

## A Case Report of Chemotherapy-induced Neuropathic Pain Treated with Oriental Medicine

Jung-hyo Cho, Jin-mi Kim, Jin-hee Kim, Young-seon Oh, Cheol-jung Kim<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, College of Oriental Medicine, Daejeon University

**Objective:** We present a case of chemotherapy-induced neuropathic pain with the aim of driving further study evaluating the effectiveness of Oriental medical treatment on patients with neuropathic pain.

**Method:** We prescribed *Bogijetong-tang* (BJT) two times a day and performed acupuncture and moxibustion once a day over one month of hospitalization. Laboratory tests were performed twice a month during this period. To evaluate the therapeutic effect, Total Symptom Score (TSS) or Visual Analog Score (VAS) was examined at intervals of 7 days.

**Result:** Laboratory data showed no abnormal signs compared with those of initial examination. The patient's subjective symptoms were rapidly relieved within one month. Also, the sums of TSS scores (upper limbs/lower limbs) decreased from 13.64/7.32 to 3.32/3.32 points, and VAS scores (upper limbs/lower limbs) improved from 19/10 to 6/8 points.

**Conclusion:** This case presents a possibility that Oriental medical treatment may offer potential benefits (from an approach aimed at relieving of pain) for patients with chemotherapy-induced neuropathic pain.

**Key Words :** Neuropathic pain, chemotherapy, Oriental medicine.

### Introduction

Neuropathic pain is a common side effect of frequently used chemotherapeutic agents such as cisplatin, paclitaxel and vincristine that occurs in 50% to 90% of patients treated with those agents<sup>1)</sup>. It may sometimes bring about severe and disabling pain, lower quality of life, and lead to compliance problems with cancer treatment. Recently, neuropathic pain-related mechanisms have been proposed such as local nerve injuries, sodium channels in injured axons, calcium channels in injured nerve endings, sympathetic-related pain, action of special cytokines, central inhibitory pathway deficiencies, etc.<sup>2)</sup> However, little is known

about the mechanisms of chemotherapy-induced neuropathy<sup>3)</sup>.

Currently, developments of new treatments are being attempted and various drugs are being tested for chemotherapy-induced neuropathy. However, patients' satisfaction with the control of neuropathic pain is still disappointing. In fact, there is no gold-standard treatment to control chemotherapy-induced neuropathic pain<sup>3)</sup>.

In this study, we report a case of neuropathic pain induced by chemotherapy in a 51-year-old woman with ovarian cancer. It is our aim to drive further study evaluating the effectiveness of oriental medical treatment on chemotherapy-induced neuropathic pain.

• Received : 31 August 2010

• Revised : 18 October 2010

• Accepted : 20 October 2010

• Correspondence to : Cheol-jung Kim

Dept. of Internal Medicine, College of Oriental Medicine, Daejeon University.

Tel : +82-42-229-6806, Fax : +82-42-229-0252, E-mail : choajoa@dju.ac.kr

## Case Report

A 51-year-old woman with abdominal and lower back pain was referred to our hospital in August 2009. Two years ago, stage III ovarian cancer was diagnosed and total hysterectomy, adnexectomy on both sides, proctocolectomy, cholecystectomy, and splenectomy were done at the National Cancer Center of Korea. After this wide carcinomectomy, she received chemotherapy with 6 cycles of paclitaxel and carboplatin. Since then she had been healthy and tumor-free for one year. However, distant metastasis was found in her lower posterior pelvic cavity in August 2009. The medical team of the National Cancer Center recommended restarting chemotherapy with paclitaxel and carboplatin, but she hesitated owing to her negative memories of her previous chemotherapy. She decided to receive Oriental medical treatment jointly for the purpose of relieving adverse effects and preventing recurrence.

