Case Report: Painful Peripheral Neuropathy Following Treatment With Docetaxel for Breast Cancer

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Peripheral neuropathy is a common side effect of many chemotherapy agents. As many as 60% of patients receiving taxane therapy report symptoms such as numbness, tingling, burning, pain, and, in severe cases, weakness in a stocking and glove pattern. These symptoms are associated with problems in physical mobility and decreased quality of life, yet few articles in the literature discuss collaborative interdisciplinary assessment and treatment of this population. This article describes the care of a patient with diabetes and docetaxel-induced, painful peripheral neuropathy by a multidisciplinary team of nurses, physicians, and physical therapists. Because nurses are often the first clinicians to recognize symptoms of chemotherapy-induced peripheral neuropathy, they provide the essential coordination of care by appropriate medical and rehabilitative services. This case also raises important questions about the relationship between diabetes mellitus and persistent, painful peripheral neuropathy.

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function can be assessed using a safety pin to test sharp sensibility or tubes of warm and cold water to assess temperature perception (Sweeney; Wilkes). Because healthcare providers do not know when peripheral neuropathy symptoms usually appear or resolve, nursing assessment should be performed at each clinic visit when patients are on treatment and during subsequent follow-up visits (Sweeney).

The Standardized Nursing Care Plan for the Patient With Peripheral Neuropathy (Barton-Burke, Wilkes, Berg, Bean, & Ingwerson, 1996) provides guidance in the assessment of symptoms associated with peripheral neuropathy as well as goals and nursing interventions to maximize patient quality of life during and after chemotherapy treatment. Interventions may include patient education regarding the consequences of diminished sensation or pharmacologic treatment of neuropathic pain. Most importantly, patients should be educated to discuss their symptoms with their healthcare providers so that symptoms may be addressed early rather than allow them to become severe and potentially irreversible.

A recent study of patients with painful, paclitaxel-induced peripheral neuropathy demonstrated quantifiable impairment of upper-extremity function (Dougherty, Cata, Cordella, Burton, & Weng, 2004). The patients with peripheral neuropathy required significantly more time to perform a grooved peg-board test, a measure of upper-extremity dexterity, when compared to control subjects. This is not surprising because large-diameter sensory nerve fibers mediate proprioception (joint position sense) and gross touch and are important for normal postural control and coordinated movements of the extremities. Although no other functional impairments have been documented in patients with taxane-induced peripheral neuropathy to date, patients with diabetic peripheral neuropathy have been shown to have problems with large-fiber nerve function, pain, balance, upper-extremity function, and quality of life (Casanova, Casanova, & Young, 1991; Galer, Gianas, & Jensen, 2000; Simonene, Ulbrecht, Derr, Becker, & Cavanagh, 1994). As with patients with diabetic peripheral neuropathy, patients with chemotherapy-induced peripheral neuropathy may benefit from a physical therapy referral so that quantitative peripheral nerve function and mobility may be assessed and treated as necessary.

Physical therapists are well trained in quantitative peripheral nerve assessment. Touch thresholds of the hands and feet can be determined using Semmes-Weinstein monofilaments, a set of 20 filaments of various stiffnesses, applied to the skin in sensory nerve patterns (Shy et al., 2003). Vibration thresholds can be determined using quantitative instruments such as the BioThesimeter® (Biomedical Instrument Company, Newbury, OH) over bony prominences in a distal to proximal manner (Bloom, Till, Sonksen, & Smith, 1984). Some therapists also are certified to perform clinical electromyographic and nerve conduction velocity testing. These instruments can be used individually or in combination with a neurologic clinical examination to monitor peripheral nerve function. In addition, physical therapists are experts in assessing physical mobility using physical performance measures and equipment such as the Balance Master® (NeuroCom International, Inc., Clackamus, OR), which assesses a patient’s ability to use vision, somatosensory, and vestibular input to control postural sway, a component of balance (Di Nardo et al., 1999).

