Peripheral neuropathy (PN) often is a side effect for patients with cancer treated with neurotoxic chemotherapeutic agents and is defined as inflammation, injury, or degeneration of the peripheral nerve fiber(s) (Wilkes, 1999). Although PN has received less attention than other symptoms and the actual incidence is unknown, researchers estimated that it occurs in 10%–20% of patients with cancer (Armstrong, Rust, & Kohlz, 1997). Having a pre-existing neuropathy or pre-existing condition known to cause neuropathy, such as HIV, diabetes mellitus, alcoholism, or vitamin deficiency (especially vitamin B), puts patients at risk for developing PN. Early symptoms of PN include tingling and numbness in the fingers and toes (stocking-glove distribution). As the condition worsens, patients may experience the loss of deep tendon reflexes, pain, impaired temperature sensation, diminished touch and position sense, and reduced muscle tone (Almadrones, 2001). Chemotherapeutic agents that can cause or exacerbate PN, particularly in higher doses, primarily are the vinca alkaloids (especially vincristine), cisplatin, and paclitaxel. The frequency of PN is increasing partly because of the wider use of high-dose chemotherapy, longer survival for many patients with cancer who experience PN as a lasting symptom, and new agents and delivery routes that target the nervous system (Almadrones). More research is needed to increase knowledge of this lesser known symptom, find better and more effective therapies, and enhance the quality of life (QOL) for these patients.

Before presenting the case study, the normal physiology of the nervous system must be reviewed. The central nervous system (CNS) and the peripheral nervous system (PNS) make up the nervous system. The CNS uses the PNS to communicate with the rest of the body. The PNS includes all nerves not found in the brain or spinal cord and consists of 31 pairs of peripheral nerves and 12 pairs of cranial nerves. The nerves of the PNS perceive pain, temperature, and sensation (Almadrones). Two types of peripheral nerves, sensory and motor, exist. The sensory nerve fibers transmit impulses from the periphery to the CNS (afferent), and the motor nerve fibers transmit impulses from the CNS to the muscles or organs (efferent). The large fiber sensory nerves control vibration and position sense, and the small fiber sensory nerves control touch, pain, and temperature. Motor nerve control movement and maintain muscle tone. Symptoms are related directly to the nerve fibers that are affected. For example, large fiber damage is associated with vibration and position sense changes whereas small fiber damage is associated with pain and temperature sensation changes. Neurotoxic chemotherapeutic agents can cause injury to the sensory and motor axons and Schwann cells and, if involved, can breakdown the myelin sheath (Wilkes, 1999). The autonomic nervous system (ANS) is part of the PNS and controls involuntary body functions, such as control of internal organs. Damage to the nerves of the ANS causes changes in the functioning of the bowel, bladder, or blood pressure, resulting in constipation, incontinence, or orthostatic hypotension (Almadrones). The cranial nerves transmit sensory and motor impulses to and from the CNS from the head and neck area. The most common cranial nerve damage caused by chemotherapy is ototoxicity. Other effects may include ocular toxicity (e.g., blurred vision, ptosis) or taste changes (Almadrones). Patients experience symptoms directly related to the portion of the PNS that is affected.

What factors place an individual at risk for developing PN? Known risk factors include having high-dose chemotherapy or cumulative doses of neurotoxic drugs; being over 60 years old; concurrently using neurotoxic drugs; having had previous radiotherapy to the spinal fields that resulted in neurologic damage; having a pre-existing neuropathy as a result of diabetes mellitus or infection with HIV or Charcot-Marie Tooth disease (a hereditary neuropathic joint disease); and being malnourished with a vitamin deficiency (e.g., B complex) (Boyle, 2000). IV chemotherapy administration or a combination of chemotherapy regimens that may increase synergistic effects (e.g., paclitaxel + carboplatin) also can create a PN risk (Boyle).

