Case Report

Carcinostatic effect of allergen removed *Rhus Verniciflua* stokes based Traditional Korean Medicine on a patient with lung adenocarcinoma; single case report

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SUMMARY

Lung cancer is one of the leading causes of cancer mortality and overall treatment outcomes for lung cancer are still to be considered disappointing despite of development of new medical therapeutics on cancer. Cytostatic agents are considered as novel medication in the treatment of cancer though its benefit is most appropriately assessed through survival end points rather than the objective-response end points. We present a case of a lung adenocarcinoma patient who showed tumor lesion in patient's two different lung sites. From the day of diagnosis, the tumor lesion stayed with the almost same size with more than 1 year of Allergen-Removed *Rhus Verniciflua* Stokes (A-RVS) based Traditional Korean Medicine treatment without any western conventional treatment. No significant side effect was noted and the patient maintained good performance status throughout the treatment period. We assume A-RVS may have cytostatic effect on NSCLC patient and our observation justifies further investigation.

Key words: *Rhus Verniciflua*; A-RVS; Lung cancer; Carcinostatic; Cytostatic

INTRODUCTION

Lung cancer is one of the leading cause of cancer mortality and despite of development of new medical therapeutics and increased medical cost, analysis based on Surveillance, Epidemiology, and End Results (SEER) data of the National Cancer Institute shows life expectancy of elderly patients after diagnosis over the period 1983 to 1997

improved minimally, with an average increase of approximately 0.6 months (Woodward *et al.*, 2007). Though some clinical results of chemotherapy have recently shown promising results, overall treatment outcomes for lung cancer are still to be considered disappointing.

These days, thanks to the advances in the knowledge of tumor biology and mechanisms of oncogenesis, some molecular target agents for cancer treatment have been developed. One of the approaches of targeted agent is the inhibition of angiogenesis, and these targeted agents usually induced cytostatic effects contrary to the most chemotherapy agents which have cytotoxic

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properties to the cancer cells (Gridelli et al., 2007).

In Traditional Korean Medicine (TKM), many medicinal herbs are used for their possible effect upon the treatment of cancer. *Rhus Verniciflua* Stokes (RVS) is one of them and according to TKM theory, it has been considered to have the function of breaking up blood stasis and purging hardness and used, for example, for abdominal masses and amenorrhea from blood stasis (Bensky, 1993). In this report, we demonstrate a 50-year old woman with Non-small cell lung cancer (NSCLC) and she was treated with Allergen-Removed *Rhus Verniciflua* Stokes (A-RVS) based TKM. The result shows that this treatment has prevented further progress of cancer mass in this patient and this can be considered as treatment with carcinostatic effect.

Case presentation

A 50-year-old female patient paid her first visit the clinic on Nov 2006 for the treatment of NSCLC. Initially she had thyroid enlargement since Dec 2005 which turned out to be malignant by fine needle aspiration and the cell type was papillary carcinoma. She had planned to get thyroidectomy but cancelled it due to newly detected lung cancer before the surgery. She complained of anorexia, fatigue and mild cough without sputum. Her ECOG (European Cooperative Oncology Group) performance status was 0, which means she is fully active, able to carry on all pre-disease performance without restriction. She had no history of smoking or alcohol drinking with no significant past history.

After confirmed by biopsy that the tumor is adenocarcinoma (Fig. 1), she was recommended to have an operation (lobectomy) on her lung but the patient refused to have a surgery to know the risk of removing up to 3 lobes that was infiltrated and possible lowered quality of life after surgery. Computerized tomography (CT) of chest which was taken 11 Nov 2006, was compatible with adenocarcinoma in the LUL and two mixed ground-glass opacity (GGO)s in the RLL suggesting adenocarcinoma or bronchioalveolar carcinoma.

Fig. 1. Biopsy slides A. Lung adenocarcinoma B. Microphotograph from a section of thyroid lobe showing.

But Positron Emission Tomography (PET)-CT showed hypermetabolic lesion in the LUL, while no abnormal FDG accumulation in the RLL nodule, so the nodule in RLL was considered as benign tumor though it was not histologically confirmed.

