eAppendix 1.

Studies of Differential Effects of Cancer and Chemotherapy Intervention Based on Age[a]

Study	Design and Timing of Measures	Population and Drug	Measures of PNP/Mobility or Function	Results	Conclusions/Functional Implications Relevant to This Case Report
Argyriou et al, 2006[b]	Prospective cohort with measurements at baseline, third, and sixth cycles of chemotherapy and up to 3 mo after cessation	35 patients (mean age=62.5 y, SD=7.3) without baseline PNP or systemic disease and with satisfactory liver and renal function who were about to begin 6 cycles of paclitaxel or cisplatin for NSCLCA or breast cancer were grouped by age (group 1: mean age=56.3 y, range=50–64; group 2: mean age=69.1 y, range=65–77)	Nerve function: modified PNP score of clinical symptoms and signs (cranial nerve, joint position, pinprick, vibration, strength, and DTR) and electrophysiological testing Mobility: Hughes Functional Grading Scale, with grades of 0 (healthy), 1 (fully capable of manual work), 2 (able to walk >10 m unaided), 3 (able to walk >10 m with a walker or support), 4 (bed-bound or chair-bound), and 5 (requiring artificial ventilation for at least part of the day)	Incidence and severity of CIPN were similar between the 2 age groups. CIPN occurred in 50% of the younger cohort (n=18) and was graded as mild in 16.7%, moderate in 22.2%, and severe in 11.1%. CIPN occurred in 52.9% of the older cohort (n=17) and was graded as mild in 23.5%, moderate in 17.6%, and severe in 11.8%. Distal numbness of the fingers and toes or stocking-and-glove pattern were most common, but signs extended to the knees and elbows in 2 patients in each age group. Mobility was similar between age groups and influenced by CIPN at similar rates.	CIPN incidence and severity, and subsequent functional impact, may be comparable among young-old and mid-life cohorts, but no comparison was made with those younger than 50 y, and no one older than 77 y was included. Additionally, the 6-point scale used to assess mobility may lack responsiveness to change induced by CIPN, and it appears that function after chemotherapy may have been compared between groups without consideration of baseline mobility.
Argyriou et al, 2005[c]	Prospective cohort with measurements at baseline, third, and sixth cycles of chemotherapy used to predict outcomes up to 3 mo after cessation	46 patients without baseline PNP or systemic disease who developed CIPN after treatment with 6 cycles of paclitaxel, cisplatin, or combined therapy for nonmyeloid malignancy	Nerve function: modified PNP score of clinical symptoms and signs (cranial nerve, joint position, pinprick, vibration, strength, and DTR) and electrophysiological testing	Age (20- to 55-year-old group compared with 56- to 75-year-old group) was not associated with higher severity of CIPN Worse outcome was associated with: (1) numbness/paresthesia, (2) decreased vibration perception combined with decreased DTR, and (3) decrease of sural sensory action potential >50% of baseline value	Young-old adults (age=56–75 y) may not be at risk for more severe CIPN compared with their younger counterparts; however, there is no evidence that any subsequent functional deficits would be of the same severity.
duBois et al, 1999[d]	Prospective comparison with age-matched controls Measurements taken at baseline, before every chemotherapy dose, and about 6, 12, and 18 wk after cessation	38 women aged 23–71 y (divided into 3 groups: age 23–50 y, 50–60 y, and 60–71 y) receiving paclitaxel for ovarian or metastatic breast cancer, most with prior platinum therapy but without baseline PNP or neurotoxic systemic disease. Female controls were free from neurotoxic disease.	Motor: self-report of motor function for tasks such as walking, stair climbing, buttoning; diadochokinesis Sensory: self-report of sensory symptoms, joint position sense, vibration threshold, stereognosis, 2-point discrimination Reflexes: DTR Coordination: Romberg test, walking a line for 10 steps	Age was an important risk factor for CIPN, and increasing age was associated with increasing neurotoxicity A tandem walk test was sensitive for neurotoxicity, and deviations from the line were seen only in those >50 y of age	In women with prior platinum chemotherapy, paclitaxel-related CIPN may be more likely to occur with advancing age and more severe when it does occur. Incident walking difficulty with high-level dynamic balance tasks after neurotoxic chemotherapy may be related to age.

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eAppendix 1.