The purpose of this case study is to describe the onset, treatment, and progression of painful peripheral neuropathy in a woman with insulin-dependent diabetes mellitus who received docetaxel for breast cancer. This study also describes the collaboration among her healthcare team, including a medical oncologist, pain physician, nurse, and physical therapist, during her treatment of chemotherapy-induced peripheral neuropathy.

**Case Report**

The patient was a 54-year-old, right-handed woman of African American descent who was treated for breast cancer. Her relevant medical history included well-controlled diabetes mellitus for 14 years, bilateral carpal tunnel syndrome that resolved four years earlier, and lumbar discectomy surgery for sciatica that resolved 21 months earlier. The patient denied any complaints of pain, numbness, or tingling in her hands or feet immediately before her treatment for cancer, suggesting that she had no overt diabetic peripheral neuropathy or other peripheral nerve pathology prior to initiation of chemotherapy. Two stereotactic core biopsies demonstrated invasive lobular and invasive ductal carcinoma. By clinical examination, her breast mass was 6 x 9 cm, and breast magnetic resonance imaging scan (MRI) showed a 5.4 x 5.7 x 8.0 cm mass and axillary lymphadenopathy. A metastatic workup that included computed tomography (CT) and bone scans was negative. Thus, the patient’s clinical stage of disease was stage III. Because of the large size of her tumor, her neoadjuvant therapy plan included four cycles of doxorubicin (60 mg/m²) and cyclophosphamide (600 mg/m²), one cycle every three weeks for a total of 12 weeks, followed by four cycles of docetaxel (100 mg/m² per cycle), one cycle every three weeks over a 12-week period. She was premedicated with low-dose dexamethasone (up to 18 mg) prior to each cycle of chemotherapy to protect her from hypersensitivity reactions. The patient reported that her glucose levels were very high (from 150–375 mg/dl) for the first three days after a chemotherapy treatment. Her glucose control would return to normal fluctuations just before her next cycle of chemotherapy. Following her neoadjuvant chemotherapy treatment, the patient underwent a bilateral breast reduction and mastopexy (breast lift) and axillary lymph node dissection. This type of surgery allowed the patient to conserve breast tissue but also allowed for clean excision of her tumor.

The patient’s symptoms and the events described in this case began at week 1, the week of her first docetaxel treatment. Three days after completing her first cycle of docetaxel, the patient reported to her nurse that she had difficulty walking, swollen feet (left foot more than right), a “raw” feeling in both feet (left more than right), and numbness and tingling in her feet. Her medical oncologist prescribed gabapentin (300 mg, once a day at bedtime [qhs]), an analgesic noted for its efficacy in treating neuropathic pain. This medication did not relieve her pain. She then was treated with antibiotics for cellulitis of the left lower extremity. This improved her symptoms but did not completely resolve them. On weeks 2–10, she received the remaining three cycles of docetaxel. Throughout this time period, her pain neither worsened nor completely resolved.

In week 16, at her presurgical appointment, the patient reported a new symptom—left sciatica pain similar to the pain she had experienced before her lumbar discectomy two years earlier. The numbness of the plantar surfaces of her feet (left more than right) also had worsened. Her symptoms were noted, and her surgery was performed as planned. Docetaxel reduced the size of the tumor by 50% (2.5 x 4 cm), and the surgeon performed a left partial mastectomy, sentinel node biopsy, axillary lymph node dissection (18 nodes removed), and right breast reduction and mastopexy to raise and reshape the right breast. The surgery went without incident, and initial recovery progressed as expected.

