

# Case report of a patient with chemotherapy-induced peripheral neuropathy treated with manual therapy (massage)

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## Abstract

**Purpose** Chemotherapy-induced peripheral neuropathy (CIPN) is a common, miserable, potentially severe, and often dose-limiting side effect of several first and second-line anti-cancer agents with little in the way of effective, acceptable treatment. Although mechanisms of damage differ, manual therapy (therapeutic massage) has effectively reduced symptoms and improved quality of life in patients with diabetic peripheral neuropathy.

**Methods** Here, we describe application of manual therapy (techniques of effleurage and petrissage) to the extremities in a patient with grade 2 CIPN subsequent to prior treatment with docetaxel and cisplatin for stage III esophageal adenocarcinoma. Superficial cutaneous temper-

ature was monitored using infrared thermistry as proxy for microvascular blood flow.

**Results** By the end of the course of manual therapy without any change in medications, CIPN symptoms were greatly reduced to grade 1, with corresponding improvement in quality of life. Improvements in superficial temperature were observed in fingers and toes.

**Conclusions** Manual therapy was associated with almost complete resolution of the tingling and numbness and pain of CIPN in this patient. Concurrently increased superficial temperature suggests improvements in CIPN symptoms may have involved changes in blood circulation. To our knowledge, this is the first report of using manual therapy for amelioration of CIPN.

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## Abbreviations

CIPN Chemotherapy-induced peripheral neuropathy  
FDA Food and Drug Administration

## Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a common, potentially severe and often dose-limiting side effect of cancer treatment that substantially impairs quality of life and can compromise continuation of treatment [1]. Little is available in the way of prevention or effective and acceptable palliation or cure [2, 3]. Incidence of CIPN varies according to agent(s) used (including platins, taxanes, epothilones, plant alkaloids, bortezomib, thalidomide), treatment scheme, and method of assessment [4–6].

Rates may be as high as 60–70% with taxanes [7, 8] and platin [9–11]; two agents frequently used as first and second-line treatment for several common malignancies. CIPN may be transient or permanent and can last for many years. Susceptibility is poorly understood but increased among patients who are malnourished, have had gastrointestinal surgery, a personal or family history of neuropathy, or active diabetes, and recent evidence suggests there may be genetic contributors [12]. Mechanisms and types of neural damage are only partially understood [13, 14]. The number of patients affected is expected to increase with use of more aggressive treatments, and as patient survival with distant metastases improves [4]. CIPN is of sufficient concern that it is a priority of National Cancer Institute's Symptom Management and Health-related Quality of Life Steering Committee [15].

At present, no FDA-approved therapeutic options exist to treat CIPN. Off-label uses of medications (e.g., steroids, antidepressants, anti-epileptics, opioids for severe pain) remain largely ineffective and/or have debilitating side effects. Several promising agents are under investigation and behavioral techniques (meditation, relaxation), physical exercise, and counseling can help in coping with symptoms, but adequate and effective treatment has not yet been established [1–3]. Given the disappointing progress with pharmacotherapeutics, interest in “alternative” approaches is increasing, particularly among patients.

Manual therapy, also called therapeutic massage, is known to reduce cancer pain and anxiety [16, 17] and has the general benefits of relaxation and stress-reduction which can be beneficial for coping with cancer treatment [18, 19]. Moreover, it can be readily implemented in clinical practice. Apart from an early study suggesting syncardial massage could reduce symptoms of diabetic neuropathy in some patients [20], the English-language medical literature on use of massage for neuropathy is scant [21, 22].

One of us (PF) previously found that manual therapy brings relief to CIPN patients in the pain clinic setting, reducing pain, tingling and impaired sensation, and returning feelings of warmth to extremities chronically cold due to CIPN. Here, we report on a patient with stage III adenocarcinoma of the distal esophagus who had grade 2 CIPN, subsequent to treatment with docetaxel and cisplatin.