PN affects both sensory and motor nerve fibers. Early symptoms include tingling, numbness, and burning in the fingers and toes; symptoms usually are experienced bilaterally and are worse in the lower extremities. This is described as the sensation of wearing a sock or glove, referred to as “stocking-glove” distribution (see Figure 1). Later, symptoms may progress to pain and the loss of deep tendon reflexes, two-point
discrimination, and vibratory, temperature, touch, and position sense (i.e., awareness of the position of body parts without visual cues) (Almadrones, 2001; Boyle, 2000). Symptoms of autonomic neuropathy include constipation, incontinence, urinary retention, and acute abdominal distress (e.g., ileus) (Boyle). Symptoms that result from cranial nerve toxicity are directly related to the specific nerve that is affected. For example, tinnitus or hearing loss could be the result of damage to cranial nerve VIII, and blurred vision could result from damage to cranial nerve II.

Case Study

M.C. is a 49-year-old premenopausal woman with cancer in her left breast, stage II-A, T1N1M0, with one of 14 positive lymph nodes affected. She has completed four cycles of adjuvant doxorubicin and cyclophosphamide followed by four cycles of adjuvant paclitaxel after lumpectomy with axillary node dissection. Her last dose of paclitaxel was several days ago. She currently is being evaluated for a course of radiation therapy to her left breast. M.C. has no other medical problems and is on no medications. She does not drink alcohol or take drugs. She lives with her husband and teenage daughter and works full-time as an undercover agent. Her mother is alive and has insulin-dependent diabetes mellitus; her father is deceased. M.C. returns unscheduled to the clinic complaining of a vague sensation of pins and needles in her toes and feet bilaterally. She stated that the soles of her feet sometimes feel “funny” and that her symptoms are worse with prolonged walking or standing. Because her job requires her to be on her feet and is, at times, physically demanding, she is worried that these new symptoms will interfere with her job responsibilities in the future. On physical examination, she has decreased temperature sensation in her toes and feet.

Considering this scenario, answer the following questions about M.C.

1. What symptoms associated with PN are M.C. experiencing?
2. What should be included in an assessment of M.C.’s symptoms?
3. What are some of the major chemotherapeutic drugs known to cause PN?
4. What should be included in patient teaching, with particular attention to risk for injury?

Discussion

Question 1: M.C. is experiencing side effects most likely because she received paclitaxel recently. Paclitaxel is associated with symptoms of small nerve fiber damage. The sensation of pins and needles in her toes is one typical early symptom and often presents in a bilateral stocking-glove distribution. A decrease in temperature sensation in her toes and feet is consistent with this type of damage. Because paclitaxel also affects the large nerve fibers, delayed symptoms may progress to loss of muscle strength and diminished reflexes. M.C. potentially could experience a change in her functional status. Safety precautions, particularly those related to her job, may be necessary to prevent injury. This, in turn, could affect her future ability to participate in activities that require fine motor skills or meet the physical requirements of her job.

Question 2: M.C. currently is being evaluated for radiation treatment for stage II cancer in her left breast. In reviewing M.C.’s history for factors that would put her at risk for developing PN, the nurse notes that she had adjuvant chemotherapy that included four cycles of paclitaxel that was completed several days ago. Her past medical history reveals that she has no other metabolic or hereditary disorders, is not taking any medications, does not drink alcohol, and has no prior exposure to neurotoxic agents. Her physical examination reveals decreased pain and temperature sensation in her toes and feet bilaterally. To assess this decrease in sensation, the nurse used a pinprick on the skin and held hot and cold items against the skin, working distally to proximally. M.C. demonstrates normal muscle strength, and deep tendon reflexes are present. No difference in blood pressure is found when taken lying or standing. She reports no obvious change in her bowel or bladder habits, vision, hearing, or gait.

