

## Clinical Study

### Clinical trials of lung cancer after chemotherapy and traditional medicine (12 cases)

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#### Abstract

**Objective:** In this paper, we have reported the retrospective study of lung tumors under remission, with the combination chemotherapy and traditional medicine or traditional medicine alone. Study on effect of some traditional herbal drugs on cancer patient after chemotherapy. **Methods:** All 12 patients with lung tumors were in progressive at hospitalization. The criteria of complete remission (CR) and/or partial remission (PR) is according to the rules where physicians have in common with in clinics. **Results:** During the schedule of drug administration, 8 patients were treated with different dosage of combination chemotherapy in conjunction with traditional medicine. Two of them were undergoing chemotherapy 5-Fu and antitumor capsule. Another lung cancer was given the combination chemotherapy plus targeting oncogenic receptor EGFR gefitinib therapy, which was in stable disease for 8+ months. A short CR following combination chemotherapy and traditional medicine was obtained in a boy with malignant mesothelioma. The other 4 lung tumors were using traditional medicine alone. The survival times were over 6 months to 1 year 4 cases, 1-2 years 3 cases, 8+years 1 case, over 10 years 3 cases, the longest survival time in one lung cancer was 17 years, and he died in his lung cancer relapse. **Conclusion:** In this study, a CR was a pivotal influencing factor in those longer survival cancers, and traditional medicine was also recommended. Targeting oncogenic receptors are currently the third-line setting, especially advanced cancers.

**Keywords:** Advanced lung cancer; Oncogenic receptor EGFR; Chemotherapy; Traditional medicine

#### Introduction

Chemotherapy is a major skillful to the treatment of cancer. One of this approach, traditional plant medicine occupied its important advances in the field of treatment. In this paper, we are in retrospective study of those lung cancer under remission, with a small dosage of chemotherapy in adjuvant traditional medicine or traditional herbs alone.

#### Case reports

**Case 1.** A breast cancer after mastectomy was well until in August, 1993 while an attack of osteodynia involving lower extremities was admitted into hospital. At admission on MRI examination showed a 3x3cm metastatic mass in her left lung. The diagnosis of her metastatic lung cancer was made. PR was

achieved by the approach to PHA and combination chemotherapy. On repeated CT scan the remains of only two lymph nodes (each a pea size) in the hilus of her left lung were clearly visible during the course of PHA. Total dosage of PHA 880mg. The PR was obtained for 10+months. At 1 year later, she died in metastatic carcinoma of bone.

**Case 2.** A 64-year-old man was admitted into the hospital due to his right lung cancer on November 6, 1994. He had a history of recurrent episodes of cough and symptoms of catching a common cold frequently for half a year, and blood-tinged sputum for one month. He was immediately to the emergency ward owing to the total volume of one bowel of his bloody sputum near 3 days. On examination chest x-ray revealed a mass of 3x5cm in the middle of his right lung with indistinctly outlined shadow, and the side chest x-ray further demonstrated a mass shadow with indistinctly boundary, which is localized between lower poster of his lung hilus and spinal. The tumor mass was

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remarkably receded by the use of antibiotics in full dose with adjuvant prednisone, and intensively staunched the bleeding of his lung. The traditional medicine was continuous to be taken for late 3 months in another hospital. He obtained a disease-free survival with 17 years. In 2011, he died in his lung cancer relapse.

**Case 3.** A 40-year old man was admitted into hospital on April 27, 1996 due to an attack of dyspnea (short breathing), complicated by progressive weakness, weight loss and loss of appetite. On CT examination showed much malignant hydrothorax with a 4.5x4.9 cm mass in the cavity of his left lung. A protocol was mainly by a 6 months of traditional medicine, with the combination of a small dosage of CTX (0.4g), 5-FU (0.75g) and PHA (100mg) therapy. A CR (disease-free survival) with 10 years was achieved and in recovery of his job again.

