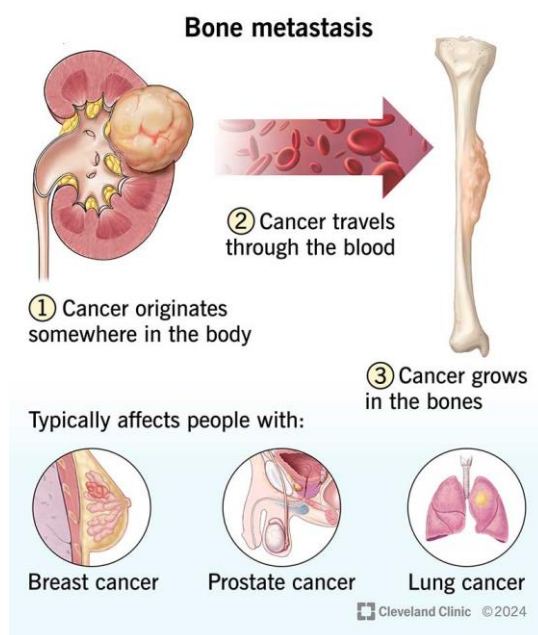


Biology of Bone Metastases

Maxime Coles MD

A bone metastasis occurs when cancer cells spread from their original site to a bone or any tissue around. Nearly all types of cancer can spread (metastasize) to the bones or elsewhere. Some have a predilection for bone, like breast, lung and prostate attacking typically the long bones of the extremities, especially the arms and legs.



A bone metastasis is manifested when cancerous cells move from one place to another location in the body or spread to another bone. Often seen with people suffering from breast or lung cancers as well as prostate cancer but in fact any cancer can metastasize to soft tissues or bones. There may not be any cure at this stage but there are treatments to ease the symptoms and to try to prevent further deterioration of the one suffering. Bone metastasis is common partly because people are living longer with an incidence that seems to increase by 3% increase per year following the

discovery of the first metastasis but by 8% within the 10 years following the diagnosis.

The most common symptom of a bone metastasis is bone pain when it involves bone giving the sensation of either a dull ache which gets worse at night either a sudden sharp and localized pain. The bone can become so fragile at time that a fracture can happen without any trauma or fall. Any bone of the body can be involved but generally, the spine, the ribs, the pelvis are the most common involved. The same can be seen for the long bones like the humerus, the femur and even the skull. Once the case is advanced, a metastasis can show up at any site.

Such fracture through a metastasis is called a pathologic fracture. Severe pain is a hallmark of such fractures. Once one develops a pathologic fracture is seen, we can expect the patient suffering from it to have a hypercalcemia and precautions will have to be taken because of the general complications on the body with confusion, constipation, loss of appetite, nausea and vomiting. Many patients with spinal vertebrae fractures may develop pain and spinal compression, low back pain, weakness to the upper or lower extremities. They may be unable to control their urine (urinary incontinence) or their stools (rectal incontinence).

Two bone cells are important in the bone turnover metabolism: the osteoblasts responsible of the bone formation (new bone) and the osteoclasts responsible of the bone turnover, dissolving and breaking down the old damaged bone cells. Too much bone formation by the osteoblasts may form osteoblastic or osteosclerotic lesion. The bone can present punched out or osteolytic lesions because of an osteoclastic activity rendering the bone weak and easy to break. Up to 85% of bone metastasis from prostate have an osteoblastic activity, while 75% of metastatic breast cancer have an osteolytic activity.

Several diagnostic tests are available. Blood and Urine tests can be diagnostic demonstrating damages to the tissues. Often regular X-Rays as, CT Scan, MRI Studies, Positron Emission Tomogram (PET Scan) will be useful in helping diagnosing and treating different lesions. Each metastasis is approached differently and the specialist can provide proper treatment depending on the staging of the lesion. Different medications can be prescribed as well as appropriate treatment to keep the lesion from getting worse.