A previous positron emission tomography - computed tomography (PET-CT) scan in September 2009 had shown a suspicious mass of peritoneal metastasis in the lower posterior pelvic cavity. Otherwise, no definite abnormal hypermetabolic lesions were observed. However, laboratory tests revealed elevation of tumor marker CA125. All other blood parameters were in normal ranges. She started 6 more cycles of chemotherapy combined with Oriental medical treatment. Fortunately, we could dispel her worries about severe complications of chemotherapy after the 1st cycle. She presented alleviation of symptoms on visit, rather than severe complications. She felt just slight dizziness, fatigue and pain in extremities. However, she complained of severe pain, burning sense, tingling and numbness of extremities after the 6th cycle. We checked frequency and intensity of pain using TSS and VAS (Table 1). We used a modified TSS scale for both limbs, because the original TSS has limitations in the

**Table 1.** Total Symptom Score (TSS): scoring system for neuropathic symptoms

Items	Symptom Frequency		Symptom Intensity	
	Absent	Slight	Moderate	Severe
	Absent	0	0	0
	Occasional	1.00	2.00	3.00
	Frequent	1.33	2.33	3.33
	(almost)Continuous	1.66	2.66	3.66
1. Stabbing pain	<input type="checkbox"/> Occasional <input type="checkbox"/> Frequent <input type="checkbox"/> (almost) Continuous		<input type="checkbox"/> Absent <input type="checkbox"/> Slight <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	
2. Burning pain	<input type="checkbox"/> Occasional <input type="checkbox"/> Frequent <input type="checkbox"/> (almost) Continuous		<input type="checkbox"/> Absent <input type="checkbox"/> Slight <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	
3. Paresthesias	<input type="checkbox"/> Occasional <input type="checkbox"/> Frequent <input type="checkbox"/> (almost) Continuous		<input type="checkbox"/> Absent <input type="checkbox"/> Slight <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	
4. Numbness	<input type="checkbox"/> Occasional <input type="checkbox"/> Frequent <input type="checkbox"/> (almost) Continuous		<input type="checkbox"/> Absent <input type="checkbox"/> Slight <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	

evaluation of lower limbs. She showed high scores in sum of TSS (13.64/7.32; upper limbs/lower limbs) and VAS (19/10; upper limbs/lower limbs). She also complained of anorexia, fatigue and abdominal discomfort. However, laboratory data showed no abnormality including CA125. So, we decided to focus on rapid pain relief in our treatment.

We first decided to give *Bogijetong-tang* (BJT; Korean pronunciation for 補氣制痛湯) twice a day for the purpose of alleviating extremity pain during the one month of hospitalization. BJT had clinically been used in Daejeon University Hospital for the treatment of patients with neuropathic pain induced by diabetes mellitus (Table 2). In a previous study, BJT showed good response for diabetes-induced neuropathic pain<sup>4)</sup>, so we expected BJT could be also effective in relieving this patient's pain. We also applied acupuncture once a day on the acupoints of Palpung (Korean pronunciation for 八風), Palsa

(Korean pronunciation for 八邪), LI-4, Liv-3, S-36 and TE-5, and moxibustion on the acupoints of H-8, K-1 and CV-12. As a rule, a follow-up of TSS and VAS at intervals of 7 days was checked. Also, laboratory tests were performed twice a month during the hospitalization period.

There were no adverse events during the hospitalization period. Laboratory data showed no aggravations compared with those of the initial examination (Table 3). Her subjective symptoms were relieved rapidly and the sum of TSS score (upper limbs/lower limbs) decreased from 13.64/7.32 to 3.32/3.32 points, and VAS score (upper limbs/lower limbs) improved from 19/10 to 6/8 points within one month (Fig. 1). The abnormal sensation had completely disappeared at two months after the finish of Oriental medical treatment. She has been living in a healthy state without any recurrence or disease progression as of August 2010.

