

Case Report

## Two Cases of Endometrial Cancer Treated with Palliative Herbal Medication *Hangam-dan* (HAD)

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**Background :** Advanced-stage endometrial cancer patients show a poor prognosis because of limited success from surgery, radiotherapy or chemotherapy. Recently, the uses of complimentary and alternative medicines have gained popularity for these patients.

**Cases :** The first case is a 46-year-old patient with FIGO stage IVb endometrial cancer who had distant metastasis on her supraclavicular LNs area; the second, a 72-year-old stage Ib patient who could not be treated with surgery or chemotherapy because of chronic heart disease and her refusal of radiation therapy due to her advanced age. They remain alive and in stable condition under a strict traditional herbal medicine regiment 41 and 52 months, respectively, after diagnosis.

**Conclusion :** We present two cases of endometrial cancer patients who desire to be treated by traditional herbal medication with no further development.

**Key Words :** Endometrial cancer; complimentary and alternative medicines; herbal medication; *Hangam-dan* (HAD)

### Introduction

Endometrial carcinoma mostly occurs in postmenopausal age, and is more prevalent in developed countries as a result of the westernized lifestyle and diet. Incidence rates in Korea have also been increasing over the past decade. Surgery is one effective treatment method to support a low death rate while adjuvant therapies such as chemotherapy or radiotherapy have not yet been fully proved to improve survival rate and quality of life.

Especially in advanced stages, endometrial cancer shows a poor prognosis because surgery and other chemotherapy or radiation therapies are often not beneficial<sup>1)</sup>.

Recently, the uses of complimentary and alternative medicine (CAM) have gained popularity. Cancer patients, in particular, have shown a greater desire to explore these forms of treatment<sup>2)</sup>. We report two cases of endometrial adenocarcinoma patients treated with traditional herbal medication. Both patients showed stable disease condition after 41 and 52 months follow-up period, respectively.

### Case 1.

In Oct 2002, a 46-year-old female was diagnosed with FIGO stage IVb endometrial carcinoma and had received a total abdominal

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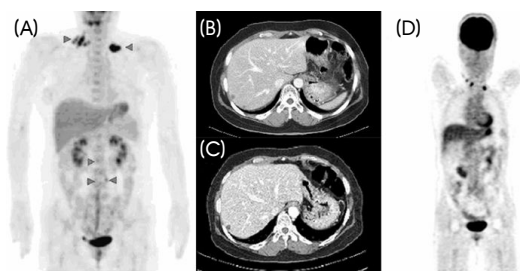
hysterectomy with bilateral salpingoophorectomy and selective pelvic/paraortic lymph nodes (LNs) dissection. Metastatic diseases were indicated in supraclavicular and paraortic LNs by positron emission tomogram (PET) (fig. 1A) and proved by biopsy. She had a complaint of palpable breast mass that was also detected as a metastatic endometrioid adenocarcinoma. She had started to receive 9 cycles of combination CAP chemotherapy, cyclophosphamide (700mg), doxorubicin (70mg) and cisplatin (70mg), from Nov 2002 to July 2003. Interval follow-ups by PET showed a partial response after 6 cycles of chemotherapy, but new liver metastases were evident in the subsequent abdominal computerized tomography (CT) scan (July 2003, fig. 1B). The patient refused to take further chemotherapy and decided to be treated instead through traditional medicinal techniques. She was treated by the guideline of wheel balance therapy (WBT) protocol in the East-West cancer centre (EWCC) at Daejeon University Oriental Medical Hospital from Oct 2003. She took *Hangam-dan* (HAD) (1,500mg/day), three times daily from Oct 2003

to Dec 2005.

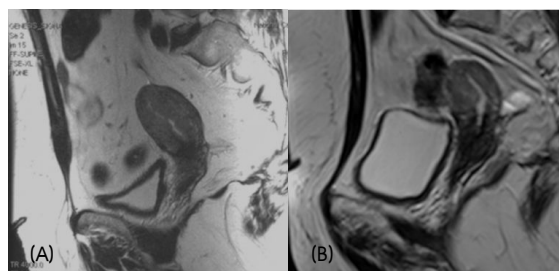
Chest and abdomino-pelvic CT scans were performed in June 2004 and showed no interval change of the liver metastasis, S7, while Lt. supraclavicular LN enlargement had decreased in size since September 2003 (fig. 1C). PET CT scan (Dec 2004) reported residual mass in Lt. lateral cervical and Rt. paratracheal LN (fig. 1D). Also, neck CT and abdominal CT (July 2005) reported small supraclavicular LNs and liver metastasis without interval change. She is alive and in stable condition at the present time (Nov 2006). After being diagnosed with metastatic liver disease, she has continued to survive for the last 41 months by adhering to a strict traditional herbal medicine regiment with partial regression (from July 2003 to Nov 2006).

## Case 2.

A 72-year-old female presented at a gynecologic clinic with vaginal bleeding. Endometrial biopsy revealed grade II adenocarcinoma with deep myometrial invasion and magnetic resonance imager (MRI) scan showed no



**Fig. 1.** Whole body PET on Nov 2002 shows metastatic lymphadenopathy in both supraclavicular LNs area & paraortic LNs (A) and two nodules newly appeared in liver S7, suspicious of liver metastases in abdominal CT on July 2003 (B). No interval change of liver metastasis, S7 in CT on June 2004 (C) and residual mass in Lt. lateral cervical and Rt. paratracheal LN in PET CT scan (Dec 2004, D).