### Description of case

The patient is a married 45-year-old African-American male with a 14-year history of gastroesophageal reflux. He initially presented to our cancer center with a 6-month history of epigastric discomfort and dysphagia with solids. These symptoms had progressively increased concurrent

with weight loss of more than 25 lb. Esophagogastroduodenoscopy revealed a tumor from 35 to 45 cm from the incisor, biopsy positive for adenocarcinoma. Endoscopic ultrasound revealed celiac lymphadenopathy and biopsy confirmed malignant cells. His distal esophageal adenocarcinoma was stage T3N1M1a. At the time of presentation, he was active and robust, recently retired from the navy. He had smoked cigarettes for 8 years, quitting 15 years prior to presentation. He had a long history of sleep apnea previously treated with surgery and now managed with CPAP (continuous positive airway pressure). He did not have diabetes or any known neurological condition. Family history was unremarkable except for diabetes.

During Tumor Board discussion, a multimodality approach was recommended with concurrent chemoradiation followed by surgery. After 1 cycle of induction chemotherapy with docetaxel 75 mg/m<sup>2</sup>, cisplatin 75 mg/m<sup>2</sup>, and 5-fluorouracil 750 mg/m<sup>2</sup>/day (CIV days 1–5), he developed grade 3 mucositis, and 5-fluorouracil was left out of the second and third cycles. Subsequently, he underwent an Ivor Lewis esophagectomy, with final surgical pathologic stage T0N1. Three months later, the patient resumed chemotherapy with cisplatin 35 mg/m<sup>2</sup> and docetaxel 45 mg/m<sup>2</sup> (q14days×4 cycles with Neulasta support). CT subsequently showed interval enlargement of a gastrohepatic lymph node and new left paraaortic lymph node. Biopsy from a paraaortic lymph node confirmed recurrence, and he was then treated with irinotecan, capecitabine, and oxaliplatin; chemotherapy was subsequently suspended for a hernia repair.

While on induction chemotherapy (docetaxel, cisplatin, 5-fluorouracil) the patient reported that his hands and feet, which had previously been warm to the touch, became cold with a blue color, and he developed symptoms of neuropathy. This began in his feet as tingling in the plantar surface and a tight feeling in the pads beneath the toes. His lifestyle became sedentary, in part because the tingling was not evident when he was lying down. These symptoms intensified overtime, his hands became hypersensitive and weak and he began to experience peeling of the skin and had difficulty with normal dressing and other activities of daily living. He also noted that he had difficulty keeping his body warm. He was placed on a treatment break multiple times to improve his quality of life.

After about 8 months with CIPN in all extremities (i.e., about 6 months after last chemotherapy), the patient began a 6-week course of manual therapy given in three sessions per week by two licensed massage therapists. At this time, he had grade 2 CIPN. Medications included Lortab Elixir, vitamin D, and ferrous sulfate; no new medications were added during the course of manual therapy. Treatment was administered as a combination of effleurage (stroking with a light, soothing touch) and petrissage (deep kneading and

wringing in a downward and outward motion) on each extremity. Treatment sessions began at about 9:30 AM and were conducted in a massage therapy room at 77°F (25°C) with low light and peaceful music. The patient was acclimatized to these conditions for 10–15 min, lying in a supine position on the massage table and covered with a sheet. Treatment was applied by the two therapists simultaneously, first to the lower extremities from just below the knees downward through tips of the toes, and then to the upper extremities from just below the elbows through the tips of the fingers. Each extremity received 12.5 min of massage, beginning with firm effleurage to warm the skin, followed by a deeper petrissage. After therapy was completed, the patient remained on the massage table in a relaxed state, covered with a sheet, for another 30 min. Therapists alternated sides each treatment session. The procedure was developed by the lead therapist (PF) based on his experience with diabetes-induced neuropathy and applied in this case because no evidence-based guidelines are available for CIPN.

Before each session, the patient was asked to complete the MD Anderson Symptom Inventory [23] to describe his symptoms over the past 24 h on an 11-point scale, with 0 as not present and 10 as the worst imaginable. Before the first manual therapy session, he rated his pain as 4 and numbness and tingling as 10. By the end of the treatment course, the patient's pain decreased to a zero in all extremities. Numbness decreased to a zero. Tingling decreased to a 1 (grade 1 CIPN), now being very light and only in his toes and fingers, no longer involving palms or soles. His hands and feet, which at each previous session had been cold to the touch, were now warm without any changes in dress or external temperature. Three weeks after completion of manual therapy, his CIPN symptoms were stable and unchanged since his last treatment. After a further 3 months (4 months total), symptoms remain stable in his upper extremities; he reports return of some pain in his feet but no increase in tingling or numbness. We are continuing to follow the condition of this patient.