**Case 4.** A 10-year-old boy who entered the hospital due to his malignant mesothelioma on July 5, 1996. He developed the symptoms of dyspnea two months duration. On CT examination showed much malignant hydrothorax with irregular pleural elliptical mass in his right pleural cavity. The protocol of combination chemotherapy (VCR, 1mg/wk; CTX 200-400mg/wk; 5-FU 250mg/day, PHA 20mg/day) was given four courses of therapy. A short complete response after four time sequential chemotherapy with the combination of traditional medicine, and the results showed in the chest x-ray the disappearance of hemorrhagic pleural effusion, with the remains of pleurisy. Total dosage of cytotoxic drugs: VCR 4mg, CTX 660mg, 5-Fu 7.5g, MMC 4mg, PHA 870mg. He was allergic rash in response to PHA administration and in recovery from skin rash when stopping PHA, which possibly indicates over PHA dosage.

**Case 5.** On January 4, 2001, A 46-year-old man was the complaint of his blood-tinged sputum for 15 days, accompanied with attack of cough and chest pain three months duration, and metastatic lymph nodes in right cervical region. On CT examination showed hemorrhagic hydrothorax with a 5.5x4.0cm mass in his right hilus pulmonis, complicated by right bronchlarctia and pulmonary atelectasis at right middle lobe. Moreover, metastatic lymph node was detected at his mediastinum. The diagnosis of central type of lung cancer with pulmonary atelectasis was made. He was firstly given the combination chemotherapy of 5-Fu (0.25g/wk) plus CTX (0.2-0.4g/wk), then the combined protocol of VCR, CTX and Adriamycin (ADM). After two courses of treatment, alternative approach to cisplatin infusion. During chemotherapy he was also taken the adjuvant treatment of traditional medicine. Three months later, he obtained complete response, with the remains of pleurisy, and 6 months later, he died in his lung cancer relapse.

**Case 6.** A 58-year-old man with lung cancer was admitted into hospital on September 4, 2004. He presented his previous history of cough and short breathing following alcohol one month ago. On CT scan showed a 4.5x4x3cm soft mass at hilus pulmonis, complicated by obstructive pneumonia. Histologically under broncho fiberscope, there existed the ingredients of necrotic tissue and some poorly differentiated cancer cells. He was undergoing the combination chemotherapy of PDD plus etoposide in another tumor hospital. The remainder of two courses of combination chemotherapy was continuous to be performed on September 11, 2004 and on October 16, 2004. A therapeutic protocol consisted of CTX (0.2-0.6g) plus MMC (4mg) drugs, and interleukin-2 immunotherapy. After having completed chemotherapy, he was treated in other hospital.

**Case 7.** A 75-year-old female was the chief complaint of hoarse voice for three months duration. In April 20, 2008 chest CT showed the diagnosis of lung teratoma (4x3cm) at her mediastinum (figure 1). A protocol was mainly by traditional medicine alone. The traditional medicine consists of *Taraxacum mongolicum* H, *Scrophularia ningpoensis* hemsl, *Ophiopogon japonicus* ker-gawl, *trichosanthes kirilowii* maxim, *Astragalus memberanaceus* bunge, *Poria cocos* (schw) wolf, *Citrus reticulata* Blanco (orange peel), Licorice, Blackberry lily, *Sophora subprostrate* chun T. chen, *Lasiosphaera fenslii* reich, *Scutellaria barbata* D. don, *Oldenlandia diffusa* roxb. A 10-years of follow up she remained well.



**Figure 1.** On CT scan showed tumor mass at her mediastinum

**Case 8.** A 62-year-old woman with advanced lung cancer was the complaint of pricking chest pain for one month on November 25, 2008. On CT examination showed a

38x40x40mm mass with much malignant hydrothorax in the cavity of her left lung, complicated by pulmonary atelectasis. A hydrothorax smear was further diagnosed as her advanced lung cancer. Treatment concluded a small dosage of 5-Fu and antitumor capsule tablets. The disappearance of hemorrhagic pleural effusion was achieved by traditional herbs, which consisted of *Cordate houttuynia*, *Solanum nigrum* L, *Lobelia chinensis* Lour, *Scutellaria barbata* d. don and *Oldenlandn diffusa* roxb. She was in stable disease for 6+ months without hemorrhagic hydrothorax relapse. She was near 1 year survivor.

