All About Bone Metastases

What are bone metastases?

Bone metastases, also called "bone mets," occur when cancer cells break off from a primary tumor that is somewhere else in the body. These cells travel through the bloodstream or lymph system to a part of the bone and become metastatic cancer cells. This is different than a primary bone tumor, which starts in the bone. When metastatic cancer cells reach the bones, they release substances that turn on either osteoclasts or osteoblasts. Osteoclasts lead to breakdown of bone without new bone being made, which weakens the bones. Osteoblasts lead to new bone being made without the breakdown of old bone first, which makes the bones abnormally hard.

Let's use an example to better understand metastases: a lung cancer is first formed in the lung tissue, but tumor cells can break off from the original mass and travel through the bloodstream or lymph system. These cells can make their way to other areas of the body, including the bone. This spreading of the tumor is known as "metastasis." When a lung cancer metastasizes to the bone, this "bone cancer" is actually made up of lung cancer cells. If a pathologist looked at these cells under a microscope, they would look like lung cancer cells. It is important to understand the difference between primary bone tumors and bone metastases because they are treated differently.

Metastases can occur in any bone in the body, but are most often found in bones near the center of the body. The spine is the most common site of bone metastasis. Other common sites are the pelvis (hip), upper leg bone (femur), upper arm bone (humerus), ribs, and the skull. The lesions are referred to as either osteolytic or osteoblastic lesions, depending on the effect of the cancer cells on the bone.

The cancers most likely to metastasize to the bone are breast, prostate, lung, thyroid, and kidney. More than 2 out of 3 primary breast and prostate cancers metastasize to the bone before any other site. About 1 out of 3 primary lung, thyroid, and kidney cancers will spread to the bones.

Signs, Symptoms, and Diagnosis

The most common signs of bone metastases are pain, fracture (broken bone), spinal cord compression, and a high calcium blood level. Your provider will monitor you closely during treatment of your primary cancer for these signs and symptoms. You should notify your provider if you start to experience any symptoms of bone metastases.

Bone pain is usually the first symptom of bone metastases. The pain usually starts intermittently (comes and goes), is worse at night, and is usually relieved with movement. It may progressively worsen and become constant. There are many medications that can be used to treat the pain.

Bone metastases can weaken bones and even result in fractures (breaks). Fractures that are the result of bone metastases are called "pathologic" fractures. The fractures could be caused by trauma, but if the bone is weak enough, it can break just by doing an everyday activity.

Cancer that has spread to the spine can cause pressure on the spinal cord, which is called spinal cord compression. Signs of spinal cord compression include new or worsening pain in the back or neck, numbness and weakness in the body below the tumor and difficulty walking. Spinal cord compression can lead to nerve damage and even paralysis if not treated promptly.

Some bone metastases can cause calcium to leak from the bones into the bloodstream. This can lead to high calcium levels (hypercalcemia) in the blood. Hypercalcemia can cause constipation, nausea, loss of appetite, extreme thirst, frequent urination, dehydration, fatigue, and in very serious cases confusion and even coma.
Imaging studies such as a bone scan, x-rays, CT scan, PET, or MRI, may be used to diagnose bone metastases, depending on the particular situation. You may also have blood tests drawn to check your calcium level or to check for tumor markers. A high calcium level or an elevated tumor marker level may indicate that cancer has spread to the bones. If there is a bone lesion found but it is unclear what it is, your provider may suggest a biopsy. A biopsy is a procedure that removes parts of a tumor or areas of bone that may be affected by cancer cells. A pathologist then views this sample under a microscope to determine what type of cells make up the tumor. The type of biopsy used depends on where the tumor is located.

**Treatment Options**

Treating bone metastases is important because treatment can improve symptoms and quality of life. Treatment options depend on the type of cancer, the location and extent of the metastases, and the patient’s overall health. Most providers believe the most important treatment for bone metastases is treatment directed against the primary cancer (the original cancer).

The two general types of treatment for bone metastasis are systemic (affecting your whole body) or local (treatment is directed at a specific area). Systemic therapies enter the bloodstream, either through a pill taken by mouth or a medication injected directly into a vein (IV, intravenously), and can reach cancer cells that have spread throughout the body. The treatments directed at only the metastases are called local treatments. Each therapy may be given alone or may be given in combination with another therapy depending on the situation. Each therapy is detailed below:

**Systemic Therapies**

**Medical Therapies**

Medical therapies, including chemotherapy, targeted therapy, immunotherapy, and hormone therapy, are known as systemic therapies because they can travel throughout the body to kill cancer cells. Because metastatic cancer cells have broken off from the original tumor and are somewhere else inside the body, chemotherapy has a chance of reaching them and killing them.