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Study	Design and Timing of Measures	Population and Drug	Measures of PNP/Mobility or Function	Results	Conclusions/Functional Implications Relevant to This Case Report
Satariano et al, 1990[e]	Case-control comparison of mid-life, young-old, and older women with breast cancer; interviews conducted 3 and 12 mo after diagnosis	422 patients in the Metropolitan Detroit Cancer Surveillance System who were diagnosed 3 mo earlier were divided into 3 age groups (group 1=55–64 y, group 2=65–74 y, and group 3=75–84 y); 478 controls of the same age were compared	Self-report of difficulty with tasks requiring upper-body strength, including light lifting and pushing and lifting heavy objects	3 mo after diagnosis, age groups 1 and 2 reported more difficulty with upper-body tasks than controls, whereas little difference was seen between patients and controls of age group 3. At 1 y, age group 1 had continued difficulty only with pushing and lifting heavy objects, but group 2 had difficulty with this task and light lifting.	The permanence of functional decline after breast cancer in middle-aged to older adults may be greatest in the 65- to 74-year-old age group; however, these findings are limited to upper-body function and to self-report.

[a] PNP=peripheral neuropathy, CIPN=chemotherapy-induced peripheral neuropathy, NSCLCA=non–small cell lung cancer, DTR=deep tendon reflexes.
[b] Argyriou AA, Polychronopoulos P, Koutras A, et al. Is advanced age associated with increased incidence and severity of chemotherapy-induced peripheral neuropathy? *Support Care Cancer*. 2006;14:223–229.
[c] Argyriou AA, Polychronopoulos P, Koutras A, et al. Peripheral neuropathy induced by administration of cisplatin- and paclitaxel-based chemotherapy. Could it be predicted? *Support Care Cancer*. 2005;13:647–651.
[d] du Bois A, Schlaich M, Luck HJ, et al. Evaluation of neurotoxicity induced by paclitaxel second-line chemotherapy. *Support Care Cancer*. 1999;7:354–361.
[e] Satariano WA, Ragheb NE, Branch LG, et al. Difficulties in physical functioning reported by middle-aged and elderly women with breast cancer: a case-control comparison. *J Gerontol*. 1990;45:M3–M11.

eAppendix 2.

Studies of the Effects of Cancer and Chemotherapy on Balance, Mobility, and Function in Older Adults[a]

Study	Design and Timing of Measures	Population and Drug	Measures of PNP/ Mobility or Function	Results	Conclusions/ Functional Implications Relevant to This Case Report
Bakitas, 2007[b]	Qualitative, exploratory study; interviews conducted 3–198 mo (mean=34) since diagnosis; 18% were no longer receiving chemotherapy	28 people (mean age=59 y, range=46–81; 71% female) with CIPN after treatment for any cancer (50% breast, 21% hematologic) with any neurotoxic drug (43% paclitaxel, 25% docetaxel); recruited from a rural comprehensive cancer center	Self-report: audiotaped semistructured interview	LE pain and numbness led to problems with balance, walking (falls), driving, sports (running, hiking, biking, tennis, baseball, basketball), hobbies (gardening), and shopping. The need for canes and wheelchairs was reported, as well as holding walls and other people when walking.	Mid-life and older adults with cancer reported a number of balance and mobility problems affecting ADL, IADL, and hobbies during or after intervention with neurotoxic chemotherapy.
Wampler et al, 2007[c]	Descriptive case-control; measurements taken up to 30 d after cessation of taxane-based chemotherapy and 1 wk later for reliability; controls were measured upon enrollment	20 women (aged 30–60 y) with breast cancer who had received final taxane infusion in the past 30 d; controls were matched for age, height, and weight; participants in both groups were excluded for preexisting vestibular, visual, orthopedic, somatosensory, and neurologic disease	Nerve function: Modified Total Neuropathy Score Postural control: static using COP forceplate data in 4 positions; dynamic using NeuroCom SOT Clinical balance: TUG; FABS, including tasks such as tandem walking, unilateral stance, walking with head turns	Compared with controls, women with breast cancer who received taxane had: - Higher COP velocities, especially with occluded vision or altered vestibular input, and worse SOT equilibrium scores - Poorer FABS and TUG scores Even though the severity of CIPN was classified as "mild," results of postural control testing in the taxane group was comparable to "severe" diabetic PNP	Compared with age-matched controls, postural control and clinical balance and walking tasks were impaired in young to mid-life adult women who finished taxane chemotherapy within 30 d, although pre-taxane measurements were not taken, so the degree of decline with chemotherapy cannot be established, and preexisting subclinical neuropathy cannot be excluded. Additionally, no long-term follow-up is available to determine prognosis.
Wenzel et el, 2007[d]	Randomized phase III trial with measurements at baseline, before cycle 4, and 3 to 6 wk and 12 mo after treatment	399 women randomized to receive IV Cis/P or IV paclitaxel plus IP Cis/P for stage III ovarian cancer; ~80% were aged 41–70 y; 279 women completed 12-mo follow-up	Self-report: FACT-Neurotoxicity (scores range from 0 to 44; higher score=greater symptoms); includes questions about walking difficulty and weakness	FACT-Neurotoxicity scores were only ~3.3 before treatment and ~6 before cycle 4, but 3–6 wk after treatment worsened to ~13 and remained high (~12) 1 year later	In a sample that included mid-life to older women, neurotoxic symptoms appeared to persist 1 year after treatment has ended.