**Table 2.** Prescription of *Bogijetong-tang* (補氣除痛湯)

Herbal name	Herbal medicine	Amount (g)
黃芪	Astragali Radix	30
人蔘	Ginseng Radix	4
當歸	Angelicae Gigantis Radix	7.5
熟地黃	Rehmanniae Radix Preparat	10
川芎	Cnidii Rhizoma	5
赤芍藥	Paeoniae Radix Rubra	7.5
丹蔘	Salviae Miltiorrhizae Radix	12
桃仁	Persicae Semen	7.5
紅花	Carthami Flos	7.5
谿血藤	Spatholobi Caulis	12
淫羊藿	Epimedii Herba	10
地龍	Lumbricus	5
葛根	Puerariae Radix	8
金毛狗脊	Cibotii Rhizoma	10
合歡皮	Albiziae Cortex	12
釣鈎藤	Uncariae Ramulus et Uncus	12
木瓜	Chaenomelis Fructus	8
牡蠣粉	Ostrae Concha	12
Total amount		180

**Table 3.** Changes of Blood Chemistry Findings in Patient

Tests	Unit	Range		20091228	20100111	20100122
		From	To			
AST	IU/L	0	40	25	22	20
ALT	IU/L	0	40	23	13	12
ALP	IU/L	30	120	66	75	72
$\gamma$ -GTP	IU/L	0	64	16	14	14
LDH	IU/L	140	271	120	153	123
Creatinine	mg/dl	0.4	1.5	0.7	0.7	0.6
BUN	mg/dl	5	24	19.8	19.2	12.9
WBC	$10^2/\mu\text{l}$	45	110	32	53	43
RBC	$10^4/\mu\text{l}$	400	600	333	359	338
Hemoglobin	g/dl	12	16	10.1	11.0	10.5
Hematocrit	%	36	46	31.0	32.7	31.2
Platelet	$10^4/\mu\text{l}$	15	45	17.9	27.5	23.0
CA125	U/ml	0	35	9.6	5.0	5.8

## Discussion

Commonly-used chemotherapeutic agents, such as cisplatin, paclitaxel and vincristine, can easily damage the peripheral nervous system. Individual symptoms are related to the type of nerve. In general, there is predominantly a sensory or sensory-motor neuropathy in chemotherapy-induced neuropathy<sup>5)</sup>. Compared with motor nerves, sensory nerves are more vulnerable to chemotherapy-associated damage. Most chemotherapeutic agents are not able to enter the well-protected central nervous system, where the cells of motor nerves sustaining important functions are located. Therefore, patients often undergo sensory symptoms such as tingling, burning sensations, or numbness<sup>6,7)</sup>. Moreover, the onset and progressive course of symptoms are variable. Some drugs may cause neuropathic pain during or immediately after chemotherapy, whereas others like platinum compounds show a delayed onset of symptoms. In some cases, symptoms show up several weeks after the last dose. Also, the degree of symptoms is related to the dose and frequency of the drug received. Patients who have experienced

neuropathic pain induced by chemotherapy in the past are at higher risk for severe and long-lasting neuropathic pain<sup>6,7)</sup>.

In the present case, the patient received carboplatin, which is a platinum compound, for 6 cycles. Her symptoms were delayed until 1 week after the last dose. Moreover, she had pre-existing peripheral neuropathy induced by the same chemotherapy agents. In this situation, symptoms can become severe and long-lasting, generally. However, she showed a rapid alleviation of symptoms and did not evidence any sequelae. The results imply that there is possibility of our treatment's positive effect rather than recovery by natural course.

It is unclear how long it takes for neuropathic pain to resolve because there have been no studies that have examined these questions<sup>8)</sup>. In general, diminishment of neuropathy may take several months. In some cases, the recovery from neuropathic pain is often incomplete or irreversible<sup>5)</sup>. Understandably, the concern with neuropathic pain induced by chemotherapy has been growing recently; various drugs are being tested to treat chemotherapy-induced neuropathy. However, data are very limited

