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## Case Report

# A Case of T Cell Lymphoma Treated by Korean Medicine Therapy Alone

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## Keywords

Korean medicine therapy · Atypical peripheral CD4 T cell lymphoma · Hyunamdan · Hangamdan S

## Abstract

This case report is aimed to investigate the effects of Korean medicine therapy (KMT) alone including oral herbal medicine on treating a patient with atypical peripheral CD4 T cell lymphoma. The oral medicine used is Hyunamdan made of heat-processed ginseng and Hangamdan S. An 87-year-old man who was diagnosed as having atypical peripheral CD4 T cell lymphoma on November 30, 2015 was treated with KMT from December 23, 2015 until October 22, 2016. The effectiveness of therapies was evaluated with PET-CT scan as well as the change of the main sign of lymphoma. The sizes of the right axillar and right external iliac lymph nodes decreased. These results suggest that KMT can be an effective method to treat atypical peripheral CD4 T cell lymphoma.

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## Introduction

As lymphoma is a disease group that undergoes malignant alternation via various differentiation stages of immunocytes, different subtypes of lymphoma present varying morphology, immunophenotyping, and clinical findings from highly mild ones to aggressive types. While some lymphoma cancers are expressed in white blood cells (invading bone marrow and blood), other tumors are found only as lymphoma (solid tumor in the immune system) [1]. According to the 2011 data published by the Korea Central Cancer Registry, during 2009, 4,093 people were diagnosed with malignant lymphoma in South Korea, with a standardized incidence rate of 8.2 per 100,000. Although this figure is relatively lower than that in North America or Europe, where 10–15 per 100,000 people are diagnosed with the disease, Hodgkin lymphomas account for 5% (220 patients) and non-Hodgkin lymphomas account for 95% (3,873) of the total [2]. Different countries show different prevalent types of malignant lymphoma. In South Korea, first, Hodgkin lymphoma is rarely found; second, among non-Hodgkin lymphomas, low-grade lymphoma such as follicular lymphoma is rare; and, third, lymphoma derived from T lymphocytes or NK lymphocytes is relatively common. Non-Hodgkin lymphoma, which accounts for the vast majority of the overall lymphoma patients, was the ninth most prevalent type of tumor in 2009. Among 69,780 people who died of cancer in 2009, 1,302 had non-Hodgkin lymphoma. The prognosis of non-Hodgkin lymphoma is determined based on 5 risk factors: age 60 or older; stage III or IV (Ann Arbor staging system); more than one involvement sites other than the lymph node; in the physical activity index of the patient, ECOG 2 or higher and Karnofsky 70 or lower; and, lactate dehydrogenase increase. According to the number of these risk factors, the patients are divided into (1) 0 or 1: low-risk group; (2) 2: low-to-moderate risk group; (3) 3: moderate-to-high risk group; and (4) 4: high-risk group [3].

The standard treatment of non-Hodgkin lymphoma involves radiotherapy and combination therapy, and treatment results vary according to the grade of the sign of lymphoma. South Korean patients tend to share characteristic malignant lymphoma but show a variety of side effects due to application of a unified treatment. We aimed to report the case of an elderly patient with lymphoma (stage III) who was treated by Korean medicine therapy (KMT) alone for 6 months and showed improvement in symptoms such as a decreased number of lymphomas spread throughout the body.

## Case Presentation

The patient was an 87-year-old male in whom a mass accompanied by pressure pain was found in the left inguinal region (axillary lymph nodes) and who subsequently visited a hospital in Seoul on November 29, 2015 where he received PET-CT and CT scan as well as aspiration and biopsy of the bone marrow and right iliac crest. The PET-CT and CT scan results showed hypertrophy of multiple lymph nodes. In the subsequent bone marrow finding, a number of cells were in metaphase and, therefore, the metaphase quality was adequate. In the analysis of 20 cells in metaphase, no clone with chromosomal abnormality was observed and the karyotype was normal. Therefore, it was concluded that there was no evidence of bone marrow involvement of the lymphoma. Finally, the patient was diagnosed with atypical

peripheral CD4 T cell lymphoma (follicular helper type, stage IIIA) and was recommended to receive chemotherapy at the hospital in accordance with the standard treatment guideline. However, first of all, his guardian and medical doctor suggested that the patient was unlikely to withstand chemotherapy, considering his age. Secondly, the patient was not within the normal range of standard body weight. Thirdly, the patient rejected chemotherapy due to unbearable pain and poor appetite and general weakness. Subsequently, the patient visited our hospital on December 23, 2015. At that time, there was no chief complaint caused by the diagnosis, and the patient complained of low energy and indigestion, among others. In the images he brought to our hospital, we found abnormal lymph node hypertrophy in the left intracarotid lesion, both cervical level II, left supraclavicular, both axillar, both mediastinal and interlobar, common hepatic artery, aortocaval, left iliac chain, right external iliac and inguinal lymph nodes. The blood pressure of the patient was 127/84 mm Hg, his temperature was 36.0°C, his pulse rate was 91, his respiration rate was 18, his weight was 47.95 kg, his height was 163.6 cm, and he had a history of carotid artery stenosis s/p (status post) stent insertion and compression fracture, and a body of T9 and T11 (osteoporotic lesion). As of September 9, 2016, the patient had been receiving only KMT and a regular blood test, CT, and PET-CT scan were performed, according to the treatment progress.

