



Burnell Shively. *The Awakening* (detail), 1998. Oil on canvas, 33" × 40".

Vertebroplasty and kyphoplasty studies for treatment of metastatic spinal tumors have made significant improvements in pain, mobility, and vertebral height restoration.

Palliative Strategies for the Management of Primary and Metastatic Spinal Tumors

Paul E. Kaloostian, MD, Alp Yurter, BS, Arnold B. Etame, MD, PhD,
Frank D. Vrionis, MD, PhD, Daniel M. Sciubba, MD, and Ziya L. Gokaslan, MD

Background: *Technological advances during the last few decades have improved the success rate of surgery for the treatment of malignant spinal tumors. Nonetheless, many patients present with widespread tumor burden and minimal life expectancy, which excludes them from being surgical candidates. For these patients, palliative management is recommended.*

Methods: *The authors reviewed prospective and retrospective clinical studies as well as case series regarding palliative treatments for primary and metastatic spinal tumors.*

Results: *Analgesics, ranging from nonopioids to strong opioids, may be used depending on the degree of pain. Steroids may also improve pain relief, although they are associated with a number of adverse events. Vertebroplasty and kyphoplasty are conservative treatments with high rates of pain relief and vertebral body stabilization. Radiotherapy is the gold standard for palliative management, with approximately 60% of patients experiencing a decrease in tumor-related spinal pain and up to 35% experiencing complete relief. Stereotactic radiosurgery delivers high doses of radiation to patients to provide pain relief while also sparing delicate anatomical structures.*

Conclusion: *Palliative management of spinal tumors is diverse. Analgesics may be used in conjunction with radiotherapy and/or kyphoplasty or vertebroplasty to offer pain relief.*

From the Department of Neurosurgery at Johns Hopkins Hospital, Baltimore, Maryland (PEK, AY, DMS, ZLG), the Neuro-Oncology Program at the H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida (ABE, FDV), and the Departments of Neurosurgery and Orthopedics at the University of South Florida Morsani College of Medicine, Tampa, Florida (ABE, FDV).

Submitted September 30, 2013; accepted January 14, 2014.

Address correspondence to Ziya L. Gokaslan, MD, Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, MD 21287. E-mail: zgokasl1@jhmi.edu

Dr Vrionis receives grants/research support from Globus Medical, DePuy Synthes, and Spine360. He also is a consultant for Orthofix. Dr Gokaslan receives research grants from AO North America, the Neurosurgery Research and Education Foundation, Medtronic, Integra Life Sciences, Depuy Spine, and K2M. He receives honoraria from the AO Foundation and is a stock shareholder of US Spine and Spinal Kinetics. No significant relationship exists between the remaining authors and the companies/organizations whose products or services may be referenced in this article.

Introduction

The management of primary and metastatic spinal tumors is quite diverse. During the last few decades, improvements in surgical strategies and technology have had high success rates and have increased disease-free survival rates in patients with a wide variety of malignant tumors that were once thought to be inoperable. Despite these advances, many types of patients present with such widespread tumor burden and minimal life expectancy that surgical treatment cannot be medically or ethically recommended. In such patients, palliative management is recommended. Palliative strategies are rarely discussed in the literature but are viable management options for advanced spinal oncological disease. Such methods include medical management, pain management consultation, vertebroplasty, and radiotherapy.

Pain and Medical Management Strategies

Pain is one of the most common symptoms in patients with cancer, occurring in 30% to 50% of patients in the early stages and more than 70% of patients with advanced disease.¹ A variety of medical treatments are available to manage advanced spinal oncological pathology. These strategies are based on the updated World Health Organization (WHO) analgesic ladder scale published in 1997² and the updated European Association for Palliative Care recommendations.³ In these guidelines, cancer pain may be diminished by opioid administration alone or in conjunction with adjuvant analgesic agents. The authors describe a 3-step framework for treating cancer pain.^{2,4} Step 1 refers to the nonopioid analgesics for mild pain; step 2 recommends the use of weak opioids for moderate pain; and step 3 recommends the use of strong opioids for severe pain. Data have demonstrated that an understanding of the pain type (ie, nociceptive, neuropathic, or both) can help alleviate cancer pain, although not completely.^{2,4} It is thought that the WHO guidelines offer a pain relief rate ranging from 70% to 80%.⁵