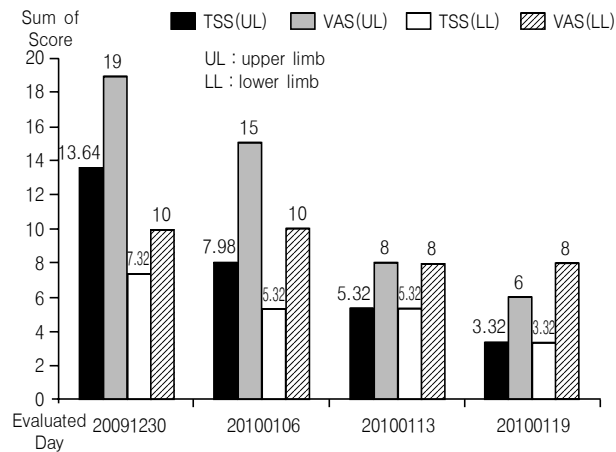


Fig. 1. Changes of TSS and VAS Score

with regard to chemotherapy-induced neuropathy.

Most drugs used in diabetic neuropathic pain are also tested with cancer patients<sup>9,10</sup>. In a previous study, we saw pain-relieving effects of BJT and acupuncture in eight patients with diabetic neuropathic pain. Though the mechanisms of chemotherapy and diabetes-induced neuropathic pain may be different, the general viewpoint of Oriental medicine about pain is the same. The point of pain relief is that if there is no free flow, there is pain; if there is free flow, there is no pain (痛則不通 通則不痛). Hence, the circulation of *ki* and blood (氣血循環) is one of the most important solutions in pain relief.

BJT is composed of herbs for promoting blood flow to remove blood stasis (活血祛瘀藥) and invigorate and replenish (補益藥). Acupuncture and moxibustion were also prescribed to enhance the circulation of *ki* and blood in the whole body or localized area<sup>4</sup>). It is presumed that circulation of *ki* and blood is helpful for regeneration of damaged nerves, although there is no evidence to confirm this hypothesis. It is essential to find the mechanism of BJT, acupuncture and moxibustion on the neuropathic pain induced by chemotherapy through further studies.

Herein we have described a case of ovarian cancer with neuropathic pain induced by chemotherapy. This case gives us some evidence that Oriental medical treatment offers potential benefits (from an approach aimed at relieving pain) for patients with neuropathic pain induced by chemotherapy.

## References

1. Armstrong T, Gilbert MR. The Female Patient: Chemotherapy-induced peripheral neuropathy. Chatham, Ob/Gyn ed. 2002; 27-30.2.
2. Ro LS, Chang KH. Neuropathic pain: mechanisms and treatments. Chang Gung Med J. 2005; 28(9):597-605.
3. Quasthoff S, Hartung HP. Chemotherapy-induced peripheral neuropathy. J Neurol. 2002; 249:9-17.
4. Kim JM, Cho CS, Kim CJ. Clinical Study of 8 Diabetic Patients with Paresthesia. J Orient Int Med. 2010; 31(2):372-379.
5. Özdogan M, Samur M, Bozcuk H, Aydin H, Çoban E, Savas B. Venlafaxine for treatment of chemotherapy-induced neuropathic pain. Turkish Journal of Cancer. 2004; 34(3):110-113.

6. Chaudhry V, Rowinsky EK, Sartorius SE, Donehower RC, Cornblath DR. Peripheral neuropathy from taxol and cisplatin combination chemotherapy: clinical and electrophysiological studies. *Ann Neurol.* 1994; 35(3):304-311.
7. Forsyth PA, Balmaceda C, Peterson K, Seidman AD, Brasher P, DeAngelis LM. Prospective study of paclitaxel-induced peripheral neuropathy with quantitative sensory testing. *J Neurooncol.* 1997; 35(1):47-53.
8. Available from URL:<http://www.cancersupportivecare.com/nervepain.php>
9. Goodnick PJ. Use of antidepressants in treatment of comorbid diabetes mellitus and depression as well as in diabetic neuropathy. *Ann Clin Psychiatry* 2001; 13:31-41.
10. Morello CM, Leckband SG, Stoner CP, Moorhouse DF, Sahagian GA. Randomized double-blind study comparing the efficacy of gabapentin with amitriptyline on diabetic peripheral neuropathy pain. *Arch Intern Med.* 1999; 159:1931-7.