The patient has been treated at our hospital with pharmacopuncture and oral herbal medicine. Comparing the first time the patient visited us in 2015 with his visit in March 14, 2016, the first therapy did not show improvement in the symptoms perceived by the patient. As a result, the prescription was changed from Sojongdan to Hyunamdan, and Yeon-goehwan was added. Subsequently, the sizes of the axillary lymph nodes and those in the inguinal region perceived by the patient began to decrease; the result of PET-CT and abdomen and chest CT scan on April 11, 2016 showed a reduction in the lymph node size (Table 1; Fig. 1). During the 8-month treatment, the lymph node size did not increase but continually decreased, and  $\beta_2$ -microglobulin in the blood test repeatedly fluctuated without a change, showing a similar pattern to the fluctuation of lactate dehydrogenase levels (Table 2). Indigestion and discomfort in the stomach after a meal, which had been a continuous complaint of the patient, have subsided, allowing the patient to have normal meals. Currently, the patient does not have any symptom that interferes with daily life.

## Discussion

Treatment of malignant lymphoma is divided according to the classification of Hodgkin and non-Hodgkin lymphomas. For Hodgkin lymphoma, radiotherapy can play an important role along with chemotherapy; however, for non-Hodgkin lymphoma, chemotherapy is used as a main treatment method. Treatment of non-Hodgkin lymphoma is determined based on the tissue form, stage and overall condition of the patient. The patient in question was recommended active chemotherapy; however, the patient and his guardian chose KMT in order to treat the symptoms. We applied pharmacopuncture and used oral herbal medicine to treat the patient, all of which were prepared by the pharmacy in our hospital.

For pharmacopuncture, a Korean medicine doctor injects liquid medicine prepared by using medicinal herbs into selected meridian points in the abdomen. Oral herbal medicine is prepared in the forms of pills, capsules, or distillate by using one or more medicinal herbs.

From December 25, 2015 until March 14, 2016, we prescribed Soramdan S and Hae 50 to be taken twice per week. The patient visited the hospital twice per week and during this time he received injections of 1 ml prunellae spica pharmacopuncture on 3 points of the abdomen: ST25, CV12, and CV13. The patient took Sojongdan 3 times per week, and 1,000 mg b.i.d. of Hanganmdan S every day. Subsequently, from March 15, 2016 until August 25, 2016, Soramdan S and Hae 50 were taken once per week, and 1 ml prunellae spica pharmacopuncture was injected once per week on a meridian point on the abdomen. Also, instead of Sojongdan, Hyunamdan and, additionally, one sachet of Yeongoenhwan were taken every day (Table 3).

Although it may be hasty to discuss the efficacy of KMT on lymphoma (stage IIIa) based on this case alone, such a case report can serve as part of a clinical ground for using oral medication like Hyunamdan, Hanganmdan S, Sojongdan, and Yeongoenhwan in KMT for the treatment of lymphoma (stage IIIa). To be sure, we believe it is necessary to prove the efficacy of KMT on treatment of various types of tumors through further case reports and clinical studies.

