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CLINICAL STUDY

Effect of compound Kushen injection on T-cell subgroups and natural killer cells in patients with locally advanced non-small-cell lung cancer treated with concomitant radiochemotherapy

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Abstract

OBJECTIVE: To observe effect of compound Kushen injection on T-cell subgroups and NK cells in patients with locally advanced non-small-cell lung cancer (NSCLC) treated with concomitant radiochemotherapy.

METHODS: We randomly divided 60 patients with locally advanced NSCLC who were treated at our hospital between May 2011 and May 2013 into a treatment group and a control group by drawing. The treatment group (n = 30) received concomitant radiochemotherapy plus compound Keshen injection, and the control group (n = 30) received only radiochemotherapy.

RESULTS: After treatment, levels of CD3+, CD4+, CD4+/CD8+ and CD16+/CD56+ cells had significantly increased, and CD8+ cells had significantly decreased, in the treatment group compared with both their pretreatment levels and with levels in the control group. In the control group, post-treatment levels of CD3+, CD4+, CD4+/CD8+ and CD16+/CD56+ cells were not significantly changed from pretreatment levels. The two groups did not significantly differ in their rates of toxicity reactions ($P > 0.05$).

CONCLUSION: Compound Kushen injections can increase immunologic function in patients with locally advanced non-small cell lung cancer who receive concomitant radiochemotherapy.

Key words: Compound Kushen injection; Carcinoma, non-small-cell lung; T-lymphocytes; Killer cells, natural; Chemoradiotherapy

INTRODUCTION

Patients with non-small cell lung cancer (NSCLC) account for about 80% of patients with lung cancer. Among them, locally advanced NSCLC (LA-NSCLC) accounts for 40%-50% of NSCLC.[1] For LA-NSCLC, successful excision is less probable, and concomitant radiochemotherapy (CRCT) is the primary treatment at present. However, compared with single-mode radiotherapy or chemotherapy, CRCT increases toxicity and decreases immunologic function, leading to decreased tolerance that may curtail treatment in severe cases.[2] Traditional Chinese Medicine holds that in treating tumors, eliminating pathogenic factors and strengthening genuine *Qi* are of equal importance; eliminating pathogenic factors is killing tumor cells by using radiotherapy or chemotherapy, and strengthening genuine *Qi* protects immunologic functions of the organism by

using drugs, increasing immunity of the organism.[3,4] Clinically, Chinese drugs with functions of strengthening genuine *Qi* to consolidate the constitution, promoting blood circulation to remove blood stasis, and clearing heat and removing toxic substance are more used for strengthening genuine *Qi* at present. Compound Kushen injection (CKI) is made from the extract of Kushen (*Radix Sophorae Flavescentis*) and Tufuling (*Rhizoma Smilacis Chinae*), containing the chemical components such as oxymatrine, matrine, sophocarpine, sophorine, sophoridine, and kurarinone.[5] Modern study indicates that CKI has many pharmacologic properties, such as anti-tumor, anti-inflammation, analgesia, and immunity-enhancing activity, and is widely used for accessory treatment of cancers including that of the digestive tract, NSCLC, and primary liver cancer. Since January 2011, our department has used CKI to increase immunity of patients with LA-NSCLC with CRCT, achieving a good clinical therapeutic effect, as reported in the following.

MATERIALS AND METHODS

Clinical data

We selected 60 patients (32 men and 28 women) with LA-NSCLC who were treated at our hospital between May 2011 and May 2013. They were assigned to a treatment group or a control group (n = 30 for both), by using a random drawing. This experimental study was approved by the Ethics Committee of the Hospital. All of the patients provided signed informed consent forms.

Inclusion criteria

We included patients for whom (a) NSCLC was established as adenocarcinoma or squamous carcinoma, by pathological or cytological detection after aspiration biopsy; (b) the patient had phase Ⅲa or Ⅲb disease (IASLC2009 staging criteria); [6] (c) The patients had not received previous radiotherapy or chemotherapy; (d) patient's Karnofsky performance score (KPS) ≥ 70, and predicted living time ≥ a half year; (e) electrocardiogram, routine blood tests and liver function and renal function were normal; and (f) the patient provided informed consent.

Exclusion criteria

We excluded patients who had (a) obvious pulmonary emphysema or respiratory function decompensation, (b) autoimmune disease, or (c) phase IIIa disease that required surgery.

Treatment methods

Both the control and treatment groups received 3-dimensional conformal radiation therapy (3D-CRT) with a concomitant regimen of duoxitasai + cisplatin (DP). The treatment group received CKIs at the same time.

For the 3D-CRT: The body position was fixed with a body model, with Toziba 16-row CT modeling location and scanning layer thickness 5 mm, and the figure was transferred into the planning system (3DTPS). Clinical target area volume (CTV) included the primary focus of the lung, the hilus of lung of the same side and the draining area of mediastinal lymph nodes. The margin was 0.6-0.8 cm outside the tumor volume (GTV), shown by the lung window in the CT slice. The planned target volume (PTV) was extra-spreading 0.8-1.5 cm on the basis of CTV; 95% of the isodose curve covered the PTV, with lung dose: V20 ≤ 20%; heart: ≤ 30 Gy; spinal cord: ≤ 40 Gy. Patients received 6MV-X radiation therapy at 4-6 conformal visual fields, 2.0 Gy/f, 1 f/d, 5 f/w; after the tissue dosage reached to 40 Gy/4 w, chest CTs were rechecked. According to any changes of the focus, the primary focus was then radiated with DT 60-70 Gy over the reduced area.

The DP (duoxitasai +cisplatin) regimen was Duoxitasai (Jiangsu Hengrui Medical Limited Company, Batch No. H20031227, Lianyungang, China) 20 mg/m^2, intravenous drip, on the first day; cisplatin (Jiangsu Haoshen Pharmacy Limited Company, Batch No. H20050563, Lianyungang, China) 30 mg/m^2, intravenous drip on the first day. The chemotherapy was concomitantly carried out on the first day of radiotherapy, once a week, until the end of radiotherapy. During chemotherapy, patients received treatments for inhibiting acid and nausea, and protecting the liver.

In the treatment group, at the beginning of radiochemotherapy, compound Kushen injection (Shanxi Zhendong Pharmacy Limited Company, Chinese medicine permit No. Z14021231) 20 mL plus 200 mL saline was given, intravenous drip, at 40-60 drips each min, once a day for 15 days.

Observation indices

Patients' peripheral blood T-lymphocyte subgroups (CD3+, CD4+, CD8+) and natural killer (NK) cells (CD16+, CD56+) were detected with a flow cytometry one day before treatment and one week after the end of the treatment in both groups. Ratios of CD4+/CD8+ were calculated.

Statistical analysis

Statistical analysis was carried out with SPSS13.0 software (SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation ($\bar{x} \pm s$). Independent sample t-tests were used to compare the two groups. Toxicity reactions in the two groups were compared with χ^2 tests. $P < 0.05$ was considered significance.

RESULTS

Comparison of basic data of the patients

At last, 60 patients (32 men and 28 women) with