SECOND ISSUE IN THE 2013 SERIES

SECOND ANNUAL

CONQUERING THE CANCER CARE CONTINUUM™

Introduction to Oncology Pain Management

Lillie D. Shockney, RN, BS, MAS

In part 2 of our *Conquering the Cancer Care Continuum* series, the focus is on pain management. Despite dramatic improvements in pharmaceutical agents, as well as surgical procedures designed to help control pain, we still have a long way to go to be successful on behalf of our patients.

Lillie D. Shockney, RN, BS, MAS

I was recently watching a few minutes of an old, black-and-white western movie. A cowboy had been shot by a gunslinger, and as the town doctor attempted to remove the bullet from his chest, another cowboy gave the wounded man a bottle of whiskey to drink and a knife to bite between his teeth. I'm sure back in the day this was how people coped with pain – liquor to numb them and something hard to bite on. This is far from ideal.

Today all patients who enter a hospital environment, whether it be an inpatient unit or a clinic visit with their doctor, are asked to complete a pain measurement tool that provides some expression of whether they are presently in pain, and to what degree. Patients have trouble, however, interpreting what to circle (a happy face or a very sad face) if their pain was bad in the morning but not so bad now because they took a pain pill before coming to see the doctor. Furthermore, is this information actually reviewed by anyone during their visit? Sometimes it is, and sometimes it is not.

Certainly one of the greatest fears expressed by cancer patients is the fear of pain and suffering and the inability to overcome it effectively, fearing they will die while in great pain. Family members, too, commonly respond that their greatest fear is having to witness their loved one in great pain without a way to ease the suffering. Family members fear these will be the final images they witness before their loved one dies.

Many organizations have developed measurement tools and practice guidelines for the purpose of helping providers effectively manage pain associated with cancer and its treatment. The following articles provide you with a wealth of information associated with these tools and guidelines. They also promote that thoughtful care be taken to ensure that all of us address with our cancer patients the pain they are experiencing and implement ways to relieve it. Pain steals away social time, psychological well-being, and physical endurance and can make quality of life virtually absent for some patients. Accurate assessment and adequate treatment for effective pain management need to be priorities for all of us working in the cancer field.

I feel confident you will find these articles thought provoking and containing valuable information that will assist you in reassessing your current patients as well as developing more effective ways to help your future patients have quality of life by having pain effectively managed. ■

Classifying and Managing Pain in the Oncology Patient

Beth Faiman, PhD(c), MSN, APRN-BC, AOCN
Cleveland Clinic Taussig Cancer Institute, Cleveland, Ohio

Mrs S is a 58-year-old female who presented to the nurse practitioner complaining of fatigue and mid-thoracic back pain that had become worse in the last few weeks. She works full time as a fourth-grade teacher and cares for her 3 grandchildren every weekend while her daughter works. The youngest grandchild is 18 months old. Initially, Mrs S attributed the fatigue and back pain to "long hours and not enough rest," or that she may have "pulled a muscle" when lifting the grandchildren. Now Mrs S rates her back pain a "9/10," with 10 being the worst pain imaginable, with intermittent "shooting" pains down her right leg. She has no other complaints except for insomnia as a result of the pain. She recalls no trauma. She has no additional health concerns except for controlled, mildly elevated blood pressure over the past 3 years. She takes Norvasc 5 mg po daily but is on no other medications.

Beth Faiman, PhD(c), MSN, APRN-BC, AOCN

On physical examination, Mrs S had point tenderness to her lower thoracic spine on palpation. She had no weakness in her legs, and results from a neurologic examination of the upper and lower extremities were normal. A chemistry panel and complete blood count (CBC) were ordered, as well as a urinalysis to rule out a urinary tract infection as the source of her back pain.

Chronic pain develops over a longer period. Chronic pain can occur following an initial pain-provoking event such as tumor invasion.

The CBC revealed anemia with hemoglobin 9.8 g/dL (range, 12-15 g/dL). Serum creatinine was 1.2 mg/dL (range, 0.5-1.4 mg/dL), and serum calcium was 11.1 g/dL (range, 8.5-10.2 g/dL). An x-ray revealed compression fractures at T9 and T10 vertebral bodies. Magnetic resonance imaging (MRI) of the thoracic and lumbar spine was planned as she was admitted to the hospital for pain control, evaluation, and management of her hypercalcemia.

Overview of Oncology Pain

Part 2 of the *Conquering the Cancer Care Continuum* series on Palliation in Cancer Care focuses on pain management in oncology. Cancer pain remains a commonly feared yet widely undertreated aspect of cancer.[1] Many definitions of cancer pain exist, including one from the Committee on Taxonomy of the International Association for the Study of Pain, in which pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." The National Comprehensive Cancer Network, World Health Organization (WHO), and several other organizations have logical and systematic ways to diagnose, monitor, and treat cancer pain.[2,3] Each entity agrees that cancer pain must be promptly diagnosed for appropriate and rapid intervention. Thus, the importance of diagnosis and practical recommendations will be reviewed as they relate to our case study.

