

Bone Metastases From Advanced Cancers: Clinical Implications and Treatment Options

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Bone metastases are associated with considerable morbidity and can result in skeletal-related events (SREs), including pathologic fractures, the need for palliative radiotherapy, spinal cord compression, the need for surgery to bone to prevent or treat a pathologic fracture or spinal cord compression, and hypercalcemia of malignancy. Such SREs have been associated with decreases in survival and increases in healthcare costs. Skeletal morbidity and bone pain from metastases can also reduce patients' functional capacity and undermine their quality of life. Patients who develop bone metastases from advanced cancers commonly receive bisphosphonates to not only delay the onset of SREs and reduce their frequency but also provide clinically meaningful palliative effects for bone pain. Ongoing research may lead to improvements in skeletal health monitoring and management for patients with malignant bone disease.

The skeleton is the most common site for distant metastasis in patients with cancer. For example, bone metastases form in more than 70% of patients with breast or prostate cancer, in 60% of patients with thyroid cancer, and in about 35% of patients with lung cancer or renal cell carcinoma (Coleman, 2004). Patients with multiple myeloma also develop bone lesions from myeloma colonization in the bone marrow that can affect bone metabolism. Bone metabolism involves resorption of old or damaged bone (osteolysis) by osteoclasts and the generation of new bone matrix by osteoblasts, the actions of which are stimulated by growth factors that are released during osteolysis. The bone microenvironment can provide fertile "soil" in which some metastasizing tumors may grow (Mundy, 1997). Many tumor cells that reach the bone can locally stimulate the body's osteoclast cells to increase their rates of osteolysis, resulting in increased release of growth factors from the bone matrix in the areas near the metastatic tumor cells. Those growth factors, in addition to their effects on osteoblasts, can stimulate tumor growth (Mundy).

This "vicious cycle" of tumor growth and bone destruction can result in considerable morbidity for patients. Indeed, bone metastases are associated with skeletal-related events (SREs), which include pathologic fractures, bone pain requiring palliative radiotherapy, spinal cord compression, the need for surgical interventions, and hypercalcemia of malignancy (Coleman, 2004). Patients with bone metastases typically experience bone pain as their first symptom, and acute pain episodes may occur despite analgesia ("breakthrough pain") (Simmonds, 1999). Moreover, because pain can be a symptom of the underlying bone pathophysiology (increased osteolysis resulting from malignant bone disease), the cause of bone pain is important to consider when selecting treatment for pain management.

At a Glance

- ◆ Bone metastases place patients at risk for considerable morbidity and can result in skeletal-related events (SREs).
- ◆ Bisphosphonates can prevent and delay the onset of SREs.
- ◆ Bisphosphonates can reduce bone pain from metastases.

In large-scale clinical trials, SREs occurred in about 50% of patients with bone lesions (Berenson et al., 1998; Lipton et al., 2000; Rosen et al., 2004; Saad et al., 2004; Yarbrow, O'Kelly, de Mattos Pimenta, Caponero, & Aranda, 2003) (see Figure 1), and patients experienced an average of 1.5–3.7 SREs per year, depending on the primary cancer: 1.5 for prostate cancer, 2.2 for

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