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

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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
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 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, *Scerophularia ningpoensis* hemsl, *Ophiopogon japonicus* ker-gawl, *trichosanthes kirilowii* maxim, *Astragalus memberancacuse* bunge, *Porica cocos* (schw) wolf, *Citrus reticulata* Blanco(orange peel), Licorice, Blackberry lily, *Sophora prostrate* chuneb T. chen, *Lasiosphaera fenslii* D. don roxb. *Scutellaria barbata* D. don, *Oldenlandia diffusa* roxb. A 10-years of follow up she remained well.
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 bronchilarctia. 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, Portia cocos (schw) wolf, Cremasra appendiculata makino, Bulbus fritillariae cirrhosae, Adenophora borealis, Stemona, Solanum nigrum L., Solanum lyramtum, Fructus trichosanthis, Rhizoma bletilliae, Almond, Coix lachryma-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 bronchilarctia. 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 cantheradin 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 antineoplastic 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 hemeostasis and many pathological processes, particular tumor formation. Ablerrant 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; Ulrich, 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.
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.

References


Gallant JN, Sheehan JH. 2015. EGFR kinase domain duplication (EGFR-KDD) is a novel oncogenic driver in lung cancer that is clinically responsive to afatinib. Cancer Discovery, 5:1155-1163.


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