**Case 9.** A 68-year-old man was admitted into hospital on November 9, 2008 due to his central type of lung cancer. On CT examination showed a 9x9x10cm mass at hilus pulmonis on upper lobe, complicated by left bronchlarctia. Histologically central type of differentiated squamous carcinoma of the lung was further diagnosed after biopsy of tumor tissue under broncho fiberscope. A therapeutic protocol of 5-Fu (300#) and antitumor capsule (400#) tablets, with mainly traditional medicine. The prescription of traditional medicine consisted of Lily, *Pseudostellaria heterophylla*, *Astragalus membranaceus* (fisch) bunge, *Ophiopogon japonicus* kergawl, *Poria cocos* (schw) wolf, *Cremastra appendiculata* makino, *Bulbus fritillariae cirrhosae*, *Adenophora borealis*, *Stemona*, *Solanum nigrum* L, *Solanum lyratum*, *Fructus trichosanthis*, *Rhizoma bletillae*, Almond, *Coix lachryina-jobi* L, *Trichosanthes kirilowil* maxim, *Scutellaria baicalensis* georgi, *Cordate houttuynia*, *Scutellaria barbata* d. don and *Oldenlandn diffusa* roxb. He was in stable disease, and tumor was receded to 8x8cm. In the follow up, he was over 1.5 years survivor.

**Case 10.** A 79-year-old man was admitted into hospital on March 2, 2009 due to an attack of recurrent episodes of bad cough, short breathing, and severe edema in his extremities, complicated by progressive weakness. On CT examination showed much hydrothorax with 2.0cmx2.6cm mass in the cavity of his left lung. The patient with lung cancer was considered. A protocol was mainly by three months of traditional medicine with L-asparagine tablets. With relief symptoms of cough and edema disappearance, he obtained remission in disease. He died in tremendous prostatomegaly with unable to surgery. He was over 1.5 years survivor.

**Case 11.** A 62-year-old man was admitted into hospital on March 31, 2012 because of metastatic lung cancer. He presented the symptoms of cough and blood-tinged sputum. There was an egg-like lymph node palpable on his right supraclavicular fossa. On CT examination showed a 5x3.5cm mass, accompanied with metastatic lymph node at hilus pulmonis. He had about 40 years of smoking. A therapeutic protocol was mainly by traditional medicine for four months. Repeated CT scan presented available

stable disease. He was near 1 year survivor.

**Case 12.** A 64-year-old female was diagnosed as left lung cancer on July 29, 2013 due to the tumor at her left lung complicated with bronchlarctia. Metastatic lymph nodes were detected at left axillary, mediastinum and hilus pulmonis, with one lymph node 2.2x2.0cm. She was given two courses of combination chemotherapy, with hereafter cantharidin compound and oncogenic EGFR (epidermal growth factor receptor) gefitinib target therapy. She remained in stable disease for 8+ months, and she had over 1.5 years survivor.

### Results and discussion

In this study, a series of 12 cases of lung cancers were reported. All patients were used by different dosage of chemotherapy and traditional medicine or immunotherapy. The objective responses were obtained in 5 patients (long-term CR in 2 cases, short CR in 2 cases and PR in 1 case), other 5 patients obtained in stable disease for over 6 months to 2 years, and 1 patient with pulmonary tumor at mediastinum remained well after 10 years of follow up. The detail data were summarized in table 1.

In vitro, phytohemagglutinin (PHA) stimulate host immune lymphocyte activity, inducing the generation of T-cell growth factor (interleukin-2, IL-2). In this study, PHA and IL-2 immunotherapy was indeed the stimulation of lymphocytic kill cell activity, thereby exhibiting its anti-neoplastic activity. Thus, A CR (case 3, case 4) and PR (case 1) was obtained through combination chemotherapy and immunotherapy.