At week 19, the patient reported balance problems as well as increased bilateral lower-extremity pain. At the same time, her...
postsurgical breast pain was improving. At week 20, she reported that the pain in her legs and feet was severe (8–10 where 10 is most severe), present 24 hours a day, and had associated severe muscle cramping. Physical examination and MRI of the cervical, thoracic, and lumbar spine showed broad disc bulges of C5-6 and C6-7 and enhancement of paraspinal muscles at levels L3-5. The MRI was negative for a lumbar disc bulge. The patient was given oxycodone hydrochloride (20 mg twice daily [bid]), hydromorphone (6 mg as needed [PRN]), hydrocodone/acetaminophen (5 mg/500 mg PRN), and gabapentin (600 mg three times daily [tid]) with limited relief. Two weeks later, at week 22, her pain medication regimen was changed to oxycodone hydrochloride (40 mg tid), gabapentin (600 mg tid), hydrocodone/acetaminophen (5 mg/500 mg PRN), and cyclobenzaprine (10 mg tid). Her nurse recommended that she receive a physical therapy (PT) referral.

After physician orders were received, the patient was assessed initially by a physical therapist during week 22. The patient’s PT assessment, including measures of sensation, balance, pain, and physical performance, is summarized in Table 1. The patient presented with no positive cerebellar signs (such as ataxia), vestibular signs (confirmed by a negative Hall Pike test), as well as a negative CT scan of the brain (confirmed by chart review). Her strength was within normal limits with gross manual muscle testing. Her primary impairments were limited to somatosensory deficits. A chart review found that the patient had fluctuating electrolytes during and after chemotherapy treatment, but these laboratory values had stabilized at the time of her PT evaluation, thus ruling out electrolyte imbalance as the cause of her sensory deficits. PT treatment for her balance problems was postponed until the completion of radiation therapy (6040 cGy), which was scheduled in weeks 27–32. At week 35, the patient also was referred to a pain clinic and a new pain management regimen was started: methadone (10 mg tid increasing to 100 mg bid by week 37), baclofen (10 mg bid), amitriptyline (50 mg qhs increasing to 75 mg qhs by week 37), and cyclobenzaprine (10 mg PRN). The patient was reassessed by the physical therapist at week 38. Significant reduction of her pain had occurred, particularly the pain she experienced when the bedsheets brushed over her legs and feet. However, her functional skills, particularly balance, still were compromised (see Table 1).

The patient began a four-week integrative balance program consisting of 45- to 60-minute sessions twice a week with a physical therapist and a home exercise program. The balance training included static and dynamic balance activities performed in a progressively challenged multisensory environment (e.g., eyes open, eyes closed, on firm surfaces, on soft surfaces, head still, head turning). The patient progressed in stability during her participation in this program because she was able to perform more difficult tasks given to her by the physical therapist. However, the objective test scores in her assessment at week 41 revealed a decrement in her balance, upper-extremity grip, and physical performance. When questioned, the patient reported that the physician had begun to taper her methadone dose to 20 mg bid the week prior to her final PT assessment. At this time, her Pain Quality Assessment Score demonstrated that her pain was nearly as severe as the pain she had