Different medications and treatments can be offered. Pain medicine like Acetaminophene, Motrin, Morphine, Talwin, Gabapentin etc. Other medications like the Biphosphonates (Pamidronate or Zoledronic (Zometa), medications to treat osteoporosis, may support in avoiding fractures and in bone can strengthen the bone. They may control the amount of calcium in the blood stream avoiding any risks of hypercalcemia.

Chemotherapy drugs and Hormonal therapy can also help in the control of bone metastases. Monoclonal antibody Therapy (Denosumab or Prolia or Xgeva) will also reduce the the risk of fracture. Radiation therapy can help in pain control from a single bony metastasis especially when dealing with spinal cord lesions or compression fractures. Corticosteroids can be also added to the regimen.

Surgical treatment has also a role in bony metastases. From a Kyphoplasty or Vertebroplasty both procedures in the armamentarium of the orthopedic surgeons to treat aggressive spinal metastases. These procedures can be performed by Orthopedists as well as Neurosurgeons and even Interventionist Radiologist under C-Arm radiographic control. Other surgical procedures may be necessary to stabilize the spine or other long bones following metastatic fractures in offering as well a "de-bulking of the metastatic tumor and relieve the compression of the tumor over the spinal cord.

Bone metastases has a tendency in raising the calcium in the blood (Hypercalcemia) which can easily lead to a coma if left untreated. Often a metastasis left without any treatment will weaken the bone and produce a subsequent fracture, affecting the ability to walk of the patient suffering from the lesion. The pain can be so intense that will affect the quality of life and the daily living abilities to have a functional life. Pathologic fractures will follow and if the spine is involved, paralysis may follow.

Bones metastases mean a form of advanced state of a cancer requiring medical care and support. The survival rate depend on the type of the primary but roughly, six months to some years will depend on the stages of the lesions. Many studies were performed on different types of cancer demonstrating different survival rate, by example survival rate too lung cancer metastasis to bone, taking six to seven months compared to 53 months from prostate cancer to metastasize to bone. In patients with a stage 1 cancer, a metastasis was less often seen when compared to a stage 4 at diagnosis. For other type, metastases to bone were found within 10 years, in 28% of people in a stage IV of the disease.

A cancer can be in remission and a new metastasis may be discovered. It is often seen in orthopedic practices among women treated for breast cancer following a long period free of disease but suddenly, developing a metastatic lesion in a long bone, especially the hip area. Remission is a term used for this asymptomatic period with no sign of cancer in the body. Tests can also confirm the absence of disease but if new lesions are discovered, we may use the term of "Recurrent disease" and more treatment will be needed.

Bone metastasis can affect the quality of life especially with the daily living pain and discomfort. One may need to take supportive measures to encourage healthy eating habits. Once you know that you have cancer, you have to deal with the possibility of having metastasis especially bony metastasis, especially because it can affect the quality of life. Palliative services will deal with the symptoms in providing pain medication and pain management support. More psychological counseling may help in the management of the mental issues. There are also new alternatives especially in dealing with kidney cancer treatment.

Finally, hospice care can be offered when there is no possibility of cure especially when the patient experiences poor quality of life and a life expectancy less than six months. Hospice can provide physical comfort, managing the patient's comfort. Metastasis to the spine can also produce spinal cord compression especially when the bone is eaten away by the tumor resulting in a pathological fracture.

One has to differentiate between Bone cancer and Bone Metastasis where a bone cancer started in the bones like an Ewing Sarcoma or Osteosarcoma and then spread to other bones of the body. A bony metastasis may become the first manifestation of a disease, causing pain and affecting your quality of life. A good examination and appropriate radiographical studies will help in the diagnosis. Metastatic bone disease may also spread from a primary organ site to bone and the spine is commonly involved.



A lateral view of the lumbar spine with a sclerotic metastatic lesion of a L2 vertebra. Patient is a 50-year-old gentleman with no apparent fracture.

Breast and Lungs like to spread to bone in almost 80% of the cases. Prostate and Lungs will spread as well in 80% of cases in men, leaving the 20% in both sexes to metastases from kidney, thyroid and other organs. Pain out of proportion, night pain in any patient after the age of 50 may give the suspicion of a metastatic disease, although it is not specific. Diseases of bone like Paget, or bone infection and osteomyelitis will as well manifest with bone pain.