The Etiology of Oncology Pain Is Important

The therapeutic intervention to control cancer pain can only occur after the pain is appropriately classified. Cancer pain can manifest itself as acute or chronic in nature. The onset of acute pain occurs within a relatively short time and is often the result of a traumatic event. Chronic pain develops over a longer period.[2] Chronic pain can occur following an initial pain-provoking event such as tumor invasion. Regardless of time and etiology, inadequate pain management remains prevalent, costly, and harmful to patients with cancer.[4]

Cancer pain can be categorized as nociceptive or neuropathic. *Nociceptive* pain occurs as a result of ongoing damage or tissue destruction to the somatic and visceral structures. Thermal, mechanical, or chemical processes lead to damaged pain receptors in the skin, muscles, and connective tissues. Nociceptive pain can be acute or chronic. *Neuropathic* pain results after damage to the nerve fibers that arise from the central and peripheral nervous systems.[5] Neuropathic pain

Table 1. Assessment of Cancer-Related Pain: the Pain History

Key Pain-Related Concept	Questions for the Patient and/or Caregiver
Location	Where is the pain located?
Intensity	How is the pain rated on a scale?
Quality	Is it sharp or dull; does it radiate or move around?
Duration	How long has the pain been bothering you or limiting your activities?
Aggravating/alleviating factors	What makes the pain worse or better (eg, does lying down help; does moving or sitting relieve the pain)?
Trauma	Was there any one traumatic event or any specific incident that provoked the pain (eg, cough, sneeze, falling down)?

can cause a variety of sensations from numbness and tingling to shooting and/or burning.[1,2] The treatments of nociceptive and neuropathic pain differ as adjunct medications can be more useful in neuropathic pain control that addresses the nerve damage. Therefore, incorrect diagnosis of the etiology of pain can lead to inadequate pain control.

Assessment of Cancer Pain: History and Physical Examination

Appropriate assessment of the individual's cancer-related pain can lead to prompt diagnosis, treatment, and improved quality of life. A thorough evaluation of pain begins with taking a pain history. The pain history guides the clinician toward the etiology of the pain. Key considerations when assessing pain are shown in **Table 1**.

Once the clinician obtains a thorough pain history, a physical examination is then performed. Attention to physical examination findings is critical to provide clues to the etiology of pain. Key components of the physical examination include locating the site of pain, examining the area, and performing a neurologic assessment. In our case study, mid-thoracic back pain was the major complaint. Therefore, percussion of the spine and localization of the pain provided the opportunity to order the appropriate radiologic imaging.

For all individuals with back pain, it is also imperative to determine if signs of spinal cord compression (SCC) are present. These include weakness in the lower extremities, hyperreflexia, falls, incontinence, or loss of sphincter tone. If SCC is suspected on neurologic examination or based on clinical history, further imaging is required to rule out this oncologic emergency because SCC can lead to paralysis.

Laboratory and Radiologic Assessment of Pain

Following the history and physical examination, the clinician considers laboratory and radiologic testing to further elucidate the etiology of the pain. A chemistry panel with serum calcium, alkaline phosphatase, and serum creatinine identifies if hypercalcemia of malignancy and associated renal dysfunction are present. Specific bone and disease markers appropriate to the cancer type can confirm disease progression if a known cancer diagnosis exists. A CBC with differential will identify anemia, thrombocytopenia, or neutropenia. Abnormal CBC findings may suggest tumor invasion within the bone marrow microenvironment.[6,7]

Metastatic cancer cells produce inflammatory cytokines that lead to osteolysis or bone pain. Treating the cancer itself can lead to a reduction in pain.[8,9] In patients with suspected fracture or bone metastasis as the source of cancer pain, radiographic films of the painful area will, in many cases, identify if bone destruction has occurred. Patients with breast or prostate cancer can undergo a technetium bone scan to identify if widespread tumor destruction is present. Patients with multiple myeloma should receive a bone survey. The bone survey includes radiographic images of the skull, long bones, and spine and will identify lytic lesions. However, bone scans will fail to identify lytic lesions due to the pathobiology of the plasma cell tumor.[10] It is important to note that a 30% to 40% bone loss is required before bone lesions are visible on plain x-ray films.[11]

Patients may undergo the above imaging, and the cause of the pain may still not be identified. These individuals may benefit from more sophisticated imaging techniques, which include MRI, computed tomog-

raphy (CT), and/or positron emission tomography (PET) scans. The benefit of MRI and/or CT scans of the painful area is that the clinician can visualize images within a short period, and they are more sensitive than x-rays to determine if damage to the bones or tissues has occurred. However, the MRI and CT scans are limited by not being able to detect lesions or tumors until the structural changes in the tissue are large enough to be detected. A PET scan can be used in a variety of cancers and is capable of detecting cellular and/or molecular changes that precede structural abnormalities. A limitation of the PET scan is that areas of inflammation and physiologic activity can make it unclear whether cancer is causing the pain.[12]

A PET scan can be used in a variety of cancers and is capable of detecting cellular and/or molecular changes that precede structural abnormalities.