As a proxy measure for superficial cutaneous blood circulation of the extremities, the palmar surface of the fourth fingertips and plantar surface of the tips of the great toes were monitored before and after each manual therapy session with infrared thermistry (TempTouch™ Infrared Thermometer, Diabetica Solutions, San Antonio, TX, USA). Significant changes in pre-treatment temperature over the 6-week course (measured after 10–15 min of acclimatization, just before treatment began) were observed in the hands (linear regression model, right +0.31°C per session,  $p=0.013$ ; left +0.39°C per session,  $p=0.006$ ) but not in the feet. During treatment sessions, temperature increased substantially and significantly in each extremity, lasting for at least 30 min of monitoring: mean changes were +0.96°C and +1.44°C in the hands ( $p=$

0.001 and  $p=0.008$ , right and left, respectively) and +2.27°C and +2.06°C in the feet ( $p=0.002$  and  $p=0.002$ , right and left, respectively). Total change in pre-treatment temperature from baseline to before last treatment was +8.5°C and +8.7°C in the hands and +2.1°C and +2.4°C in the feet.

## Discussion

To our knowledge, this is the first report of using manual therapy to ameliorate CIPN, and the first report of changes in superficial circulation associated with improvements in CIPN symptoms. The protocol, which was very well received by the patient, was that used by the therapist (PF) for diabetic peripheral neuropathy with similar symptom improvement.

The patient experienced mild CIPN in hands and feet fairly early in his course of anti-cancer treatment. Overtime, he reported tingling/numbness in the plantar surface, and pain/tight feeling in the bottom of the feet and especially the toes. These symptoms are classic CIPN related to both platinum and taxane toxicity. The decision for a treatment break or dose modification was not considered until functional impairment was reported. Multiple short treatment breaks yielded limited improvement in symptoms. During the course of anti-cancer treatment, CIPN progressed to grade 2 and had a major impact on his quality of life.

By the end of the 6-week course of manual therapy, the patient reported dramatic reductions in tingling and numbness in all four extremities, complete resolution of pain, and his extremities were warm for the first time since induction chemotherapy. During the past 3 months of post-therapy observation, symptoms have been stable in his upper extremities, unchanged since his last treatment. He reports return of some pain in his feet but no increase in tingling or numbness.

Although CIPN often does gradually resolve with time, it can and frequently does last for many years [1]. Based upon the stability of his symptoms prior to beginning manual therapy and their rapid improvement during the course of treatment, this is unlikely to have been a spontaneous resolution.

The mechanisms by which manual therapy may impact CIPN are not understood. Massage is reported to induce positive short and longer-term changes in circulatory measures in the extremities of type 2 diabetes, including ankle brachial index and systolic and diastolic pressures [22, 24], and to alter blood flow in treated and adjacent areas in healthy volunteers as shown by dynamic infrared thermography [25]. The changes in temperature this patient experienced in response to manual therapy were correlated with improvements in his symptoms of tingling, numbness,

and pain. While there is no known causal relationship between blood flow and CIPN symptoms, improved circulation may facilitate healing through more effective delivery of nutrients and oxygen to damaged peripheral nerves, and/or removal of residual neurotoxic compounds resulting from chemotherapy.

## Conclusion

Manual therapy, following the protocol for treating diabetic peripheral neuropathy, when administered to the extremities of this patient with CIPN was associated with greatly reduced CIPN symptoms and markedly improved quality of life. Objective evaluation of superficial cutaneous temperature suggests that reduction in symptom severity may be associated with improved local circulation. Research is needed to understand the role of manual therapy, a non-toxic, non-pharmacologic intervention, in amelioration of CIPN and to determine whether improvements in CIPN symptoms are related either directly or indirectly to changes in blood flow.

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**Conflict of interest** The authors declare that they have no financial conflicts of interest pertaining to this report other than that one coauthor is the director/president of the non-profit organization Integrative Cancer Care. The authors also declare that they have full control of all primary data, and that they agree to allow the journal to review the data if requested. Institutions and corporations involved in the work which led to the creation of this report are the Medical University of South Carolina and the Integrative Cancer Care, Charleston, SC, USA.

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