A baseline history should include questions related to the history of cancer and cancer treatment, current medications, history of presenting symptom(s), changes in activities of daily living (e.g., buttoning a shirt, tripping while walking), and past medical history of diabetes mellitus, malnutrition, or alcohol abuse (Boyle, 2000). Physical assessment of a patient who is experiencing symptoms of PN or who may be at risk for developing PN should include a review of systems. Changes in visual acuity (e.g., blurred vision), decreased hearing (e.g., tinnitus), changes in bowel (e.g., constipation) or bladder patterns, muscle weakness or falls, numbness and tingling of the hands or feet, loss of sensation (e.g., temperature, vibration, touch), or pain all are symptoms that should be assessed. Symptoms proceed in a distal to proximal fashion; therefore, assessment should begin with the fingers and toes and move proximally to detect any abnormalities on both sides. Because of the loss of temperature sensation, safety is a primary concern. Temperature sense can be evaluated by filling two test tubes, one with hot water and one with cold water, and placing them against a patient’s skin. A cold tuning fork with one or both rubberized warm with the palm also can be used to detect loss of temperature sensation. Decreased vibratory sensation often is the first sensation lost and can be tested by placing a vibrating tuning fork on a bony prominence of the ankles and knees. By moving a cotton ball or fingertip across the skin, nurses can assess a patient’s ability to sense touch. Pain can be assessed by using a pinprick and moving it from a distal to proximal direction to detect sensory changes. Asking a patient to identify a coin, key, or other object that has been placed in the palm of the hand can test fine discrimination. Vital signs can detect absent pulses and orthostatic changes. Ask the patient if he or she has noticed any change in vision, hearing, or bowel or bladder function or had any recent injuries, accidents, burns, or falls. Motor function assessment should include the evaluation of gait changes, muscle strength and tone, and reflexes. Patients are prone to wrist drop or foot drop with con-
continued drug administration as their reflex responses diminish (Almadrones, 2001; Wilkes, 1999). Through prompt recognition of symptoms, appropriate interventions, and ongoing monitoring to detect changes, nurses can promote optimal patient functioning.

Assessment of neurologic status should take place at each clinical visit when patients are on treatment and during subsequent follow-up visits, as some symptoms may be delayed in their onset. Several simple screening tools that are easy to use, time efficient, and used in clinical practice measure neurologic deficits. These tools can be used to document early changes so that a drug can be reduced or discontinued if a deficit is found. The National Cancer Institute’s common toxicity criteria are used to detect changes in sensory and motor nerves. Using a 0–4 rating scale, 0 represents no symptoms or no change whereas 4 represents paralysis or permanent loss (National Institutes of Health and National Cancer Institute, 1999). The Eastern Cooperative Oncology Group common toxicity criteria (another tool used in clinical trials) includes a section on neurologic function that grades neurosensory and neuromotor changes, as well as changes in vision, hearing, and the bowel. This scale also uses a 0–4 rating system (Oken et al., 1982). Grading of PN largely is unstandardized but these tools are commonly used. Postma and Heimans (2000) recommended using a standardized scoring system for signs and symptoms and QOL assessment. A number of general QOL instruments are available for use with patients with cancer. This combination of QOL and PN measures could provide an objective as well as subjective measure of the impact of PN on patients.

**Question 3:** Several chemotherapeutic agents, primarily vincristine, cisplatin, and paclitaxel, are known to cause peripheral neuropathies. Vincristine, a vinca alkaloid, has the greatest potential for causing neurotoxicity. Small and large nerve fibers are affected; however, small fibers are affected more severely. An early sign of vincristine toxicity is the loss of the Achilles tendon reflex. The most common symptom is paraesthesia (i.e., tingling, pins and needles, and burning) of the hands or feet. As the neuropathy progresses, motor weakness results in wrist drop or foot drop. The neuropathy usually is on both sides of the body and affects the lower extremities to a greater degree. Further motor weakness causes patients to have a broad-based stance and a slapping gait. Orthostatic hypotension or intestinal problems (e.g., constipation, abdominal colicky pain, paralytic ileus) and cranial nerve palsies (most commonly the facial nerve) with high doses also can result (Armstrong et al., 1997; Barton-Burke, Wilkes, & Ingwersen, 2001; Wilkes, 1999). Neurotoxicity can occur with a single dose (usually limited to 2 mg/wk) or with cumulative doses. Studies that use higher doses of vincristine have shown a higher rate of neurotoxicity (Weiss, 2001). The neuropathy associated with vincristine is related to the timing of the treatment and usually occurs hours or days after the treatment is completed. Cumulative doses of vinca alkaloids (e.g., vincristine) and taxanes (e.g., paclitaxel) lead to PN, especially with high-dose therapy (Fishman & Mrozek-Orlowski, 1999). Neurotoxicity occurs less frequently with vinblastine, another vinca alkaloid, except when administered in high doses (Fishman & Mrozek-Orlowski). Vinca alkaloids and taxanes also may cause jaw pain.