Even with the most sophisticated radiologic techniques, there are some individuals with cancer in whom the cause of pain cannot be reliably identified. Therefore, the clinician needs to correlate the information gained from radiologic imaging with clinical examination and laboratory findings to determine the cause of pain.

Additional Types of Oncology Pain

It has been discussed in this article that patients with cancer may experience pain as a result of the diagnosis (such as pain from nerve root compression or tumor), or the treatment itself (damage to the skin from radiation or surgery). It is essential for clinicians to further identify the etiology of cancer pain so treatment can be tailored to the individual. A common type of nociceptive pain is called incident or "functional" pain that usually occurs with voluntary movement. Incident pain is the classic type of pain that occurs as a result of skeletal metastases, but it can be involuntary as a result of a cough or sneeze. Incident pain is difficult to control in patients with cancer because a steady level of opioid medication is required to treat the peaks of pain that occur when patients are moving around performing activities of daily living.

Breakthrough pain occurs when the pain becomes unpredictably worse and requires medication to obtain relief. In patients taking long-acting opioids, additional pain medication is unpredictably required between scheduled doses of medication. In contrast, "end-of-dose failure" is a predictable occurrence of pain in which the pain recurs before the next dose of medication is due.[1]

The key to treating incident, breakthrough, and end-of-dose pain is to treat the underlying cause of the pain as effectively as possible. Palliative radiation, chemotherapy to control the disease, or adjunct medications if nerves are involved may be warranted.

Recommendations for the Management of Cancer Pain

Analgesic agents are essential to the management of cancer pain. In an effort to identify guidelines to improve the practice of pain management, the WHO developed the analgesic ladder in 1986. The 3-step cancer pain relief ladder suggests a stepwise approach to cancer pain. This includes non-opioid drugs for the first step, mild opioids either with or without non-opioids for the second step, and more potent opioid analgesics for the third step. The guidelines are reasonable but not prescriptive or all inclusive for patients.[1,13]

Nociceptive and non-nociceptive types of pain can, in most cases, be appropriately managed by a combination of pharmacologic and nonpharmacologic or adjunct therapies. Mild nociceptive pain is often controlled with acetaminophen and/or narcotic and nonnarcotic pain medications. Opioid analgesics are required to control patients with higher pain scores. A list of commonly used medications can be found in **Table 2**.

Adjunct agents are also used. These include neuroleptic drugs (eg, gabapentin or pregabalin) and antidepressants (eg, duloxetine or sertraline). Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen can be used in patients with bone pain. However, NSAIDs should be used cautiously in patients with kidney disease and elevated serum creatinine levels. In patients whose pain is not the result of tumor invasion but is musculoskeletal, physical therapy or acupuncture techniques can be used.[2]

Supportive Care: Bone Metastasis

In patients with cancer that has metastasized to the bone, bisphosphonates and monoclonal antibodies should be used. Bisphosphonates are potent inhibitors of bone resorption and are effective in decreasing pain related to metastatic cancer as well as improving bone quality over time once disease control has been achieved. While the optimal duration of therapy is unknown, in the setting of adequate renal function, monthly bisphosphonates such as pamidronate or zoledronic acid may decrease the risk of skeletal-related events.[11]

Table 2. Commonly Used Analgesic Agents for the Management of Pain

Analgesic Class	Indication	Notes
Acetaminophen	Mild pain relief	Caution in liver disease.
Nonsteroidal anti-inflamatory drugs (ibuprofen, naproxen sodium) Celecoxib (selective COX-2 inhibitor)	Mild pain relief	Caution in kidney disease.
Opioids (morphine, hydromorphone, oxycodone, oxymorphone, methadone, fentanyl, meperidine)	Moderate-to-severe pain relief	Recommend a bowel regimen as these medications can be constipating. Consider kidney and organ function when prescribing. Meperidine is not recommended for long-term pain control.
Anticonvulsants (gabapentin, pregabalin, amitriptyline)	Neuropathic pain	Relatively safe; gabapentin dose should be titrated.
Antidepressants (duloxetine, sertraline)	Adjunct to nociceptive or neuropathic pain	Patients should be screened for suicidal thoughts and counseled prior to starting antidepressants.
Corticosteroids (dexamethasone, prednisone, methylprednisolone)	Nociceptive or neuropathic pain control	Side effects may include insomnia, mood swings, and hyperglycemia and should be monitored.

Sources:
National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines)*. Guidelines for Pain Management. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed February 23, 2013.
Eisenberg E, Marinangeli F, Birkhahn J, et al. Time to modify the WHO analgesic ladder? *IASP Pain Clinical Updates*. December 2005;13(5):1-4. http://enews.iasp-pain.org/AM/Template.cfm?Section=February_2013&SECTION=Pain_Clinical_Updates1,Pain_Clinical_Updates1&TEMPLATE=/TaggedPage/TaggedPageDisplay.cfm&CONTENTID=3810&THISPAGE=2&TPLID=24&TPPID=87. Accessed January 18, 2013.
World Health Organization. WHO's pain ladder. http://www.who.int/cancer/palliative/painladder/en/. Accessed February 16, 2013.