**Fig. 2.** MRI sagittal T2WI shows endometrial carcinoma with deep myometrial invasion with no invasion to cervix on Aug 2002 (A) and no significant interval change on Jan 2005 (B).

evidence of metastatic disease in Aug 2002 (fig 2A). The patient was requested to undergo surgery but was determined to be unsuitable because preoperative electrocardiogram and echocardiography uncovered heart complications from old myocardial infarction with moderate Lt. ventricular systolic dysfunction. Radiotherapy was recommended as a substitute, but the patient and family members preferred treatment with CAM and visited EWCC on Sep 2002. The physicians of EWCC prescribed HAD (1,500mg/day) three times a day from Sep 2002 to April 2006. She was re-evaluated using MRI on Jan 2005 and there was no significant interval change since Aug 2002 (fig 2B). She is alive and in good condition at present (Nov 2006). After diagnosis with the malignant disease, she has continued to survive over the last 52 months using only traditional herbal medicines with stable condition (From Aug 2002 to Nov 2006).

## Discussion

We have treated two cases of patients with endometrial carcinoma by HAD regimen. The first case was a 46-year-old patient with stage IVb carcinoma distant metastasis to her supraclavicular and paraaortic LNs and to breast and liver. Though patients who had recurrent at distant sites generally fare poorly with local therapy, she has been stable with tolerable condition for over 40 months. The second case was a 72-year-old clinical stage Ib patient who could not be treated with surgery or radiotherapy because of chronic heart disease, age, and refusal of radiation therapy. Even though she was in the early stages of cancer, she had problems due to her age and chronic disease. Shuruti J et al. reported that the long-term outcome of endo-

metrial carcinoma patients over 63 was a significantly decreased overall survival rate and the impact of treatment related variables did not alter the age-related outcome<sup>3)</sup>. The factors that influence the survival rate of endometrial cancer patients are age, FIGO stage, grade, myometrial invasion, lymph node metastasis and peritoneal cytology<sup>1,3)</sup>. Therefore, the prognosis of these two cases was not so hopeful. In both cases, the patients chose to be treated with herbal medication. One was disappointed with her distant metastasis despite her surgery and chemotherapy while the other could not be treated with conventional therapy due to chronic heart disease.

We prescribed HAD for both cases of endometrial cancer. HAD consists of 8 herbs (botanical names, dosage per one capsule (250mg)): *Coicis Semen* 129.5mg, *Pseudoginseng Radix* 43mg, *Hippocampus* 13mg, *Cordyceps Militaris* 13mg, *Santsigu Tuber* 13mg, *Ginseng Radix* 13mg, *Bovis Calculus* 8.5mg, *Margarita* 8.5mg, and *Moschus* 8.5mg. Capsules were taken three times (500mg/time) a day after meals with no changes. HAD has antitumor, immune enhancing, antiangiogenic and antimetastatic effects *in vitro* and *vivo*<sup>4)</sup>. Especially, among constituent herbs, experimental outcomes showing antiangiogenic and immunoenhancing effects of *Cordyceps Militaris* are outstanding<sup>5)</sup>. Lee et al. also reported on 100 cancer patients including endometrial cancer treated with HAD, and concluded that HAD has antimetastatic effects via decreasing the level of b-FGF (basic fibroblast growth factor)<sup>6)</sup>. Some studies found a relationship between ER-alpha mRNA and endometrial cancer and it has also been reported that the expression of ER-alpha mRNA was

suppressed by herbal medicine<sup>7-9</sup>). We suggest that the anti-tumor effect of these herbal medicines against endometrial carcinoma might be correlated to the ER-alpha related mechanism, but further experimental studies are required.

In these case reports, we have many limitations. First, there were poor guidelines and the treatments including dosage were administered by 'experience-based prescription' from a skilled oriental medical doctor. The number of herbal medicines was too many and it was difficult to analyze the efficacies of each drug. Also, the interactions of each herb are unclear. Second, the experimental and clinical research surrounding the pre-mentioned prescription has shown poor reliability in proving anticancer effects and their mechanisms. There were no randomized controlled trials (RCTs) about the herbal prescription. Finally, there were insufficient medical records (i.e., radiological examinations, tumor markers) collected due to it being a retrospective study. Therefore, it has the original limitations of such research in its generalization.

But metastatic disease has a poor prognosis and spontaneous regression is very rare. And the quality of life (QOL) of the patients mentioned above was good and the disease free survival rate was longer than the natural history of the disease itself. The patients who have distant metastatic area show lower 3-year survival rate than local nodal disease only patients (39 % vs 93 %)<sup>1</sup>). Herbal medicines have some merits in that adverse events are rare if the skilled oriental medical doctor prescribes it by following the discipline of TOM, and it has been tested for thousand years and estimated to have significant effects to control the disease related symptoms. It is thus thought that the spectrum to help cancer

patients is broad as an adjuvant therapy. Conventional cancer treatment has many side effects and limitations to the ultimate cure for cancer and many CAM methods for cancer treatment are currently being developed. In spite of the above restrictions, these cases will provide the possibility to develop new drugs or medical protocols using natural products.

In conclusion, we experienced two endometrial cancer patients who were treated by herbal medicines and showed partial regression and stable disease respectively. We also can call them "best case series". In the future, we expect well-established experimental studies and clinical trials for the effective use of the herbal medicines based on this original case study. Although the exact triggering factor leading to regression remains unknown, this case may provide a rare opportunity for further study.

### Article Précis

We present two cases of advanced endometrial cancer treated by palliative herbal medication, *Hangam-dan* (HAD), with no progression.

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