For prunellae spica pharmacopuncture, 2 g of the floral axis of prunellae spica grown in Jiangsu, China, was freeze-dried and, by using 9 g of bamboo salt mixed with 1 L sterile water for 0.9 salinity, distilled for about 5 h in a distillation extractor, in order to obtain 2,000 mL distillate. The liquid was then filtered twice by using 0.45- and 0.2- $\mu$ m filter papers, and placed in sterilized containers in a specific quantity, which were then sealed by rubber lid, aluminum cap, and autoclave tape. Subsequently, it was sterilized by using high pressure at 120°C for 1.5 h before use. Hot water extract of prunellae spica was found to inhibit aromatase activity in a concentration-dependent manner, and suppress expression of COX-2, and, therefore, is expected to have anticancer effects [4]. For Soramdan S, 500 g mountain-cultivated ginseng from which rhizome was removed was ground by using a grinder, and then, thoroughly mixed with 500 g honey, before it was kneaded into 8-g balls that were covered with gold foil. Hanganmdan S was made by changing the ratio of *Cordyceps miliaris*, *Cremastra appendiculata* tuber, and *Panax ginseng* radix in Hangan-plus originally prescribed by the East-West Cancer Center of Daejeon University (Table 4). Kim et al. [5] reported, in a case series of patients with progressive non-small cell lung cancer who showed improvement after administration of Hangan-plus, that the prescription partially contributed to easing the symptoms and inhibiting growth of lung cancer. For Hyunamdan, fresh ginseng was cooked at high temperature over 120°C and high pressure for 3 h for sterilization, before it was thoroughly dried and ground into powder, which was then mixed with honey at a ratio of 1:1 and kneaded into 4-g pills. According to Kim et al. [6], upon heat processing at 120°C, most peaks of ginsenosides Rb1, Rb2, Rc and Rd disappeared and the contents of less polar ginsenosides 20(S,R)-Rg3, Rk1 and Rg5 were newly detected. In fact, analysis of ginsenosides contained in Hyunamdan showed Rg3 and Rh2, which are not found in fresh ginseng. It was shown that treatment of cancer cells in vivo and in vitro with Rg3 results in reduction of proliferation, metastasis and mortality [7–11]. Ginsenoside Rh2 has been shown to have an antiproliferative effect on human non-small cell lung cancer. Rh2 is able to block cell proliferation, cause G1 phase arrest, enhance the activity of capase-3 and induce apoptosis in non-small cell lung cancer A549 cells [12, 13]. For Sojongdan, *Angelicae gigantis* radix, corni fructus, cervi pantotrichum cornu, aquilariae resinatum lignum, and mountain-cultivated ginseng were mixed at a ratio of 1:1:1:0.15:0.35 g, and then, treated with alcohol

to assist in the dissolution and digestion of decursin [14], which is the main component of *A. gigantis* radix, and then immersed in distilled liquor to reduce the sour taste of corni fructus, before being dried. Then, to facilitate digestion and absorption of cervi pantotrichum cornu, it was soaked in milk and dried, before it was mixed with 3 other types of dried medicinal herbs, aquilariae resinatum lignum, and mountain-cultivated ginseng and nanocrystallized. To the powdered ingredients, a certain amount of honey was added to form pills, which were then covered with gold foil. For Yeongoenhwan, 9 kg prunellae spica, 7.5 kg *Ganodermae polyporus*, and 4.5 kg *Thallus eckloniae* were boiled for 2 h in an infusion machine, after 4 h of preheating. Then, 150 L extract was placed into a steam concentrator and concentrated into 1.8 L liquid, which was subsequently added to 3 kg powder of coicis semen and mixed for 20 min. The mixture was then made into pills by using a machine before being dried at 45°C for a minimum of 15 h. To produce Hae 50 distillate, astragali radix and *Zingiber officinale* rosc. was mixed at a ratio of 1:1 with distilled water, and then, distilled for 4 h by using an extractor. Subsequently, the extract was diluted in saline solution at a ratio of 1:5 and placed into a 50-ml glass bottle for oral administration.

### Statement of Ethics

The authors declare that there is no ethical conflict to disclose.