Denosumab is a high-affinity monoclonal antibody approved for the treatment of osteoporosis in postmenopausal women and for the treatment of skeletal metastases in breast and prostate cancer. Denosumab works most notably as a receptor activator of nuclear factor κB ligand (RANKL) inhibitor. Stimulation of osteoclasts (responsible for bone breakdown) and osteoblasts (responsible for bone repair) is controlled in part by the balance between the osteoprotegerin (OPG), RANKL, and RANK (receptor activator of nuclear factor κB) triad. RANKL binds to the RANK receptor found on the surface of osteoclasts. Binding of RANKL results in stimulation of osteoclast activity and leads to bone breakdown. OPG is a decoy receptor produced by osteoblasts. OPG inhibits osteoclastogenesis by binding to RANKL, which inactivates RANKL. RANKL is the key mediator of osteoclastogenesis. Therefore, administering a monoclonal antibody such as denosumab blocks RANKL activity.[14]

Palliative radiation is administered to tumors with the goal of local pain control. Individuals with bulky abdominal tumors or bone tumors can experience pain relief with single or fractionated doses of radiation. In patients with hematologic malignancies, it is important to spare the bone marrow repeated doses of radiation and treat the disease systemically if possible.

Surgical intervention might be warranted in patients with metastatic cancer. However, the risk-benefit ratio must be considered, depending on how invasive the surgery is. Cancer type, prognosis, general health, and functioning of the individual must be taken into consideration. Debulking of a large tumor

followed by radiation or systemic chemotherapy has been shown to improve disease control and quality of life in patients with certain cancers and can be considered on a case-by-case basis.[15]

When possible, minimally invasive surgeries are recommended, especially if vertebral compression fractures (VCFs) are the source of cancer pain, such as in the case study. Two such procedures are balloon kyphoplasty (BKP) and vertebroplasty. Both are minimally invasive outpatient techniques that form an internal "cast" in the collapsed vertebral body. The goals of the BKP procedure are to reduce the fracture and form an internal cast, and height restoration. In BKP, a bone tamp is used to inflate a balloon and create a cavity for cement to flow. The balloon is deflated but the cavity remains. Under fluoroscopy, cement called polymethylmethacrylate is injected into the collapsed vertebral body. Vertebral height is restored to some degree, and pain is decreased. With the vertebroplasty technique, thinner cement is injected into the collapsed vertebral body using a needle. While height cannot be restored, pain relief is obtained with the procedure.[16]

In the recent randomized Cancer Patient Fracture Evaluation (CAFE) study, patients with painful VCFs were randomized to receive the BKP procedure or to nonsurgical management. In patients with cancer, BKP was shown to be an effective treatment that rapidly reduces pain and improves function. BKP provided better results than nonsurgical management at 1 month in measures of pain, back function, quality of life, activity, bed rest, and analgesic use, suggesting that an early intervention is better than a delayed procedure.[17]

Case Study Outcome

Mrs S was diagnosed with metastatic breast cancer. She was given pamidronate 90 mg IV piggyback for hypercalcemia of malignancy and started on morphine 2 to 4 mg IV every 3 hours as needed for pain control via a patient-controlled analgesia pump on day 1 of hospital admission. She began gabapentin to treat the shooting neuropathic pain. However, her back pain persisted and was thought secondary to the vertebral compression fractures at T9 and T10. To treat her painful VCFs, the BKP procedure was performed to the T9 and T10 vertebral bodies and resulted in pain relief by day 4. The clinician calculated the 24-hour dose of IV morphine to a long-acting morphine sulfate continuous release (morphine CR 15 mg po every 12 hours) on day 5. Her pain was adequately controlled, but she was given a prescription for short-acting morphine for breakthrough pain management. A bowel regimen was reviewed to prevent constipation. She was discharged to home on day 6 pain free.

Conclusion

Pain can be a devastating but unnecessary consequence of cancer. Pain as it relates to cancer can also be a complex phenomenon and provide a sequelae of symptoms based on the pathophysiology of the disease. Treatment of cancer pain requires the appropriate diagnosis and management, as well as the expertise of many disciplines, with the overarching goal of controlling the disease and improving quality of life. ■

References

1. Aiello-Laws L, Reynolds J, Deizer N, et al. Putting evidence into practice: what are the pharmacologic interventions for nociceptive and neuropathic cancer pain in adults? *Clin J Oncol Nurs*. 2009;13:649-655.

2. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Multiple Myeloma*. Version 1.2013. www.nccn.org/professionals/physician_gls/f_guidelines.asp#site. Accessed February 15, 2013.