The EGF receptor (EGFR) (Cohen et al., 1982) has a key role in normal embryonic development, adult tissue homeostasis and many pathological processes, particular tumor formation. Aberrant EGFR activation becomes oncogenic due to overexpression and/or amplification of the EGFR gene or by autocrine/paracrine growth factor loops, whereas activating dimerized mutations promote EGFR signaling, which lead to ligand-independent (Zandi et al., 2007; Lainsey et al., 2013).

Phosphorylation of this oncogenic receptor at residues Tyr845, Tyr1045 and Tyr1173 leads to receptor activation and downstream signaling (Glynn, 2013; Kim, 2010; Gabitova, 2014; Ullrich, 1992; Zhu, 1992, 2013, 2016, 2017). And oncogenic receptor EGFR can transfer its oncogenic activity among cancer cells (Al-Nedawi, 2008; Robinson, 2008; O'Connor, 2008). Oncogenic EGFR mutations are found in 10% to 35% of lung adenocarcinomas, with predominant in a subset of patients

**Table 1.** Patients characteristics

Cases	Sex	Ages	History of diseases	Diagnosis	Protocol	Response following therapy	Duration of remission
1	F	43	7 years	MLC (3x3cm)	VCR,, CTX, MMC, 5-Fu	PR	8+ years
2	M	64	6 mon	Lung cancer (3x5)	Antibiotics, Pred, TCM	CR	17 years
3	M	40	3 mon	Lung cancer (4.5x4.9)	CTX, 5-Fu, PHA, TCM	CR	10 years
4	M	10	2 mon	Malignant mesothelioma	VCR, CTX, 5-Fu, PHA, TCM	Short CR	3 months
5	M	46	3 mon	Lung cancer (5.5x4)	VCR, CTX, 5-Fu, ADM, TCM	CR	6 months
6	M	58	1+mon	Lung cancer (4.5x4x3)	PDD, etoposide, CTX,IL-2	remission	unknown
7	F	75	3+mon	Lung teratoma (4x3)	TCM	Stable disease	10 years
8	F	62	1+mon	Lung cancer (3.8x4x4)	5-Fu, antitumor capsule	remission	10 months
9	M	68	6+mon	Lung cancer (9x9x10)	5-Fu, antitumor capsule	PR	1.5 years
10	M	79	2+mon	Lung cancer (2x2.6)	TCM	Stable disease	1.5 years
11	M	62	3+mon	MLC (5x3.5)	TCM	Stable disease	10 months
12	F	64	6+mon	Lung cancer	Chemotherapy, gefitinib	Stable disease	1.5 years

with non-small cell lung cancer (NSCLC) (Godin-Heymann, 2007; Rosell, 2011; Karachaliou, 2014). These mutations, which commonly occur as either small inframe deletions in exon 19 or point mutations T790M and L858R in exon 21 within the EGFR tyrosine kinase domain, confer constitutive activity and sensitivity to EGFR tyrosine kinase inhibitors (TKI) (Gallant, 2015; Konduri, 2016). Recent, Gallant (Gallant, 2015) identified a novel EGFR alterations in lung cancer. EGFR exon18-25 kinase domain duplication (EGFR-KDD). EGFR-KDD is oncogenic and oncogenic EGFR-KDD- transformed cells are sensitive to the EGFR-TKI afatinib. Konduri and colleagues (Konduri, 2016) reported five patients with metastatic lung cancer whose tumors harbored EGFR fusion, most commonly RAD5, are recurrent in lung cancer. Four of whom were treated with EGFR-TKI erlotinib with documented antitumor response for 5, 6, 8 and 20 months respectively. These patients whose tumors harbored EGFR fusions are oncogenic in preclinical studies. In mouse model, transgenic mice expressing EGFR L858R in type II pneumocytes developed atypical adenomatous hyperplasia and multifocal adenocarcinoma, and gefitinib inhibited tumorigenesis completely (Ichihara, 2009). In this study, we use gefitinib in keeping stable disease in a patient with lung adenocarcinoma, and using gefitinib in more patients are under investigation.

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