Cisplatin affects the large sensory nerve fibers; the loss of vibratory sense is one of the first symptoms. Neuropathy usually begins with sensations of burning, tingling, and numbness in a stocking-glove pattern, as well as hypersensitivity to pain. Decreased deep tendon reflexes progress to impair position sense. Occasionally, bowel and bladder function are affected. The extent of injury is dose-related, especially as cumulative doses approach 300–500 mg/m² (Weiss, 2001). The effect usually is delayed for weeks or months after treatment and may be brought on by Lhermitte’s sign, which is a type of lightning sensation down the spine when bending or flexing. As the neuropathy progresses, neuropathic pain may develop. Cisplatin can cause ototoxicity with tinnitus as an early symptom (Barton-Burke et al., 2001; Wilkes, 1999). Tinnitus may be reversible. Hearing loss can be permanent, especially if the patient has a pre-existing hearing impairment.

Oxaliplatin, a platinum compound, currently is being studied in clinical trials. In a phase I/II study, 27 men and women with non-small cell lung cancer were given oxaliplatin and vinorelbine to determine the dose-limiting toxicity, maximum-tolerated dose, and recommended dose for this combination. Neurologic toxicity was limited to grade 1 PN, defined as “paresthesia and/or numbness of short duration with complete recovery before the next cycle” (Monnet et al., 2001, p. 460). Neurologic toxic effects included dysesthesias (i.e., unpleasant abnormal sensations caused by touching [Monnet et al.] (96%), pharyngolaryngeal dysesthesias (63%), paresthesias (63%), and cramps (37%).

Paclitaxel primarily affects small nerve fibers and causes a decrease in pain and temperature sensation. The large fibers also are affected, which causes a loss of deep tendon reflexes, muscle strength, and fine motor movement. Symptoms begin with sensations of burning, tingling, and numbness in hands and feet in a stocking-glove pattern. PN is increased especially when administered with cisplatin, when paclitaxel is given in doses greater than 200 mg/m², when high cumulative doses are given, and in patients who have a pre-existing condition, such as diabetes mellitus or alcoholism (Wilkes, 1999). The neuropathy associated with paclitaxel is related to the timing of the treatment and usually occurs hours or days after treatment has been completed. Paclitaxel currently is being administered using different dosing schedules, and some schedules are under investigation. The intensity, severity, and duration of symptoms of PN vary with the different regimens. With weekly one-hour infusions of paclitaxel, severe neurotoxicity occurs at doses of more than 100 mg/m² (Seidman et al., 1997). Many recent studies using paclitaxel as a single agent (in different dosing schedules) have included patients with a variety of cancer types, advanced or recurrent disease, and prior treatment with a platinum-based chemotherapy regimen; therefore, these patients already are at risk for developing symptoms of PN. Less toxicity seems to be reported with docetaxel.

Other cancer treatment-related causative agents include procarbazine, etoposide, interferons, thalidomide, metronidazole, high-dose cytarabine or carboplatin, and vinorelbine (Almadrones, 2001). The susceptibility of the nervous system and the ability of a chemotherapy drug to cross the blood-brain barrier are important to the process of neurologic effect (Armstrong et al., 1997). Often, toxicities are dose-related; therefore, ongoing assessment of neurologic status is essential to reduce or prevent the loss of function. PN often is a dose-limiting toxicity of some regimens. The exact incidence is unknown; however, incidence is increasing with greater use of high-dose chemotherapy (Fishman & Mrozek-Orlowski, 1999). Overall, symptoms may be more severe and have a faster onset in patients who receive higher doses or combination therapy or who have a pre-existing neuropathy.