3. World Health Organization. Pharmacovigilance. www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/index.html. Accessed February 15, 2013.

4. Sarzi-Puttini P, Vellucci R, Zuccaro SM, et al. The appropriate treatment of chronic pain. *Clin Drug Investig*. 2012;32(suppl 1):21-33.

5. Rayment C, Hjermstad MJ, Aass N, et al. Neuropathic cancer pain: prevalence, severity, analgesics and impact from the European Palliative Care Research Collaborative – Computerised Symptom Assessment study [published online ahead of print November 21, 2012]. *Palliat Med*.

6. Riccio A, Wodajo F, Malawer M. Metastatic carcinoma of the long bones. *Am Fam Physician*. 2007;76:1489-1494.

7. Morgans AK, Smith MR. Bone-targeted agents: preventing skeletal complications in prostate cancer. *Urol Clin North Am*. 2012;39:533-546.

8. Lipton A, Uzzo R, Amato RJ, et al. The science and practice of bone health in oncology: managing bone loss and metastasis in patients with solid tumors. *J Natl Compr Canc Netw*. 2009;7(suppl 7):1-29.

9. Raje N, Roodman GD. Advances in the biology and treatment of bone disease in multiple myeloma. *Clin Cancer Res*. 2011;17:1278-1286.

10. Roodman GD. Mechanisms of bone metastasis. *N Engl J Med*. 2004;350:1655-1664.

11. Van Poznak CH, Temin S, Yee GC, et al. American Society of Clinical Oncology executive summary of the clinical practice guideline update on the role of bone-modifying agents in metastatic breast cancer. *J Clin Oncol*. 2011;29:1221-1227.

12. Debergh I, Vanhove C, Ceelen W. Innovation in cancer imaging. *Eur Surg Res*. 2012;48:121-130.

13. Gordon DB, Dahl JL, Miaskowski C, et al. American Pain Society recommendations for improving the quality of acute and cancer pain management: American Pain Society Quality of Care Task Force. *Arch Intern Med*. 2005;165:1574-1580.

14. Henry DH, Costa L, Goldwasser F, et al. Randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma. *J Clin Oncol*. 2011;29:1125-1132.

15. Yu HH, Tsai YY, Hoffe SE. Overview of diagnosis and management of metastatic disease to bone. *Cancer Control*. 2012;19:84-91.

16. Hussein MA, Vrionis FD, Allison R, et al. The role of vertebral augmentation in multiple myeloma: International Myeloma Working Group Consensus Statement. *Leukemia*. 2008;22:1479-1484.

17. Berenson J, Pflugmacher R, Jarzem P, et al. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. *Lancet Oncol*. 2011;12:225-235.

Clinical Decision Making in Assessing and Treating Cancer Pain

Steve Stricker, PharmD, MS, BCOP

JB is a 57-year-old male who presents to the emergency department complaining of acute left-sided chest pain (8/10 on a numeric pain scale) that has been ongoing for approximately 48 hours following a fall at home. He has taken ibuprofen and acetaminophen with no relief. Chest x-ray reveals 3 fractured ribs, and laboratory evaluation is suspicious for multiple myeloma (MM). This diagnosis is later confirmed following bone marrow biopsy, serum protein electrophoresis, and comprehensive laboratory analysis.

Steve Stricker, PharmD, MS, BCOP

Like JB, patients with MM often initially present to medical attention with pathologic fractures due to the presence of widespread osteolytic bone lesions. While the attention of hematology/oncology providers frequently focuses on the diagnosis and management of the patient's MM, palliation of pain symptoms is a critical concern related to the patient's quality of life over the short term that must be addressed as quickly as possible, usually prior to the initiation of chemotherapy. Over the natural course of the disease, MM patients often become idealized cases for teaching cancer pain management as many require opioids for acute pain, the use of bisphosphonates in the adjuvant setting for the relief of bone pain and the prevention of skeletal-related events, and management of treatment-induced neuropathic pain resulting from the use of immunomodulatory drugs such as thalidomide or proteasome inhibitors such as bortezomib. As an oncology pharmacist, I am often consulted to make recommendations for the management of the complex and ever-changing pain symptoms that this population experiences. As we assess the needs of the model patient described above, let us also evaluate the management of cancer-related pain in general, focusing on selection of the best medication management and the application of clinical practice guidelines.

Acute Pain Management

Pain associated with cancer is one of the chief complaints of patients, affecting their quality of life. It has been estimated that as many as 50% of all cancer patients experience pain during treatment. Pain is more commonly associated with metastatic disease and end-of-life scenarios, yet it frequently requires medical intervention even in patients with early-stage disease treated with curative intent.[1,2] For patients with acute pain management needs, the World Health Organization (WHO) algorithm has historically served as a reference for initiating therapy. Utilizing a strategy by which pain management is escalated based on the patient's self-report of pain intensity, objective physical assessment, and the patient's history of opioid and non-opioid drug therapy, this algorithm attempts to appropriately tailor the selection of initial analgesic medication in an individualized manner.[3] In the case of JB, a pain level of 8/10 on a numeric rating scale would be classified by WHO criteria as moderate/severe pain. Assuming that JB is opioid-naive, the WHO pain ladder recommends initiation of therapy with a short-acting opioid such as hydrocodone or oxycodone.

