Bone Metastases and Pain

Painful bone metastasis is a common complication of advanced cancer. Bone is the most common metastatic site for breast, prostate, and lung cancers, which account for 73% of bone metastases. About 200,000 new cases of bone metastases are diagnosed in the US each year. The spine and long bones are commonly involved. The bone environment is highly vascular and provides a good medium in which metastatic tumors can grow.

Not only does the incidence of metastasis to bone vary by cancer type, but the pathophysiology of metastatic disease also varies. For example, breast tumors secrete parathyroid hormone-related protein (PTHrP), part of a cascade that activates osteoclasts to resorb surrounding solid bone matrix. This weakens the bone and can lead to both hypercalcemia and pathological fractures. Moreover, transforming growth factor-beta is released from resorbed bone, further stimulating PTHrP production in a vicious cycle. In contrast, prostate cancer is more likely to produce osteoblastic lesions, pathologic new bone. Prostate cancer cells secrete an osteoblast-regulating factor, dickkopf homologue-1 (DKK-1). This brief description is a gross oversimplification, of course, and most cancers display varying degrees of both pathological processes.

Not every patient with bone metastases has pain, but, like other painful conditions, there is a wide variation in pattern and severity. A recent study characterized the pain of bone metastases:

- 83% of patients had pain

- There is typically a background pain made significantly worse by movement
- 50% of patients had breakthrough pain (spontaneous or movement-related) that lasted less than 30 minutes; 25% reported it lasted less than 15 minutes
- 52% of patients felt that breakthrough pain episodes were unpredictable.

Recent research has found that bone pathology that leads to pain has a unique character that incorporates both inflammatory and neuropathic features. This finding may lead to new treatment approaches. All parts of the bone are innervated by sensory nerves. Tumor invasion, bone weakening, and bone remodeling can lead to injury of these nerves. Osteoclasts produce a highly acidic environment that may contribute to pain. A number of pain-inducing cytokines and other proteins are released by tumor cells and immune cells.

Currently, management of pain from bone metastases is nearly always multimodal. External beam radiation, opioid analgesics, and bisphosphonates are commonly employed. Bisphosphonates stabilize bone, are tumoricidal, and may have analgesic properties. Non-steroidal anti-inflammatory agents (NSAIDS) and, occasionally, steroids are also used. The evidence base for NSAID use is weak, however. If the disease is chemoresponsive, systemic chemotherapy may be included. A recent review suggests that radionuclide therapy, indicated specifically for painful bone metastases, is underutilized. Although no clinical trials have yet been reported, animal studies suggest that gabapentin and its analogs may be effective adjuvants.
because of their ability to target neuropathic pain. Even 5HT3 antagonists (e.g., ondansetron), recently found to have analgesic properties, may have a role. COX-2-specific inhibitors have an anti-inflammatory/analgesic effect, but may also slow cancer progression. Pre-clinical research with several agents that focus on new targets for bone metastases is in progress.

Only about 50% of patients report adequate relief of pain from bone metastases. Reasonable control of background pain can often be achieved through combinations of treatments as described above. Treatment for breakthrough pain remains a major challenge. The onset of action of opioid analgesics lags behind the short but severe duration of spontaneous or movement-evoked pain. Transmucosal fentanyl has the fastest onset and shortest duration of available opioids, but may not be able to provide adequate analgesia in an adequate time frame for many patients.

Journal Watch
- Hermansen-Kobulnicky CJ. Measurement of self-advocacy in cancer patients and survivors. Supportive Care in Cancer. 2008 Apr 2. [Epub ahead of print]
- Gender, Pain, and the Brain. Pain: Clinical Updates 2008;16(3).

Online Resources
- Health Promotion for Breast Cancer Survivors: An Interview with Dr. Tish Knobf, Yale School of Nursing. Also available as iTunes podcast.
- Rating cancer risks
- Treating bowel dysfunction
- Caring for Cancer Survivors (Oncology STAT—free registration required)
- Quick Facts (for patients & families) from GetPalliativeCare.org.

Books of Note
- Chen P. Final Exam: A Surgeon’s Reflections on Mortality.
- IASP. Pain Management for Older Adults: A self-help guide

Continuing Education
Yale
- Schwartz Center Rounds: Monthly multidisciplinary forum where professional caregivers discuss difficult emotional and social issues that arise in caring for patients. 12:00 Noon, YNHH East pavilion, 9th Floor Conference Room. CME.
  - June 16 – Caring for a health care professional
  - Schwartz Rounds resumes in September

Elsewhere
- Jun 5 – 6. The Art & Science of Palliative Care Nursing. Newton, MA.
- Sep 12. Eastern Pain Association Annual Meeting

Online
- End-of-Life Care: Improving Communication Skills to Enhance Palliative Care CNE
- NCCN Nursing Program: Role of the Advanced Practice Nurse in Quality Oncology Care (CNE; Medscape) (Medscape)
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References


