



PALLIATIVE CARE CASE OF THE MONTH

“Bad to the Bone: Management of Cancer Pain Related to Bone Involvement” by

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Case: Mrs. S. is a 74-year-old woman with non-small cell lung cancer and extensive metastatic disease to the liver, adrenal glands, and bone. She was admitted for worsening pain in her left upper extremity. Imaging revealed a large expansive lytic lesion in her left scapula as well as lytic lesions in the vertebral body of T8 and right-sided ribs. Her home pain medications included fentanyl patch 25mcg every 3 days, oral hydromorphone 2mg every 3 hours as needed for pain, and acetaminophen 500mg every 6 hours as needed for mild pain.

Mrs. S. was continued on her fentanyl patch and started on a hydromorphone PCA given the severity of her pain. However, the PCA caused visual and auditory hallucinations and her pain remained significant. Her fentanyl patch was escalated, and she was rotated to a morphine PCA. Her pain was better managed on this regimen, however, she remained somewhat drowsy, constipated, and with significant limitations in the movement of her left upper extremity due to severe pain. The question is what non-opiate therapies could be used to help with her pain?

Discussion: Bone pain is the most prevalent type of cancer pain.¹ It is most commonly due to metastatic disease, usually from solid organ tumors of the lung, breast, and prostate, or multiple myeloma. Bone pain is present in one third of the patients who have bone metastases.

The etiology of bone pain has historically been categorized as nociceptive and further subcategorized as somatic pain due to a prominent inflammatory component. Bone homeostasis is regulated by RANK-ligands which maintain the balance of bone resorption and formation. When healthy bone is invaded by cancer cells, RANK-ligand expression is increased leading to increased osteoclast activity and bone destruction resulting in osteolytic lesions. These types of lesions are most commonly found in multiple myeloma and non-small cell lung cancer. Disruption of bone homeostasis also causes a dysregulation of bone deposits leading to osteoblastic lesions, most commonly found in prostate cancer. It is important to note that the distinction between osteolytic and osteoblastic lesions is complex and many diseases often have a combination of both types. Metastatic breast cancer is an example of this.²

Despite the usual classification of bone pain as nociceptive, there is recent evidence that a prominent neuropathic component also exists. This is due to both the direct destruction of nerve fibers which innervate the bone by cancer cells as well as sensitization of peripheral nerve fibers secondary to the acidic environment created by local inflammatory mediators.³

Treatment: Treatment of bone pain typically requires opioids, adjuvant (non-opioid) medications, interventional procedures, and complimentary or supportive non-pharmacological treatments. Opioids are considered first line therapy in severe pain related to bone disease.⁴ However, adjuvant pain medications are often very effective as well and may reduce the need for opioids. Given the nociceptive component of bone pain, non-steroidal anti-inflammatory drugs are given despite little empirical data and side effects ranging from gastrointestinal discomfort to renal failure. Acetaminophen, although it does not have significant anti-inflammatory properties, is often used in hopes of augmenting opioid effect.⁵ Systemic steroids are also used commonly in patients with severe bone pain when contraindications do not exist. The mechanism of action of glucocorticoids is not completely elucidated but is thought to be due to reduction of tumor-related edema and inhibition of prostaglandin synthesis. The choice of glucocorticoid, dosing, and duration of treatment is not evidence-based.⁶

Another class of adjuvant medication are bisphosphonates. Bisphosphonates are osteoclast inhibitors which work by reducing bone resorption.⁷ While it makes sense that these are most effective in diseases where osteolytic lesions predominate, the evidence also supports the use of bisphosphonates in metastatic breast cancer and prostate cancer.⁸ Bisphosphonates are also effective in the prevention of skeletal-related events such as pathologic fractures. Zoledronic acid and pamidronate both are administered as an intravenous infusion. Most patients will feel pain relief after one week, but it may take up to four weeks to feel the full effect. The duration of the treatment effect may be up to 12 weeks; however, most patients are treated every 3-4 weeks to achieve maximum relief.⁹ Bisphosphonates are contraindicated in renal failure.

Investigational therapies for bone pain include carbenoxolone and desonumab. Carbenoxolone, a glycyrrhetic acid with a steroid-like structure derived from licorice root may be useful for cancer-induced bone pain.¹⁰ Desonumab, a monoclonal human antibody, that has been used to help prevent fractures in patients with osteoporosis, is a novel agent for cancer related bone pain. It specifically inhibits RANK-ligand and there is some evidence that it may delay the development of pain in patients with metastatic breast cancer.¹¹

Interventional therapies also are effective for bone pain. Most commonly this involves external beam radiation therapy, often given in a single fraction to a distinct painful lesion. Single fraction radiation therapy has been shown to be just as effective as multiple doses, with pain relief being achieved for about 60% of patients.¹²

Personal details in the case published have been altered to protect patient privacy.

For palliative care consultations please contact the Supportive and Palliative Care programs at PUH/MUH, 412-647-7243, pager # 8511, Shadyside, 412-647-7243, pager # 8513, Perioperative/ Trauma Pain, 412-647-7243, pager # 7246, UPCI Cancer Pain Service, pager 412-644-1724, Magee Women's Hospital, pager 412-647-7243 pager # 8510, VA Palliative Care Program, 412-688-6178, pager # 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore and Children's pager 412-456-1518
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(Discussion Continued)

Bone-targeted radioisotopes, such as Radium-223, are sometimes used in patients with diffuse osteoblastic lesions, most commonly in men with castration-resistant prostate cancer. This bone-seeking alpha particle emitting agent distributes high-energy radiation therapy in a short distribution as it decays which helps to prevent damage to the bone marrow.¹³ Occasionally, interventional pain techniques such as a regional nerve blocks are used for severe bone pain.

Non-pharmacological measures to consider include repositioning, application of heat or ice, and the use of supportive devices such as an orthopedic sling or brace. Complimentary therapies such as acupuncture and transcutaneous electric nerve stimulation (TENS) may be considered, although there is no empirical data to support their use.

Conclusion of Case: Mrs. S. was evaluated by orthopedics and fitted for a left upper extremity soft sling. This was minimally effective in alleviating her pain. Because of her pain severity on admission, she was started on dexamethasone twice daily as well as a proton pump inhibitor. The combination of glucocorticoids and high-dose acetaminophen reduced her pain level to a more manageable level. She received external beam radiation in single fractions to her left scapula and right ribs. With this aggressive adjuvant regimen, her pain was controlled on lower doses of opioids and her opioid-related side effects were minimized.

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