### Table 1. Physical Therapy Assessment

<table>
<thead>
<tr>
<th>Assessment Criteria</th>
<th>Week 22 Initial</th>
<th>Week 38 Postradiation Treatment</th>
<th>Week 41 After Four-Week Balance Intervention</th>
<th>Week 60 After Five-Month Home Exercise Program</th>
<th>Values of Healthy, Age-Matched Woman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Quality Assessment Score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>104/200</td>
<td>43/200</td>
<td>81/200</td>
<td>51/200</td>
<td>0/200</td>
</tr>
<tr>
<td>Sensory Organization Test&lt;sup&gt;b&lt;/sup&gt;</td>
<td>37/100</td>
<td>77/100</td>
<td>62/100</td>
<td>76/100</td>
<td>82/100</td>
</tr>
<tr>
<td>Biothesiometer (volts)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Great toe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>17.5</td>
<td>11.5</td>
<td>20.5</td>
<td>NT</td>
<td>7.5</td>
</tr>
<tr>
<td>Left</td>
<td>28.5</td>
<td>32.5</td>
<td>38.5</td>
<td>NT</td>
<td>8.5</td>
</tr>
<tr>
<td>Lateral malleolus</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>13.0</td>
<td>13.5</td>
<td>13.0</td>
<td>NT</td>
<td>16.0</td>
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<tr>
<td>Left</td>
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<td>20.5</td>
<td>15.0</td>
<td>NT</td>
<td>15.5</td>
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<tr>
<td>First phalanx</td>
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<td></td>
<td></td>
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<tr>
<td>Right</td>
<td>5.0</td>
<td>4.5</td>
<td>3.5</td>
<td>NT</td>
<td>3.0</td>
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<tr>
<td>Left</td>
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<td>NT</td>
<td>2.5</td>
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<tr>
<td>Ulnar styloid process</td>
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<tr>
<td>Right</td>
<td>10.0</td>
<td>5.5</td>
<td>9.5</td>
<td>NT</td>
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<tr>
<td>Left</td>
<td>7.5</td>
<td>9.5</td>
<td>9.0</td>
<td>NT</td>
<td>6.0</td>
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<tr>
<td>Michigan Diabetic Neuropathy Score&lt;sup&gt;d&lt;/sup&gt;</td>
<td>26/46</td>
<td>24/46</td>
<td>23/46</td>
<td>19/46</td>
<td>2/46</td>
</tr>
<tr>
<td>Grip Strength (lb)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>54.5</td>
<td>62.5</td>
<td>53.0</td>
<td>NT</td>
<td>62.0</td>
</tr>
<tr>
<td>Left</td>
<td>59.5</td>
<td>61.5</td>
<td>55.0</td>
<td>NT</td>
<td>51.0</td>
</tr>
<tr>
<td>Timed Up and Go Test (seconds)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>6.72</td>
<td>5.97</td>
<td>6.66</td>
<td>NT</td>
<td>4.47</td>
</tr>
</tbody>
</table>

<sup>a</sup> Higher score indicates worse pain (Galer & Jensen, 1997).
<sup>b</sup> Lower score indicates worse balance (Ferd-Smith et al., 1995).
<sup>c</sup> Higher score indicates a worse vibration threshold (Bloom et al., 1984).
<sup>d</sup> Score > 6 indicates peripheral neuropathy (Feldman et al., 1994).
<sup>e</sup> Higher score indicates worse performance (Shumway-Cook et al., 2000).
experienced prior to methadone therapy. The patient was instructed to continue her home exercise program because she reported that she believed the exercises made her feel stronger.

At week 60, the patient returned for a follow-up visit with the physical therapist. She reported that she continued to be followed by her medical oncologist and her pain physician. Her medications included methadone (20 mg tid), tamoxifen (10 mg bid), and insulin (10/20/10 units), a significant decrease in the number of pain medications. She reported that she continued many of the exercises prescribed by the physical therapist, particularly the exercise in which she balanced on one lower extremity and moved a textured ball with the unweighted lower extremity (see Figure 1). She reported that the rough texture of the moving ball seemed to decrease the pain and numbness in her feet. As shown in Table 1, her Michigan Diabetic Neuropathy, pain, and balance scores each improved compared to initial values in week 22. Her balance strategies also improved. She was more reliant on an ankle strategy rather than a hip strategy to regain her balance. An ankle strategy is used by healthy adults after small balance perturbations.

**Discussion**

This patient developed a painful neuropathy in the distal aspects of her lower extremities three days after receiving her first dose of docetaxel. Her symptoms are suggestive of a systemic peripheral neuropathy secondary to taxane treatment because her symptoms presented in a stocking and glove pattern that did not follow a dermatomal or peripheral nerve pattern that is characteristic of a bulging disc or carpal tunnel syndrome. These symptoms worsened as the cumulative dose of docetaxel increased and continued well beyond the time period of chemotherapy-induced electrolyte imbalances. Although no nerve conduction studies were performed for this patient, the Michigan Diabetic Neuropathy Score and vibration testing demonstrated large-fiber peripheral nerve dysfunction that persisted at least 60 weeks after the initial docetaxel dose. Her symptoms were consistent with those documented in other clinical studies of taxane-induced peripheral neuropathy (Dougherty et al., 2004; Forsyth et al., 1997; Hilkens et al., 1996; Lipton et al., 1989; New et al., 1996).