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eAppendix 2.
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Study	Design and Timing of Measures	Population and Drug	Measures of PNP/ Mobility or Function	Results	Conclusions/ Functional Implications Relevant to This Case Report
Wampler et al, 2005[e]	Single case report; measurements at initial PT evaluation (12 wk after final taxane therapy or 22 wk after first dose), before initiation of PT intervention at week 38, after 4 wk of outpatient PT at week 41, and after 5 mo of HEP at week 60	54-year-old woman with 14-y history of IDDM and with no reported pre-taxane neuropathic symptoms but onset of painful symptoms and difficulty walking after first docetaxel cycle for breast cancer; history of sciatica and severe, multifactorial pain, with pharmacological management (including opioid analgesics); found to have cervical disk bulges	Pain: PQAS Nerve function: vibration threshold with biothesiometer; Michigan Diabetic Neuropathy Score; grip strength Postural control: SOT Balance and functional mobility: TUG	Results of the PQAS, biothesiometer testing, SOT, and TUG performance at week 22 differed from published norms for women who were healthy of the same age group. Many scores improved by week 38, without PT intervention. Little additional improvement was seen after 4 weeks of outpatient PT, but the patient reported increased pain at this time point. Neuropathic symptoms persisted at least 1 y after taxane therapy.	Neuropathic symptoms may persist at least 1 y after taxane chemotherapy; however, performance on mobility measures cannot be attributed to neurotoxicity, as no pre-taxane measures are available in this case with multiple medical confounders. Results of grip strength, balance, and physical performance tests related inversely to her reports of pain over the course of PT intervention.
Visovsky and Daly, 2004[f]	Exploratory pilot study; observational cohort with measurements at baseline and at 4 and 12 wk of chemotherapy	16 participants aged 28–79 y (mean=59) without potentially neurotoxic conditions; all participants had the highest normal vibration scores before receiving C/P or IFA for malignant melanoma, ovarian cancer, or NSCLCA	Nerve function: -DTR -128-Hz tuning fork -S-W monofilaments -LE strength -Orthostatic BP Balance and mobility: -Tinetti POA of balance -Tinetti POA of gait	Tinetti ordinal scale of gait was the only measure not to change after 12 wk of chemotherapy, although nerve function declined only 3%–10% in this cohort.	Declines in balance during chemotherapy may not affect gait when measured in young to old adults who have normal baseline vibration and using a semi-quantitative and somewhat qualitative measure of gait. Conclusions are limited in this underpowered study.