In addition to medical strategies, a combination of treatments may be administered to modulate pain relief. For example, adjuvant analgesics, drugs aimed at reversing the adverse events of opioids, radiotherapy, local nerve blocks, or neurolytic blocks may be used in a variety of ways to alleviate pain.⁶ Neuropathic pain typically responds to antidepressants, anticonvulsants, and local anesthetic medications. For patients with severe neuropathic pain, opioids in combination with N-methyl-D-aspartate receptor antagonists such as ketamine should be used.⁷ Cannabinoids may also be used as an adjuvant therapy to improve the quality of life of those with chronic pain, as well as treating those with chronic neuropathic pain.⁵

The use of steroids is controversial in the setting of palliative management of spinal cancer pain. Studies

have demonstrated their efficacy in inhibiting prostaglandin synthesis and reducing vascular permeability.⁸ The exact mechanism of steroid reduction of cancer pain is unclear. Some researchers propose that steroids act on every step of the nociception pathway. The proinflammatory cytokines synthesized or released during tissue injury allow for peripheral sensitization; thus, steroids act to inhibit these cytokines, decreasing nociceptor activation.⁹ In addition, glucocorticoids inhibit the expression of collagenase and stimulate the synthesis of lipocortin, blocking the production of pain-producing eicosanoids.¹⁰ In addition, as in cases of spinal cord injury, steroids have an antismelling property that aids in tumor shrinkage, thus reducing the compression of surrounding pain-producing structures.¹¹ Dexamethasone is the most commonly prescribed of these corticosteroids and causes the least fluid retention due to its decreased mineralocorticoid activity.¹² The adverse events of steroids are varied and are generally associated with long-term or high doses; these events may include immunosuppression, hyperglycemia, Cushing myopathy, osteoporosis, peptic ulceration, and psychological symptoms.¹³

Nauck et al¹⁴ studied 55 palliative units and noted that corticosteroids were used in 17.8% of patients upon admission and in 32.4% of inpatients. Gannon and McNamara¹³ discovered a high prevalence of steroid use in their patient population, with 51% of 178 patients receiving steroids until death.

Bruera et al¹⁵ studied 40 patients who had advanced cancer and bone, visceral, or neuropathic pain. Oral methylprednisolone (16 mg twice daily) or placebo was given to patients for 5 days. The patients were crossed over to the alternate treatment after 3 days of a washout period. They were then given methylprednisolone for 20 days. Visual analog scale scores for pain and analgesic intake were lower with methylprednisolone treatment for all types of pain.

Della Cuna et al¹⁶ performed a randomized, double-blind study of 43 patients with advanced cancer who were given either intravenous methylprednisolone (125 mg/day) or placebo for 8 weeks. Visual analog scale scores for pain improved in the group treated with steroids. Several case reports have proven the efficacy of steroids in the treatment of patients with bone pain. Arkel et al¹⁷ showed the utility of steroids in treating bone pain in patients with hairy cell leukemia, and Vyvey⁸ demonstrated pain relief in a patient with metastatic pancreatic carcinoid to the liver and bones.

Radiotherapy and Radiosurgery

Radiotherapy is an enduring, established means of achieving analgesia for bone metastases that dates back to 1930.¹⁸ Patchell et al¹⁹ demonstrated a benefit of surgical decompression followed by radiation therapy for patients with severe epidural metastatic

disease. Study participants who received surgery in combination with radiotherapy retained the ability to walk for a longer duration postoperatively relative to the radiotherapy-alone group. Despite these results, patients with severe spinal metastatic disease with cord compression or multiple levels of spinal disease are not generally suited for surgical palliation because they usually have limited life expectancy and significant comorbidities. As a result, radiotherapy is the gold standard of palliative treatment for patients with metastatic spine disease and is often used in combination with adjuvant steroids.²⁰

