Bone Metastasis Treatment with Medications

Bone metastases can be a part of advanced cancer. They are most common in breast and prostate cancer. Bone metastases can cause:

- Severe pain
- Bone fractures
- Life-threatening electrolyte imbalances
- Pressing down of nerves which can cause pain and/or weakness

Pain and nerves not working right can be hard to treat and affects quality of life. Often bone metastases means your cancer is advanced and not curable.

Osteolytic vs. Osteoblastic

Bony metastases are either osteolytic or osteoblastic.

Osteolytic:

- The tumor has caused bone break down or thinning
- Calcium is being released from the bone, into the bloodstream
- On X-rays these are seen as holes called "lucencies"
- Often seen in multiple myeloma, but may be present in patients with other types of cancers like breast cancer

Osteoblastic:

- Increased bone production
- Tumor signals to the bone to make extra bone cells which results in rigid, thickened, inflexible bone being formed
- Most often seen in prostate cancer

Most cancers result in either osteolytic or osteoblastic bony changes, but some can lead to both.

Why the bone?

The bone is a common site of metastasis for many solid tumors. The three reasons for this are blood flow, adhesive molecules and growth factors.

- Blood Flow: There is a high level of blood flow to the bone and bone marrow. Once cancer cells get into to the blood vessels, they can travel all over the body. They usually go where there is the highest flow of blood.
- Adhesive Molecules: Tumor cells secrete adhesive molecules that can bind to the bone marrow and bone. This interaction can cause the tumor to signal for more bone destruction and more tumor growth within the bone.
- Growth Factors: The bone is a rich source of growth factors. These growth factors signal cells to divide, grow, and mature. As the cancer attacks the bone, these growth factors are released and stimulate the tumor cells to grow. This results in a self-generating growth loop.

What are the signs of bone metastasis?

Signs of bone metastasis can be caused by many other health issues. Most people with bone pain do not have bone metastasis but it is the most common sign of a bone metastasis. Other signs are:
• Bone fracture without injury or trauma. Bone fracture is more common in osteolytic metastases than osteoblastic metastases.

• Numbness and tingling sensation in their feet and legs

• Bowel and bladder issues – either losing continence of urine and/or stool, or severe constipation and urinary retention

• Leg weakness and difficulty moving their legs against gravity. This would imply that there is tumor pressing against the spinal cord, compromising the nerves that control these functions. This is called spinal cord compression and is considered an emergency that needs medical attention right away.

A less common sign of bone metastasis is high levels of calcium in the body. High calcium can cause constipation, which can result in abdominal pain, and with very high calcium levels, confusion and mental status changes can occur.

**Diagnosis of Bone Metastasis**

Once a patient has any of the signs of bone metastasis, tests can be done to find the true cause. In some cases, bone metastasis may be found before the symptoms start. X-rays, bone scans, and MRIs are used to diagnose bone metastases.

X-rays are especially helpful in finding osteolytic lesions. These often appear as "holes" or dark spots in the bone on the x-ray film. Bone metastases often do not show up on plain x-rays until they are quite advanced.

By contrast, a bone scan can detect very early bone metastases. This test is done by placing a small amount of radio-tracing material into the vein. Special x-rays are taken a short time after the injection. The radiotracer will go to the site of the metastases and will appear as a darker, denser, area on the film. Sometimes infections, arthritis, and old fractures can appear as dark spots on the bone scan and may be difficult to differentiate from a true cancer. Bone scans are also used to follow patients with known bone metastasis.

In some cases CT scan images can show if a cancer has spread to the bone. An MRI is most useful when examining nerve roots suspected of being compressed by tumor or bone fragments due to tumor destruction (called spinal cord compression).

There are no blood tests that are currently used to diagnose a bone metastasis. There are, however, a number of blood tests that may suggest the presence of bone lesions, but the diagnosis rests with the combination of radiology testing, clinical picture (symptoms), and the type of cancer (is it one that travels to bone?). For example, elevated levels of calcium can be related to bone metastasis, but these lab tests alone cannot prove their presence.

**Treatment**

The best treatment for bone metastasis is the treatment of the primary cancer. Therapies may include chemotherapy, hormone therapy, radiation therapy, immunotherapy, or treatment with monoclonal antibodies. Pain is often treated with narcotics and other pain medications, such as non-steroidal anti-inflammatory agents. Physical therapy may be helpful and surgery may have an important role if the cancer resulted in a fracture of the bone.

**Bisphosphonates**

Bisphosphonates are a type of medications that decrease pain from bone metastasis and help make bones stronger. Bisphosphonates are a man-made version of a naturally occurring compound called pyrophosphate that prevents bone breakdown. They are used to treat or prevent osteoporosis and to treat other bone diseases (such as Paget's Disease), as well as in the treatment of elevated blood calcium. These medications suppress bone breakdown caused by cells called osteoclasts, and, can indirectly stimulate the bone forming cells called osteoblasts to make new bone. Strengthening bone and relieving bone pain has made bisphosphonates a good treatment for cancer that has spread to the bone. It is important to keep in mind that treatment of bone metastases is not curative.

Bisphosphonates can be given either orally (by mouth) or intravenously (IV). The two most commonly used in cancer care are pamidronate(Aredia) and zoledronic acid(Zometa). The typical side effects are a flu-like reaction during the first 48 hours after the infusion, nausea, low calcium levels, kidney impairment, and osteonecrosis of the jaw with long-term use.
Denosumab

Osteoclast inhibition can also be achieved with a medication called denosumab (XGEVA). This medication works a little differently – it is a type of targeted therapy (monoclonal antibody) and works by targeting a specific protein that is necessary for bone destruction to occur. By inhibiting this protein, called RANKL, denosumab stops the breakdown of bone and, in turn, reduces the chance of developing a fracture in the affected bone. It has side effects similar to the bisphosphonates, though it has a higher likelihood of causing low blood calcium, so patients are asked to take calcium and vitamin D supplements while on this treatment.

Radiopharmaceuticals

These medications carry radioactive elements which can kill cancer cells. They are given into a vein and find areas of cancer in the bones. There they give off radiation which kills cancer cells. Examples of radiopharmaceuticals are Strontium-89, Samarium-153 and Radium-223. It can be used with radiation to treat areas of pain and the same area can be treated again if the pain returns. These work best on osteoblastic areas.

The Future

Skeletal metastases remain one of the more debilitating problems for cancer patients. Research is ongoing to identify the molecular mechanisms that result in both osteolytic and osteoblastic bone lesions.