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eAppendix 2.
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Study	Design and Timing of Measures	Population and Drug	Measures of PNP/ Mobility or Function	Results	Conclusions/ Functional Implications Relevant to This Case Report
Given et al, 2000[g]	Inception cohort with measurements at 6–8, 12–16, 26–30, and 52 wk after diagnosis	907 patients aged 65 y and older with newly diagnosed breast, lung, colon, or prostate cancer	Self-report of physical function: 10-item physical function subscale of the SF-36, with items such as lifting heavy objects, participating in strenuous sports, climbing stairs, walking several blocks, bathing, and dressing	Function by cancer site: those with lung cancer were more affected (scores similar to norms for people with COPD or CHF), followed by breast and colon cancer (similar to norms for HTN or acute MI), and finally prostate cancer. Function by treatment modality: radiation had little effect, except in patients with lung cancer at 6 mo; chemotherapy lowered function, except in breast cancer. At all time points: - Patients with ≥3 comorbid conditions had lower function - Men reported higher function than women	Older adults with cancer reported functional levels comparable to those of individuals with chronic disease, even 1 year after diagnosis. Lower function is most likely with lung cancer, in older women, and in those with at least 3 comorbid conditions. Function appeared to improve 6–8 points in the first year after diagnosis; however, approximately one third of those interviewed at 6–8 wk had undergone surgery in the preceding 40 d.
duBois et al, 1999[h]	Prospective comparison with age-matched controls; measurements taken at baseline, before every chemotherapy dose, and about 6, 12, and 18 wk after cessation	38 women, aged 23–71 y (divided into 3 age groups: 23–50 y, 50–60 y, and 60–71 y), who received paclitaxel for ovarian or metastatic breast cancer, most with prior platinum therapy but without baseline PNP or neurotoxic systemic disease; female controls were free from neurotoxic disease	Motor: self-report of motor function for tasks such as walking, stair climbing, and buttoning; diadochokinesis Sensory: self-report of sensory symptoms; joint position sense; vibration threshold; stereognosis; 2-point discrimination Reflexes: DTR Coordination: Romberg test; walking a line for 10 steps	24% of patients had no neurotoxicity after taxane therapy; 37% had motor symptoms (tying shoes, buttoning); 71% had paresthesia (50% incident, 16% reported grade 3 with walking difficulty), and no patient had complete resolution 18 wk after chemotherapy. A tandem walk test was sensitive for neurotoxicity, and deviations from the line were seen only in those >50 y. Recommend test panel: vibration threshold; walking the line; self-reported paresthesia; 2-point discrimination.	Symptoms of CIPN can persist at least 18 wk after chemotherapy has ended. Implications for balance and mobility are unknown. Walking the line may have floor effects as a test of CIPN for older adults with baseline mobility impairment who are still at risk for further decline.

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Study	Design and Timing of Measures	Population and Drug	Measures of PNP/ Mobility or Function	Results	Conclusions/ Functional Implications Relevant to This Case Report
Stafford and Cyr, 1997[i]	Retrospective analysis of results of the 1991 Medicare Current Beneficiary Survey	9,745 community-dwelling elderly Medicare beneficiaries; 1,647 (mean age=75.0 y, 67% female, 90% white) reported being diagnosed with cancer other than skin cancer; those without cancer (mean age=74.4 y) were 57% female and 85% white	Self-reported: -Health status -ADL and IADL	Almost 50% of those with a history of cancer reported ADL/IADL difficulty (mean=1.04 ADL limitations, 0.92 IADL limitations). Mean ADL/IADL limitations were 1.27/1.08 for those with another chronic condition such as stroke or arthritis, and 0.46/ 0.43 for those without cancer or other chronic condition. Advanced age independently predicted ADL limitations for those with and without cancer.	Cancer may have long-term effects on the ability of older adults to perform daily activities that require mobility. Greater difficulty was reported with walking, bathing, getting into or out of a chair or bed, housework, and shopping. Although these limitations are less than for older adults with other chronic conditions, they are more than twice those of people with no history of cancer or chronic conditions.

[a] PNP=peripheral neuropathy, CIPN=chemotherapy-induced peripheral neuropathy, ADL=basic activities of daily living, IADL=instrumental activities of daily living, COP=center of pressure, SOT=Sensory Organization Test, TUG=Timed "Up & Go" Test, FABS=Fullerton Advanced Balance Scale, FACT=Functional Assessment of Cancer Therapy, Cis/P=cisplatin/paclitaxel, IV=intravenous, IP=intraperitoneal, PT=physical therapy, HEP=home exercise program, IDDM=insulin-dependent diabetes mellitus, PQAS=Pain Quality Assessment Score, C/P=carboplatin/paclitaxel, IFA=interferon alfa-2b, NSCLCA=non–small cell lung cancer, DTR=deep tendon reflexes, S-W=Semmes-Weinstein, LE=lower extremity, BP=blood pressure, POA=Performance-Oriented Assessment, SF-36=36-Item Short-Form Health Survey, COPD=chronic obstructive pulmonary disease, CHF=congestive heart failure, HTN=hypertension, MI=myocardial infarction.

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[h] du Bois A, Schlaich M, Luck HJ, et al. Evaluation of neurotoxicity induced by paclitaxel second-line chemotherapy. *Support Care Cancer*. 1999;7:354–361.

[i] Stafford RS, Cyr PL. The impact of cancer on the physical function of the elderly and their utilization of health care. *Cancer*. 1997;80:1973–1980.