In this case, hydrocodone-acetaminophen 5 mg/500 mg was selected, and JB is counseled to take 1 to 2 tablets every 4 to 6 hours as needed.

From a patient education perspective, it is important to recognize that these commonly used administration instructions for hydrocodone-acetaminophen products could result in a patient consuming 6 g of acetaminophen in a 24-hour period, thus exceeding the 4-g daily maximum dose, which could lead to hepatic injury. As such, patients and caregivers should be appropriately educated on how to responsibly use these medications and what adverse events can be reasonably expected. In addition to dosing and administration directions, patients beginning opioid-based pain management regimens, like JB, should also be educated on the risk of drowsiness, nausea, and constipation. In our practice, patients prescribed opioid pain medications are strongly encouraged to concurrently take a mild laxative such as senna or polyethylene glycol 3350 and a stool soft-

ener such as docusate to prevent constipation from becoming a serious medical issue.

While this patient case serves to illustrate the application of WHO recommendations for initiation of pain management in the moderate/severe setting, the WHO also provides guidance for the management of mild and severe pain. For mild pain, practitioners are encouraged to recommend nonpharmacologic treatment options including heat, cold, massage, and music, as well as over-the-counter (OTC) alternatives such as acetaminophen and nonsteroidal anti-inflammatory drugs such as ibuprofen or naproxen. Conversely, in the setting of severe pain, the WHO recommends stronger opiates including morphine, fentanyl, and oxycodone. Critics point out that the stepwise approach of beginning with milder treatment options, including OTC analgesics, and escalating based on the level of relief delivered by these treatments is often unsuccessful in gaining patients meaningful pain relief in a rapid manner. In fact, many publications have argued for revisions to the WHO pain ladder to include the addition of new levels incorporating surgical interventions such as the implantation of pain stimulators, which may offer significant relief to patients suffering with chronic pain not relieved with traditional medication-based approaches.

Many publications have argued for revisions to the WHO pain ladder to include the addition of new levels incorporating surgical interventions...

Clinicians should also be aware that clinical practice guidelines for the mitigation of cancer-related pain are available from the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology.[4,5] These organizations provide evidence-based approaches to the management of these patients that are often comprehensive and account for nuances in patient care not addressed by the older WHO program.

Adjuvant Pain Management Strategies

A nuclear medicine bone scan reveals that JB has osteolytic bone lesions throughout his thoracic spine, left ribs, and the distal head of the left femur.

In this case, it is apparent that JB's acute pain has resulted from the fracture of 3 ribs on the left side. While opioid analgesics are often relied on as the cornerstone of therapy for acute pain, no intervention has yet been made for this patient's bone lesions and, in particular, to reduce his risk of future fracture and corresponding quality-of-life concerns, including mobility and pain. Though not typically classified as analgesics, in this setting bisphosphonates have become a commonly used adjuvant treatment. In a study of 377 patients with MM, Berenson and colleagues demonstrated an increase in the time to first skeletal event in those patients treated with pamidronate. Additionally, bone pain and quality of life were significantly improved in those patients receiving pamidronate versus placebo. Similar results have been observed with zoledronic acid. As a result, both are described in the NCCN clinical practice guidelines for MM as highly recommended for all MM patients with symptomatic disease.[6-9] Some practitioners may inquire about the use of denosumab in this patient population. Currently, denosumab is not recommended as an alternative to bisphosphonate therapy in MM patients because an increased risk of mortality was observed in this patient population in a post hoc analysis of a large phase 3 clinical trial evaluating the efficacy of zoledronic acid versus denosumab. Ongoing clinical trials are attempting to address this question prospectively.[10] Bisphosphonates are also indicated by NCCN guidelines for similar end points of pain relief and prevention of skeletal events in other malignant diagnoses, including breast and prostate cancer.[11,12]

The decision is made for JB to begin zoledronic acid 4 mg q28 days following laboratory analysis to ensure appropriate renal function.

Clinicians are encouraged, and pharmacists should be watchful, to ensure that patients started on bisphosphonates have adequate renal function. For patients with some degree of renal impairment, specific recommendations are available for dose reduction based on creatinine clearance. Additionally, patients should have a dental assessment conducted as part of their physical exam to ensure that they do not have unresolved jaw, tooth, or gum issues that may increase their risk of developing osteonecrosis of the jaw, a serious but rare adverse event of these types of therapies.

In addition to bone-targeted therapies, patients may require any number of other adjuvant analgesics that may include antidepressants, muscle relaxers, corticosteroids, neuroleptics, psychostimulants, topical analgesics, etc.[13] Clinicians are encouraged to recognize that classic analgesic medications may lead to a greater degree of pain relief in those patients in whom adjuvant therapies are appropriately utilized.