M.C. received eight cycles of adjuvant chemotherapy, and four of these included paclitaxel. The number of cycles of paclitaxel puts her at risk for developing neurotoxicity. Depending on the dose (particularly if high-dose therapy was given), early symptoms would include burning pain in her feet and numbness that might occur within 24 hours of administration (severity of symptoms is dose-dependent). Once the drug is discontinued, symptoms improve within months.
(Barton-Burke et al., 2001). Her last dose of paclitaxel was administered several days prior to her present clinic visit, and her symptoms are mild. M.C. can expect her symptoms to decrease over time; however, sometimes they are permanent.

Question 4: The need for effective patient and family education has increased because of changes in the healthcare system and the shift in focus to patient outcomes and costs. Treacy and Mayer (2000) suggested that oncology nurses assist their patients by providing support that corresponds with the type and amount of information in a style that meets patients’ needs, contributes to better patient outcomes, and is cost-effective. Little written information is available for patients who experience symptoms of PN. Almadrones and Arcot (1999) developed a patient-education booklet that offers strategies to manage the side effects of PN and maintain safe home and work environments. They suggested that information be included in patient education regarding the performance of daily activities that require small muscle movement and coordination. With decreased sensation in the fingers and hands, patients may have difficulty buttoning buttons, opening jars, or inserting keys in keyholes. When the feet are affected, patients may lose their sense of position while standing, walk out of their shoes, or be more prone to falls and accidents. When temperature sensation is decreased, patients may be prone to heat-related injuries (e.g., cooking or bathing burns) or cold-related injuries (e.g., frostbite).

Safety issues at home and in the work environment are a priority. Patients whose jobs require balance, climbing, or driving skills may be at increased risk for injury, not only to themselves but also to others (Almadrones & Arcot, 1999). Patients need to be told what to expect; symptoms usually are not permanent, and recovery will occur in time. Neuropathy symptoms from the vinca alkaloids (especially vincristine) may persist for up to four years after treatment is completed, but they usually diminish and become less important to patients (Weiss, 2001).

Prior to the start of chemotherapy, M.C. should be instructed about potential neurologic side effects that she might expect (written information also should be provided if it is available), when it is necessary to report a change in neurologic symptoms to her doctors and nurses, and treatment that is available to help manage symptoms. Nursing measures that will help M.C. to meet her own self-care needs include teaching her how to assess for changes in hearing, vision, or bowel, bladder, or abdominal function. In addition, M.C. and her family should be instructed on how to maintain a safe environment both at home and at work. They should be taught to avoid extreme temperatures (e.g., check water temperature in the home, use gloves when washing dishes, use potholders, wear socks and gloves when appropriate), check for adequate lighting (e.g., turn on lights when entering a room), ensure that the environment is free of unnecessary clutter (e.g., remove throw rugs, wipe up spills when they happen, provide safety handles and skid-free mats in the shower), and discuss driving skills (e.g., ability to feel gas and brake pedals and the steering wheel) (Almadrones, 2001). M.C. may need to evaluate the physical aspects of her job should her symptoms interfere with her duties. Because her job requires a certain amount of physical activity, she may need to modify her activities as her symptoms worsen with prolonged walking or standing.

Summary

PN is a troublesome symptom that frequently occurs in patients with cancer and is associated with certain neurotoxic chemotherapeutic agents. By understanding the basic principles of PN and recognizing the potential toxicities of specific chemotherapy drugs, nurses can take an active role in minimizing their occurrence. Nursing assessment is critical to early identification of toxicities and successful intervention. Nurses need to educate their patients regarding potential drug side effects and review safety issues that may put them at risk for injury. Patients need to be instructed to report symptoms of PN to their nurses and physicians. Healthcare professionals, in turn, need to assess neurologic function on a routine basis, monitor those at risk, and intervene when appropriate. Ultimately, PN can be recognized as a significant symptom, such as pain or fatigue.

Current treatment options include both pharmacologic and nonpharmacologic therapies, and the success of the treatment often depends on the cause. Research is needed to find better and more effective therapies for PN.

The Neuropathy Association is a national organization that offers patients with PN the chance to contact others to share experiences and information to help them to cope with symptoms, increase public awareness of the problem, and promote the development of better therapies. This organization provides a newsletter, information booklets, and activities for members and can be contacted at 800-247-6968 or www.neuropathy.org.

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References


