). Erlotinib as second-line therapy alternating with gefitinib produced no change in our second patient. However, the serum CEA level and primary tumor size changed during treatment. Finally, both patients underwent conventional chemotherapy as first-line therapy and gefitinib or erlotinib as second-line therapy to stabilize the condition and recovery.

The prognosis of advanced NSCLC after failure of second- or third-line treatment is generally only weeks to months (Okada et al., 2004). For effective antitumor results, some patients should alternate the treatment program. Our 2 patients receiving gefitinib or erlotinib as second-line treatment still showed long-term survival.

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