This case suggests that women with preexisting diabetes mellitus may develop severe and persistent symptoms of peripheral neuropathy when treated with docetaxel therapy. This patient presented with early paresthesias and persistent large-fiber sensory dysfunction lasting at least 60 weeks. This is consistent with other data in which patients with preexisting peripheral nerve pathologies suffered early and severe symptoms after being treated with chemotherapy doses that normally are tolerated without debilitating side effects (Chaudhry et al., 2003).

Several mechanisms, including disruption of axonal transport, altered cytoskeletal structure, and reduced mitochondrial respiration, have been proposed to explain the signs and symptoms of taxane-induced peripheral neuropathy (Chaudhry et al., 2003; Dina et al., 2004; Polomano et al., 2004; Sahrenk et al., 1994). Which mechanism is responsible for the severe neuropathy experienced by the patient in this case is unclear; however, the rapid onset and persistence of her paresthesias implies that her symptoms may not be completely explained by disruption of microtubule-mediated axonal transport. Although the rate of axonal transport is as high as 400 mm per day (Brimijoin & Wiermaa, 1977), healthcare providers do not know whether the peripheral nerve axons in the patient’s feet may degenerate in the three days following docetaxel treatment. In addition, improved large-fiber function might be expected after completion of docetaxel therapy because disruption to axonal transport should be reversed, allowing for peripheral nerve regeneration. However, at week 60 she had minimal improvement in her Michigan Diabetic Neuropathy score, a test sensitive to large-fiber functional changes.

The patient presented in this case had primarily large-fiber somatosensory deficits, which have been associated with balance problems (Simoneau et al., 1994). Of note, pain also has been associated with decreased balance and physical performance (Dougherty et al., 2004; Menz & Lord, 2001). The patient’s grip strength, balance, and physical performance were inversely related to her pain reports throughout the progression of her PT treatment (see Table 1). Therefore, to maximize function during and after chemotherapy treatment, managing pain symptoms as well as large-fiber somatosensory impairments may be important.

Nurses are often the first to recognize chemotherapy-induced peripheral neuropathy symptoms because they see patients frequently during and after chemotherapy treatments. Moreover, nurses serve as a link between patients, physicians, and physical therapists and thereby can facilitate a multidisciplinary healthcare team to ensure that patients with cancer receive appropriate referrals. A multidisciplinary team allows each clinician to contribute his or her expertise for the betterment of the patient: nurses in symptom assessment, patient education, and pharmacologic monitoring; physical therapists in quantitative peripheral nerve assessment, physical mobility assessment, sensory reeducation, and balance training; and physicians in cancer treatment and pharmacologic management. This holistic approach may provide improved outcomes in physical function and quality of life during and after chemotherapy treatment for patients with cancer. Clinical research needs to be performed to identify the optimal assessment and intervention for chemotherapy-induced peripheral neuropathy and thus improve functional performance and quality of life for the oncology population.

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**Figure 1. Home Balance Exercise**

The patient is performing one of her home exercises in which she balances on one lower extremity while moving a textured ball forward and backward under her unweighted foot. The proprioceptive system of her left lower extremity is challenged during this activity, thereby promoting somatosensory input for balance control. The exercise also provides large-fiber somatosensory input to her right foot, potentially providing pain relief via a gate control mechanism. This exercise should be performed in a corner so that patients may use the walls to help regain their balance and therefore maintain safety.

![Home Balance Exercise Image](image-url)


**Rapid Recap**

**Case Report: Painful Peripheral Neuropathy Following Treatment With Docetaxel for Breast Cancer**

- Women with chemotherapy-induced peripheral neuropathy may benefit from collaborative assessment and treatment by a nurse, medical oncologist, pain physician, and physical therapist.
- Women with long-standing diabetes mellitus may be at an increased risk for developing a more severe and persistent painful neuropathy.
- A combination of pain management and balance retraining may be the most effective approach in treating physical mobility and balance problems.