A-RVS based TKM treatment was initiated from 23 Nov 2006. 1 capsule that contains 150 mg of ARV extract was given to the patient three times a day. While RVS is generally considered as toxic herb because, among its chemical components, urushiol induces allergen reaction of the skin. To eliminate urushiol, extracts from RVS were prepared using water or ethanol solution at the temperature of 90~95, with 10 times much more of solvent, under 1 atmospheric pressure for 6 h (Yoon, 2006).

Patient was followed up every other week and acupuncture treatment was given every visit to promote her overall health status. She was diagnosed as Qi deficiency status based on TKM and acupuncture points mainly used to this patient include LI4, LR3, CV12 and SP36. Supplementary herbal decoction Bo-Jung-Ik-Ki-Tang (Bu Zhong Yi Qi Tang: Tonify the Middle and Augment the Qi Decoction) was also given to treat her Qi deficiency status and promote digestive function. The components of herbal decoction include Astragali Radix, Panax ginseng C. A. Meyer, Atractylodis Rhizoma Alba, Angelicae gigantis Radix, Aurantii nobilis Pericarpium, Bupleuri Radix, Cimicifuga racemosa and Glycyrrhiza Radix.

Radiographic findings of Chest-CT on 2007. 11. 22 revealed no significant change of nodule in LUL

Fig. 2. Chronological Radiographic Findings of LUL Mass. She maintained good performance status with ECOG score 0 which is the same score from initial treatment day in Nov 2006. No significant side effect was noted.

Table 1. Interpretation Reports of Radiographic Findings

Radiographic report	
2006.10.21 Chest CT	<ul style="list-style-type: none"> ·Spiculated nodule, LUL. ⇒ R/O Lung cancer. ·Another spiculated nodule, RLL. ⇒ 2nd primary lung cancer, cannot be excluded. ⇒ R/O Focal atelectasis or pneumonic infiltration. ·Fibrocalcified old tbc sequelae, RUL.
2006.11.03 PET-CT	Findings : Hypermetabolic lesion in the LUL : r/o Lung cancer Hypermetabolic lesion in the Rt thyroid r/o Thyroid cancer No abnormal FDG accumulation in the RLL nodule r/o benign nodule, more likely.
2006.11.10 Chest CT	Findings : Compatible with adenocarcinoma in the LUL with small GGO in the LUL. Two mixed GGOs in the RLL suggesting adenocarcinoma or BAC Small tiny subpleural nodule in the LLL.
2007.11.22 Chest CT	Findings : No significant change of nodule in LUL No significant change of GGO nodule in RLL

GGO: ground-glass opacity, BAC: bronchioalveolar carcinoma

and no significant change of GGO nodule in RLL. Both thyroid glands were also showed no interval change. Until last follow up visit on 8 Jan 2008, she maintained good performance status with ECOG score 0 which is the same score from initial treatment day in Nov 2006. No significant side effect was noted.

DISCUSSION

Main treatment modalities of lung cancer include

surgery, chemotherapy and radiotherapy, but management of patients with lung cancer requires careful consideration of the patients' general health condition, cancer stage, and risk or side effect of treatment. According to the World Health Organization classification, four major cell types make up most of all primary lung neoplasms. These are squamous carcinoma, small cell carcinoma, adenocarcinoma, and large cell carcinoma. As small cell carcinomas usually show different clinical presentation with

the spread such that surgery is unlikely to be curative, the other types of lung neoplasm usually referred to NSCLC, which accounts for approximately 80% of all lung cancers. In patients with non-small cell lung cancer of stages IA, IB, IIA and IIB who can tolerate operation, pulmonary resection offers the best chance of cure. Patients with tumors which are not suitable for surgical resection can benefit from radiotherapy to the chest. Chemotherapy is also usually used to get survival benefits, symptom palliation, and improved quality of life (Kasper, 2005).

Although there is skeptical view on the value of medical interventions for lung cancer including chemotherapy of NSCLC (Woodward *et al.*, 2007), lots of efforts are still made to improve the survival and quality of lives of cancer patients. These days, cytostatic agents are being considered as novel medication in the treatment of cancer with prolonged survival period and lower toxicity compared with the cytotoxic chemotherapy agent previously used. One of the approaches of targeted agent is the inhibition of angiogenesis (Gridelli *et al.*, 2007). Because of the presumed cytostatic mechanism of action of these agents, however, the efficacy is most appropriately assessed through survival end points rather than the objective-response end points that have traditionally been used with cytotoxic agents (Ellis, 2006). Moreover, ongoing trials are attempting to integrate targeted agent into the treatment of early-stage disease as adjuvant and neoadjuvant therapy and into combined modality approaches for locally advanced disease.