**Bisphosphonates**

A group of medications called bisphosphonates can help make diseased bones stronger and can help prevent fractures. Bisphosphonates may be used along with other therapies for bone metastasis. This class of medication is often prescribed as treatment for osteoporosis (a form of bone thinning not related to cancer). Bisphosphonates can help bones affected by cancer by allowing them to hold on to calcium, making them stronger. This slows down bone damage caused by the cancer, reduces high blood calcium levels (hypercalcemia), and decreases the risk of fracture. Bisphosphonates are more effective for lytic (weakening) than blastic (thickening/hardening) types of metastases. The bisphosphonates used as treatment for bone metastasis are given intravenously. The most commonly used bisphosphonates are zoledronate (Zometa®) and pamidronate (Aredia®). Possible side effects include tiredness, nausea, vomiting, lack of appetite, low blood calcium levels, and a rare side effect called osteonecrosis of the jaw (ONJ).

The medication denosumab (Xgeva®) may be used to prevent further bone damage from cancer cells. This medication works a little differently – it is a type of targeted therapy (monoclonal antibody). It works by targeting a specific protein that is necessary for bone destruction to occur. By targeting this protein, called RANKL, denosumab inhibits the breakdown of bone and, in turn, reduces the chance of developing a fracture in the affected bone. This medication 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.

**Radionuclide Therapy**

Another form of systemic treatment is radionuclide therapy. A radionuclide is an element that is radioactive. The medication is given intravenously (IV, into a vein) and deposits itself into the areas of bone that contain cancer. The radiation is given off over a period of time, killing the cancer cells and alleviating pain. The treatment is given once, but the effect can last for several months. Samarium and strontium are the most used radionuclides for bone metastases, but radium may also be used.

Radionuclides are more effective for "blastic" metastases, those that stimulate bone growth. Prostate cancer metastases are often blastic. Most metastases from other types of cancers are "lytic," meaning they break down bone. These are not treated with radionuclides. This treatment can initially cause pain to get worse before it gets better. A main side effect is low blood...
counts, so it is used with caution in people with low counts. In addition, your care team will provide education about necessary precautions for your family members because the radiation is present for days to weeks.

Local Therapies

Radiation Therapy

Radiation therapy is the use of high energy x-rays that are delivered to the areas of metastases. These x-rays are similar to those used for diagnostic x-rays, but they are of a much higher energy. The high energy of x-rays in radiation therapy results in damage to the DNA of cells. Cancer cells divide faster than healthy cells, so their DNA is more likely to be damaged than that of normal cells. Additionally, cancer cells have a harder time repairing damaged DNA compared to normal cells, so cancer cells are killed more easily by radiation. Radiation therapy exploits this difference to treat cancers by killing cancer cells while killing fewer cells in normal, healthy tissue.

Radiation is frequently offered when patients have bone pain from a metastasis that is not relieved with pain medication. The goal of the treatment is to reduce pain. Most patients will experience at least partial improvements in their pain quite quickly; however, it can be a few weeks after treatment before maximum pain relief is achieved.

Ablation

Ablation is a technique in which a needle is placed directly into the tumor. This needle is used to introduce heat, cold, or a chemical into the tumor to destroy cancer cells. The two commonly used types of ablation are radiofrequency ablation and cryoablation. Radiofrequency ablation introduces an electric current into the tumor which produces heat to destroy the tumor. This is typically done under general anesthesia. Cryoablation freezes the tumor and kills cancer cells.

Bone Cement

In some cases, and after some treatments, a bone may need to be strengthened or stabilized. This can be done using a quick-setting cement or glue. A procedure called kyphoplasty or vertebroplasty is used to treat fractures of the spine. This involves the injection of cement to stabilize the bone. These can be used alone to stabilize a bone and manage pain or can be used with other treatments such as radiation or radiofrequency ablation.

Surgery

Surgery can be used to relieve symptoms, such as pain, and to stabilize the bone or bones. Surgical rods, screws, pins, plates, and cages can be used to stabilize bones and prevent or treat fractured bones.

Clinical Trials

Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Resources For More Information

American Cancer Society

Provides information and resources for patients and caregivers.

www.cancer.org