Recently, technological progresses in radiotherapy and radiosurgery, whether used alone or in conjunction with surgical and chemotherapeutic management, have enhanced management. Due to these advancements, a subsequent decline has been seen in surgery for metastatic disease. For example, in cases of radiation therapy, approximately 60% of patients have decreased tumor-related spinal pain, while 23% to 35% experience complete pain relief.²¹ In patients with severe metastatic disease, doses may vary from 5 daily fractions of 4 Gy to 23 daily fractions of 2 Gy, without one schedule having a statistically significant functional advantage over the other.²² Specific dose-fractionation schedules for uncomplicated metastatic spinal disease can vary. The literature suggests that no significant difference exist in complete and partial pain response rates following single fraction (8 Gy) versus multifraction regimens.²¹ Nonetheless, the likelihood of re-treatment is 2.5-fold higher in patients receiving single fraction therapy compared with those undergoing multifraction therapy. In addition, those receiving single fraction therapy have a significantly higher risk for subsequent pathological fracture.²³ Patients can tolerate re-treatment palliative radiotherapy and are not at risk for increased spinal cord toxicity.²⁴

Studies of radiosurgical techniques for metastatic spine disease have also demonstrated effective results. In a study of 294 patients with spinal metastases, Gerszten et al⁴⁵ noted that radiosurgery using CyberKnife (Accuray, Sunnyvale, California) yielded a rate of 88% for local control and an 86% rate in long-term pain reduction. Moreover, of the 32 patients with neurological deficit at the beginning of the study, 84% improved following radiosurgery. Wowra et al²⁶ found higher tumor control rates in 102 study participants with metastatic spinal disease. Single-dose fractions of 15 to 24 Gy using fiducial-free spinal radiosurgery resulted in a local control rate of 98%. In a study of 49 patients, Ryu et al²⁷ reported a local control rate of 96% and an improvement in pain in 85% of patients whose lesions were treated with single-dose radiosurgery. The 1-year survival rate was 74%, and a 5% rate of radiological progression at adjacent levels was observed.

Vertebroplasty and Kyphoplasty

Advances in vertebroplasty and kyphoplasty for the treatment of metastatic spinal tumors without epidural compression have allowed surgeons to improve the anterior column stability of the spine in conjunction with medical and radiation therapies. In particular, these conservative procedures are beneficial for elderly patients at high risk because minimal blood loss occurs in addition to less operating time under anesthesia compared with their younger counterparts. Cement injection may provide structural support to the vertebral body. Thus, pain relief is achieved via mechanical stabilization.^{28,29} The most common complication is cement extravasation into the spinal canal, venous plexus, or both, and hematogenous embolization.^{30,31} A randomized, multicenter, controlled trial demonstrated the merits of kyphoplasty for patients with oncological vertebral compression fractures.^{32,33} The authors concluded that kyphoplasty is a safe, effective procedure that reduces pain, improves neurological function, and may be used in conjunction with posterior stabilization in cases of malignancy.

Vertebroplasty and kyphoplasty studies for the treatment of metastatic spinal tumors have demonstrated significant improvements in pain, mobility, and vertebral height restoration.³³⁻⁴⁴ Vertebroplasty studies specific to spinal metastases have demonstrated pain improvement among 73% to 100% of patients.^{35,41} Although few studies exist that have documented changes in mobility, McDonald et al³⁸ observed an improvement in mobility among 70% of the 67 study participants. To our knowledge, Yang et al³⁷ conducted the largest vertebroplasty study in patients with metastatic spinal disease. A total of 196 patients were treated during the study, and a 98.5% improvement in pain was seen, as well as statistically significant improvements in vertebral body height. Studies of kyphoplasty have demonstrated pain improvement in 81% to 100% of patients.^{33,44} To our knowledge, Berenson et al³³ conducted the largest controlled, randomized multicenter study of kyphoplasty for spinal metastases. Of the 70 study participants, 65% had improved mobility and 81% had improved pain. The next most statistically powered study consisted of 50 patients, demonstrating a 96% rate of pain improvement.⁴³ Newer combination treatment paradigms have also proven beneficial, as demonstrated by Gerszten et al.⁴⁵ Twenty-six patients were successfully treated by kyphoplasty followed by CyberKnife spinal radiosurgery, and 92% saw an improvement in axial pain.

Conclusions

Palliative management of spinal tumors is diverse. Analgesics, ranging from nonopioids to opioids, may be used with adjuvant drugs, such as steroids, to treat cancer-related pain. Standard radiotherapy may also

reduce radiation-sensitive tumors, while stereotactic radiosurgery can provide concentrated doses to treat conventionally radioresistant tumors.⁴⁶ Furthermore, cement augmentation procedures such as vertebroplasty and kyphoplasty are minimally invasive procedures that can offer significant pain relief via mechanical stabilization for patients with vertebral compression fractures.

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