There are tests which can help in diagnosing of a metastatic disease: Serum alkaline phosphatase may be related to bone destruction, Serum protein electrophoresis, Urine analysis and urine protein electrophoresis, "N-telopeptide" in type 2 collagen is a marker of bone absorption which can be used.

Imaging studies like any basic study can assess the extent of a tumor and the degree of cortical erosion. Computed tomography is a more sensitive modality to detect bone destruction. MRI is a most sensitive study to assess the anatomical extent of a lesion (intramedullary or extra-osseous). Bone scanning also is a very sensitive study for the detection of occult lesions and their level of activity.

Angiography is a useful tool, to assess how a suspicious lesion is vascularized, which can be useful for the surgeon exploring the extremity or even help in assessing the biologic activity of the metastasis. This can help in pain palliation especially if such lesion can't be explored. Some lesions can be embolized prior to any surgical procedure, minimizing the bleeding. It is important for the treating physician to have a tissue biopsy to assess a pathological diagnosis from the soft tissue mass if present or from the bone

itself. It can be obtained through a percutaneous core needle biopsy or an open biopsy.

Once the biopsy of a metastasis is done, the staging of the tumor can be discussed and appropriate treatments offered by the treating team (Surgeon, oncologist, radiologist etc.) Does the lesion discovered and the primary site requires stabilization because of an impending pathological fracture? The location of the lesion in the body (extremities, pelvis, spine etc.) may matter. Studies have demonstrated that 19% of patients with such metastases will develop hypercalcemia associated with a pathologic fracture. 10% will suffer from a spinal cord compression following a vertebra pathological fracture and 9% will also develop bone marrow failure.

Patients with metastases need help in the maintenance of their basic functional skills, like ambulation in their daily living activities. Metastatic lesions often may require surgical treatment or radiation therapy (RT) especially when dealing with spinal metastases. Studies have shown that patients with spinal metastasis who are functional at the beginning of their radiation therapy will remain ambulatory at the end of their treatment. Therefore, such loss must be prevented if a surgical intervention can be avoided.

About spinal surgical procedures for patients with metastatic bone disease, it is done to eliminate pain while decompressing (debulking) the neural elements and protecting the cord function while stabilizing a segment of the involved spine (Cervical, Thoracic or Lumbar). Vertebroplasty and Kyphoplasty, in which polymethyl-methacrylate is percutaneously introduced, may also be used as minimally invasive treatment alternatives for patients with one- or two-level vertebral body compression fracture.

The management of long-bone metastases with or without impending or pathologic fractures are often approached with the introduction of a locked intramedullary rod with or without the use of cement followed by Radiation Therapy, once the surgical wound has sufficiently healed. An open procedure with plate fixation can also be offered as well as a hemi-Arthroplasty or total joint replacement prosthesis in the treatment of hip or shoulder pathologic fractures involving the joints. The use of cement will depend on the surgeon preferences.

Medications can be also used in the treatment of metastatic bone disease like Monoclonal antibody antineoplastic agents (Denosumab, Pamidronate, Ibandronate, Zoledronate etc.).

In conclusion, metastasis cause mortality and morbidity in multiple malignancies and inflict bone pain, hypercalcemia, often fractures with the inability to bear weight over the long bones and the spine with spinal compression requiring surgical treatment. Often a hypercalcemia is present. The more, we understand the mechanisms contributing to such metastasis, the more we will be able to improve the therapeutic options, maintaining the quality of life and improve the survival rate. Knowledge in the pathophysiology of bone cancer improving and relations between bone cells and cytokines will provide better opportunities of treatment

We need to question the survival period with bone metastases. Many factors will influence like the type (Prostate or Breast) which can be measure in years, while lung cancers spread to bone in months. Finally, some people may be more resilient and may live longer than expected.

Maxime Coles MD

Boca Raton FL (Dec 2024)

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