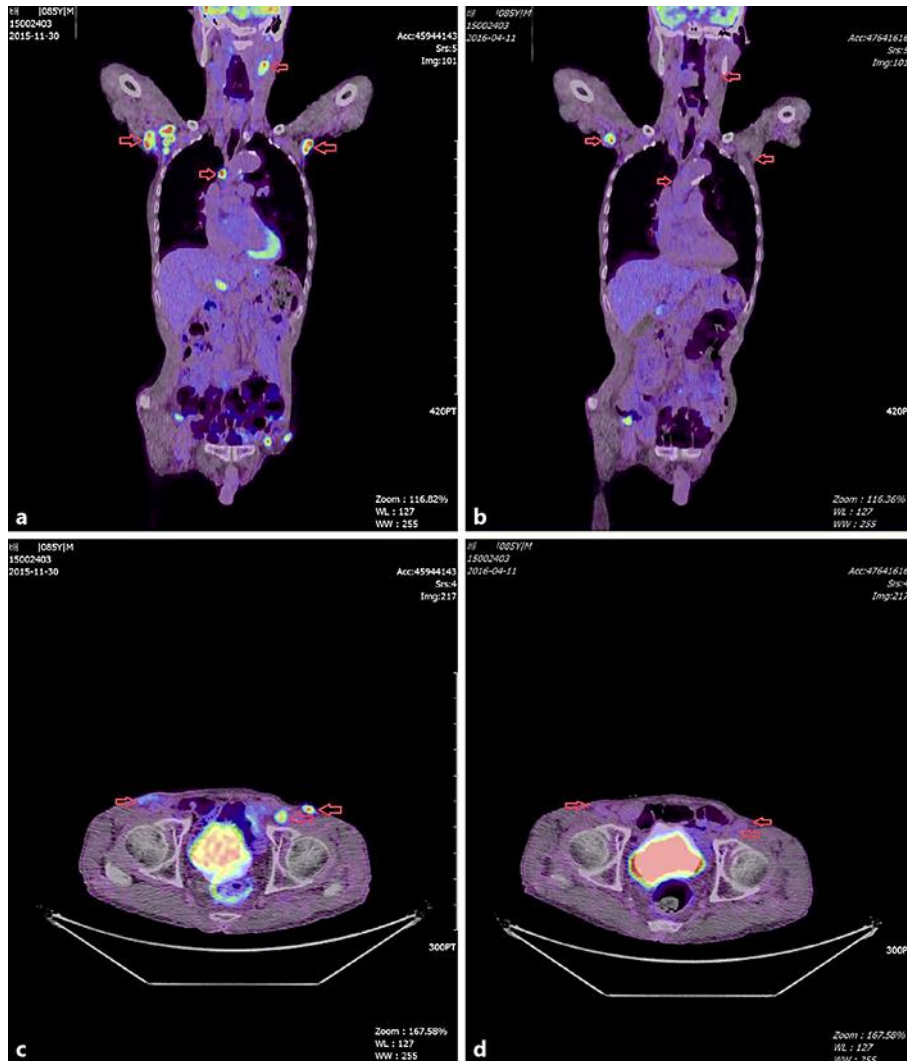
### Disclosure Statement

The authors declare that there is no conflict of interest regarding the publication of this article.

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**Fig. 1.** PET-CT scan. **a** An image of November 30, 2015. PET-CT scan of the axillary lymph node at the beginning of KMT. **b** An image of April 11, 2016. PET-CT scan of lymph node reduction in the neck and of axillary lymph node reduction after 4 months of KMT. **c** An image of November 30, 2015. PET-CT scan of the inguinal region lymph node at the beginning of KMT. **d** An image of April 11, 2016. PET-CT scan of inguinal region lymph node reduction after 4 months of KMT.



**Table 1.** Radiological image reading

PET-CT scan date	Image reading
November 30, 2015	Lymphomatous involvement of left intracarotid lesion, both cervical level II, left supra-clavicular, both axillar, both mediastinal and interlobar, common hepatic artery, aorto-caval, left iliac chain, right external iliac and inguinal lymph nodes
April 11, 2016	Residual lymphoma involvement in the right external iliac lymph node and right axillary lymph node; interval decreased metabolic activity since November 30, 2015 Disappeared/decreased activity of multiple hypermetabolic lymph node with residual hypermetabolic lymph nodes in bilateral mediastinal, hilar and interlobar lymph nodes

**Table 2.**  $\beta_2$ -Microglobulin and lactate dehydrogenase

$\beta_2$ -Microglobulin					
Dec 23, 2015	Jan 16, 2016	Feb 13, 2016	March 9, 2016	Jun 4, 2016	Jul 1, 2016
3.5 mg/L	3.1 mg/L	3.1 mg/L	3.3 mg/L	3.0 mg/L	2.7 mg/L
Lactate dehydrogenase					
Dec 23, 2015	Jan 16, 2016	Feb 13, 2016	March 9, 2016	Jun 4, 2016	Jul 1, 2016
331 U/L	288 U/L	276 U/L	350 U/L	333 U/L	296 U/L

**Table 3.** Prescription and dosage from December 25, 2015 to August 25, 2016

1st prescription	Dosage	2nd prescription	Dosage
Soramdan S	8 g twice a week	Soramdan S	8 g once a week
Hae 50	50 ml twice a week	Hae 50	50 ml once a week
Sojongdan	5 g 3 times a week	Hyunamdan	4 g q.d. (daily)
Hangamdan S	1 g p.o. b.i.d.	Hangamdan S	1 g b.i.d. (daily)
Prunellae spica pharmacopuncture	10 ml (s.q.) twice a week	Yeongoenhwan	1 g q.d. (daily)
		Prunellae spica pharmacopuncture	10 ml (s.q.) once a week

1st prescription: from December 25, 2015 to March 14, 2016. 2nd prescription: from March 15 to August 25, 2016.



**Table 4.** Prescription of Hangan-dan S

Herb	Latin botanical name	Relative amount, mg
三七	<i>Pana notoginseng radix</i>	95.2
冬蟲夏草	<i>Cordyceps miliaris</i>	71.4
山慈菇	<i>Cremastra appendiculata tuber</i>	71.4
人蔘	<i>Panax ginseng radix</i>	71.4
牛黃	<i>Calculus bovis</i>	47.6
珍珠粉	Margarita	47.6
乳香	<i>Boswellia carteri</i>	47.6
沒藥	<i>Commiphora myrrha</i>	47.6
Total amount (1 capsule)		499.8