In view of TKM, cancer is resulted from qi and blood stagnation due to dysfunctioning of organs such as spleen, lung or kidney. Depending on each patient's yin, yang, qi, blood or jangfu status, the treatment regimen is determined whether to tonify the body or remove stagnation or the combination of the two methods. In this case, we used RVS as main therapeutic treatment modality. Pharmaceutical name of *Rhus Verniciflua* is *Lacca Sinica Exsiccatae* and it's mainly grown in Korea, China and Japan.

In TKM, *Rhus Verniciflua* is herb with acrid, bitter, warm, slightly toxic properties. It is considered to have the function of breaking up blood stasis and purging hardness. One of the main symptoms of stasis of blood is pain that is fixed in one place, and is of a boring or stabbing character. Stasis of blood can derive from stagnation of qi, deficiency of qi, heat in the blood, blood deficiency and interior cold according to TKM point of view (Kim *et al.*, 2006). Use of RVS to cancer patient was initially inspired by these views of TKM (Yoon, 2006).

There are many studies that show anticancer properties of RVS. Kim *et al.* (2006) reported that exposure to an ethanol extract of RVS 50 g/ml resulted in a synergistic inhibitory effect on cell growth in AGS cells. Kitts *et al.* (2001) also reported the antioxidant, cytotoxic, and antitumorigenic activities of a fractionated, ethanol extract derived from RVS. Lee *et al.* (2005) studied that RVS glycoprotein has dose-dependent blocking activities against G/GO-induced cytotoxicity and apoptosis, increasing the glutathione peroxidase activity. Jang *et al.* (2005) showed that RCMF (the RVS chloroform-methanol fraction) is an agent which may be capable of inducing sensitive growth inhibition and apoptosis in HOS cells.

Although the study on RVS is mainly limited to *in vitro* and *in vivo* study, more and more clinical application of RVS or A-RVS is necessary to verify the effect on cancer patient. Its anticancer effect is not fully understood, but study performed by Choi *et al.* (2006) attributes the anticancer effect to antiangiogenic effect of A-RVS. Clinical applications were also made by various types of cancer patients. Yoon *et al.* (2006) reported case series of the acute lymphocytic leukemia treated with A-RVS. Jeong *et al.* (2007) showed its possible use to malignant melanoma patient.

In this case, we used A-RVS based TKM treatment to treat NSCLC patient. Before starting TKM treatment, she was recommended to have an operation on her lungs but she decided to start

A-RVS based TKM and maintained this treatment for more than 14 months. So far, the tumor has shown no interval change while maintaining the good performance status without any significant side effect. Considering these points, we assume that A-RVS based TKM treatment has induced carcinostatic effect upon this patient and its effect probably attributes to cytostatic effect of A-RVS which was proved to inhibit the angiogenesis of cancer cell (Choi *et al.*, 2006). As for other herb that showed similar effect, though *in vitro* study, is *Astragali Radix* (AR). Lin *et al* studied AR for its inhibitory effect on growth of different cancer cell lines, and AR specifically inhibits gastric cancer cells growth *in vitro* and the mechanism is mainly cytostatic but not cytotoxic or inducing apoptosis (Lin *et al.*, 2003). Cytostatic agents usually do not shrink tumors, but they do inhibit tumor growth and/or decrease the number of metastatic lesions in animal models. As with other cytotoxic chemotherapeutic agents, these cytostatic agents also need to be validated through clinical application and trials. But because these cytostatic agents do not shrink tumors but slows or stops the growth of tumors and the development of metastases (possibly with higher doses not necessarily leading to more effect), standard cytotoxic trial designs may not be effective in identifying clinically useful agents. New approach that warrants identification of effective cytostatic agents will permit clinicians not to incorrectly discard promising agents. This new approaches may include administering the cytotoxic agent first, followed by the cytostatic agent (Ratain and Stadler 2001).

This is only a case report but it has a significant meaning in that A-RVS based TKM treatment shows potential in treating lung adenocarcinoma patient by its carcinostatic effect. Considering the fact that she didn't receive any conventional western treatment, and only was treated with A-RVS based TKM, this treatment proves unique effect and justifies further investigation.

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