Neuropathic Pain

For patients diagnosed with MM, immunomodulatory drugs and proteasome inhibitors will almost certainly play a role in their treatment and, thus, these patients are all too often left with neuropathy induced by these medications. Currently, a number of medications are used to alleviate neuropathic pain associated with chemotherapy, including tricyclic antidepressants, anticonvulsants (gabapentin and pregabalin), and opioids. Concerns of neuropathy are not exclusive to the management of patients with MM. Patients treated with taxanes (docetaxel and paclitaxel) and platinum analogs (cisplatin, carboplatin, and oxaliplatin) also are likely to experience this adverse event, and practitioners should be prepared to intervene if neuropathies begin to limit activities of daily living.[14] In our practice, we have come to favor pregabalin for initial management of neuropathies because, in contrast to gabapentin, it does not require dose titration, is well tolerated, and has been reported to reduce the impairment of sensation in the hands and feet often experienced by these patients. However, I caution that often the best treatment of chemotherapy-induced neuropathy is time. While medications may have some limited impact on the symptoms patients experience, substantial time, measured as months to years, is required for nerve regeneration and return of sensation.

To date, JB's MM is in remission following hematopoietic stem cell transplantation and maintenance lenalidomide. He continues to receive monthly infusions with zoledronic acid, but his other pain symptoms have resolved completely.

Conclusion

While this exercise in cancer pain management is not intended to be a comprehensive review of clinical practice guidelines, I hope it serves to illustrate the clinical decision making pertinent to the role of an oncology pharmacist for a representative patient with cancer. Providers, including oncology pharmacists, should completely review the medical record, radiographic scans, and laboratory values of patients with cancer to create an appropriate care plan for pain management. Focus must be placed not only on the patient's acute complaints but also on the recognition that medical intervention, including chemotherapy, may induce other issues that will ultimately affect the patient's experience of pain and quality of life. In this case, the oncology pharmacist is a key member of the healthcare team, often responsible for appropriate medication selection, dose adjustment based on organ function, adverse event monitoring and prevention, and patient education.

Finally, as healthcare providers, we must remember that patients desire adequate pain relief that fits their lifestyle and allows them to pursue, to the best of their ability, the things that bring them joy. While it may be clinically appropriate to identify a goal of reducing the patient's self-report of pain intensity from an 8 to a 4 (on a 10-point scale), this may not allow the patient the freedom from pain to live a life filled with quality. Rather, I prefer the idea of identifying 1 or 2 things that pain has prevented a patient from achieving and use these tangible objectives to establish pain management goals. Ultimately, pain management in the setting of oncology is a complex, multidisciplinary problem that allows opportunities for input from various healthcare providers with congruent goals for the relief of pain that could be debilitating, not only to the patient, but also to family and caregivers. ■

References

1. Zhukovsky DS, Gorowski E, Hausdorff J, et al. Unmet analgesic needs in cancer patients. *J Pain Symptom Manage*. 1995;10:113-119.

2. Cohen MZ, Easley MK, Ellis C, et al. Cancer pain management and the JCAHO's pain standards: an institutional challenge. *J Pain Symptom Manage*. 2003;25:519-527.

3. Stjernsward J, Colleau SM, Ventafridda V. The World Health Organization Cancer Pain and Palliative Care Program. Past, present, and future. *J Pain Symptom Manage*. 1996;12:65-72.

4. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Adult Cancer Pain*. Version 1.2013. www.nccn.org/professionals/physician_gls/f_guidelines.asp#pain. Accessed February 25, 2013.

5. Ripamonti C, Bandieri E, Roila F; ESMO Guidelines Working Group. Management of cancer pain: ESMO Clinical Practice Guidelines. *Ann Oncol*. 2011;22(suppl 6):vi69-vi77.

6. Berenson JR, Lichtenstein A, Porter L, et al. Efficacy of pamidronate in reducing skeletal events in patients with advanced multiple myeloma. Myeloma Aredia Study Group. *N Engl J Med*. 1996;334:488-493.

7. Berenson JR, Lichtenstein A, Porter L, et al. Long-term pamidronate treatment of advanced multiple myeloma patients reduces skeletal events. Myeloma Aredia Study Group. *J Clin Oncol*. 1998;16:593-602.

8. Major P, Lortholary A, Hon J, et al. Zoledronic acid is superior to pamidronate in the treatment of hypercalcemia of malignancy: a pooled analysis of two randomized, controlled clinical trials. *J Clin Oncol*. 2001;19:558-567.

9. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Multiple Myeloma*. Version 1.2013. www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed February 25, 2013.

10. Henry DH, Costa L, Goldwasser F, et al. Randomized, double-blind study of denosumab versus zoledronic acid in the treatment of bone metastases in patients with advanced cancer (excluding breast and prostate cancer) or multiple myeloma. *J Clin Oncol*. 2011;29:1125-1132.

11. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Breast Cancer*. Version 1.2013. www.nccn.org/professionals/physician_gls/f_guidelines.asp#breast. Accessed February 25, 2013.

12. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Prostate Cancer*. Version 1.2013. www.nccn.org/professionals/physician_gls/f_guidelines.asp#site. Accessed February 25, 2013.

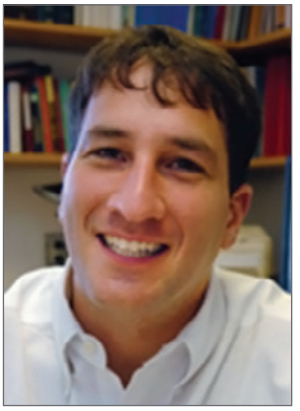
13. Lussier D, Huskey AG, Portenoy RK. Adjuvant analgesics in cancer pain management. *Oncologist*. 2004;9:571-591.

14. Niscola P, Scaramucci L, Romani C, et al. Pain management in multiple myeloma. *Expert Rev Anticancer Ther*. 2010;10:415-425.

A Physician's Perspective on Pain Management

Jeffrey D. Meyerhardt, MD, MPH

Pain management is a critical component of patient care in any medical specialty, but particularly in oncology. The 2 case presentations and discussions by Beth Faiman and Steve Stricker are common cases in which pain management is integral to the overall care of the patient. As a medical oncologist specializing in gastrointestinal malignancies, I have to consider pain due to a patient's metastatic disease, postoperative pain, and pain from treatment (eg, oxaliplatin-induced neuropathic pain). As Ms Faiman discussed, the type of pain needs to be considered when determining a relief strategy. However, sometimes pain can occur through multiple mechanisms, and a multipronged approach is required. I concur with both authors that the gamut of options needs to be considered and individualized to patients, including medications, localized intervention (eg, celiac nerve block or radiation), and surgery (eg, palliative resection of the mass contributing to the pain or kyphoplasty). Further, I would add consideration of complementary strategies that, though less tested in randomized controlled trials, seem to have benefits in certain patients, including acupuncture, massage therapy, relaxation therapy, and others.



Jeffrey D. Meyerhardt, MD, MPH

Pain management requires a team approach. Pain and palliative care services are increasing across academic and community practices as well as hospitals. As a medical oncologist, these services have become invaluable partners in the management of pain for my patients. However, I also am a strong believer that every provider for these patients needs to have an understanding and comfort level with pain management. The Massachusetts Board of Registration in Medicine has recognized this need, and since February 2012, all physicians who treat pain have been required to complete at least 3 hours of continuing medical education in pain management. At my cancer center, we have annual training in pain management. In my own practice, my team (including me as the medical oncologist, the nurse practitioner I work with, and my group's program nurses) are the frontline managers of pain medications for our patients. However, if the pain is not well controlled after multiple adjustments to long-acting and rescue medications or narcotic rotation is required (and after consideration of procedures that may help with pain control), I will involve our pain and palliative care providers to help comanage these patients. These partnerships have proven to be very successful for my patients both to improve quality of life and to continue other therapies for these patients as their performance status improves. ■

GHC106-2

2ND ANNUAL

View the series online at TheOncologyNurse.com

CONQUERING THE CANCER CARE CONTINUUM™

A 6-part series

The publishers of *The Oncology Nurse-APN/PA*, *The Oncology Pharmacist*, and *Personalized Medicine in Oncology* are proud to present our 2nd annual *Conquering the Cancer Care Continuum* series. Upcoming topics include:

IN THIS ISSUE

- Palliation
- Pain management
- Hospice care
- Treatment planning
- Survivorship care
- Biosimilars in supportive care

TO VIEW THE SERIES ONLINE PLEASE LOG ON TO:

www.TheOncologyNurse.com

#1 WITH ONCOLOGY NURSES
The Oncology Nurse-APN/PA®
The Official Publication for the Hem/Onc Nurse & Advanced Practitioner

SAVE the DATE

NOVEMBER 14-17, 2013

Fourth Annual Navigation and Survivorship Conference

Memphis, Tennessee • The Peabody Memphis

CONFERENCE CO-CHAIRS

Program Director:

Lillie D. Shockney, RN, BS, MAS
University Distinguished Service
Associate Professor of Breast Cancer
Departments of Surgery and Oncology
Administrative Director, Johns Hopkins Clinical Breast Programs
Administrative Director, Johns Hopkins Cancer Survivorship Programs
Department of Surgery and Oncology
Associate Professor, JHU School of Medicine
Departments of Surgery, Oncology, and Gynecology
Associate Professor, JHU School of Nursing
Johns Hopkins Avon Foundation Breast Center
Baltimore, Maryland

Sharon Gentry, RN, MSN, AOCN, CBCN
Breast Health Navigator
Derrick L. Davis Forsyth Regional Cancer Center
Winston-Salem, NC

AONN Academy of Oncology Nurse Navigators®

www.AONNonline.org

AONNasize20813