Cancer Related Issues:
Bone Metastases

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Disclosures
Bronwyn Long has no real or perceived conflicts of interest that relate to this presentation.

Objectives
1. Review bone physiology
2. Describe the pathophysiology of bone metastasis
3. Discuss assessment for patients with bone metastasis
4. Examine management of patients with bone metastasis
Bone Basics

- Adult human skeleton: 206 bones
- Functions
  - Structure
  - Mobility
  - Protection
  - Hematopoiesis
  - Storage
  - Acid-base balance
  - Detoxification
  - Endocrine

Cortical or Compact Bone

- Hard outer shell of bone
- Composed of mineralized collagen
- 80% of total body
- Found in the appendicular skeleton

Trabecular or Spongy Bone

- Internal
  - Load bearing, shock absorbing
  - Spongy, mesh-like
  - 20% of total body
  - Bone core with bone marrow contact
  - Found in the axial skeleton
Bone Physiology

- Remodeling: normal balance between resorption and replacement
  - Osteoblasts
  - Osteoclasts
- Renew/repair bone and maintain metabolic balance

Bone Metastases

Tumor cells travel to metastatic sites through blood vessels and lymphatic system

Ideal environment for tumor cells: easily accessible blood supply, abundance of growth factors, porous nature
Bone Metastases Physiology

• Once tumor cells have invaded the bone matrix they produce growth factors that can directly or indirectly stimulate osteoclasts to degrade bone

• Growth factors that can stimulate tumor cell growth are released from bone, thus establishing a vicious cycle of bone destruction and local tumor growth

Types of Bone Metastases

- **Osteolytic Lesions**
  - Tumor produces substances that activate resorption
  - Increased bone destruction
  - Breast, lung, thyroid, renal, melanoma, GI
  - Multiple myeloma
  - Plain film

- **Osteoblastic Lesions**
  - Tumor produces cytokines that activate osteoblasts
  - Increased bone formation
  - Unbalanced osteolytic activity and marked bone turnover
  - Prostate, breast, lung, carcinoid
  - Bone scan

Most Common Site of Metastasis

- Axial skeletal sites have the greatest risk for developing bone metastasis
  - Spine 69%

- Ribs and lumbar spine most common area
  - Upper Limbs 10-15%
  - Pelvis 41%
  - Femur 25%
  - Rib Cage 58%
  - Skull 14%

*Source: About Cancer*
Clinical Consequences

- Skeletal-related events (SREs)
  - Pathological fractures
  - Spinal cord compression
  - Hypercalcemia
- Shortened survival
- Bone pain
- Anemia
- Reduced mobility
- Decreased quality of life

Symptoms of Bone Metastasis

- **Bone pain**
  - Intermittent to constant
  - Dull, aching or boring
  - Worsens throughout day and into night; with bed rest
  - Percussion tenderness
  - Back pain may be due to spinal cord compression or vertebral collapse
  - Acute pain may represent fracture

Symptoms of Bone Metastasis

- **Not all bone metastases cause pain**

- **Hypercalcemia**
  - Constipation, nausea, anorexia, extreme thirst, polyuria, fatigue, muscle weakness, confusion

- **Neurological impairment**
  - Spinal cord compression
    - Numbness, tingling, muscle weakness in extremities
    - Back pain
    - Difficulty with urination or bowel movements
Physical Exam

• Identify areas of discomfort
• Tenderness to palpation
• Acute or chronic pain locations
• Back pain
  • Radiates around to front
  • Numbness
  • Tingling
  • Loss of sensation below compression site
  • Change in bowel and bladder function
  • Muscle/motor weakness

Diagnostic Work-Up

• Plain film x-rays
• Bone Scan
• CT Scan
• MRI

Treatment Strategies

• Goals of treatment
  • Relieve pain
  • Preserve function
  • Maintain skeletal integrity
  • Prevent skeletal-related events (SREs)
  • Improve quality of life

• Modalities
  • Radiation, surgery, hormonal therapy, chemotherapy, and bisphosphonate therapy
  • Other medications
Radiation Therapy
- Standard of care for bone metastasis
- External beam is local treatment to treat pain and stabilize bone
  - Single fraction of 8 Gy
  - Multiple fractions
- Stereotactic body radiation therapy (SBRT)

Surgical Treatment
- Goal is to promote mobility and reduce pain
- Stabilization of the bone that is fractured or has impending fracture
- Fixation of the femur, humerus, pelvis and vertebrae are indicated

Radioisotopes for Bone Metastasis
- Radioisotopes have an affinity for bone
- Strontium-89 is a high-energy beta particle emitting radioisotope
  - Has been effective in decreasing pain
- Samarium-153 is also effective in alleviating pain in bone metastasis
- Both have bone marrow toxicity
- Osteoblastic lesions
- Multiple lesions
Chemotherapy
- Aimed at controlling the primary tumor
- Used to stabilize disease progression
- May not help with bone integrity

Diet and Exercise
- Diet
  - Calcium
  - Vitamin D
  - Limit alcohol intake
- Exercise
  - Regular exercise program
  - Moderate to intense weight bearing exercise
  - Strength/resistance training

Medication Management
- Pain Medications
  - NSAIDs
  - Corticosteroids
  - Opioids
  - Adjuvant
- IV Bisphosphonates
- RANKL Inhibitor
- Hormones
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Reduce inflammation and pain
- Aspirin
- Ibuprofen
- Naproxen
- Ketorolac
  - IV loading dose
- Risk of GI bleed, ulcer
- Monitor renal function

Corticosteroids

- Reduce inflammation and pain
- Rapid pain control
- Dexamethasone
- Risk of insomnia, psychosis

Opioids

- Long-acting analgesia
- Breakthrough pain relief
- Bowel regimen
- Monitor for urinary retention
Adjuvants

- Opioid-sparing regimen
- Acetaminophen
  - Monitor total daily dose
- Topical analgesia
  - Lidocaine 5% patch
- Anxiolytics
  - Benzodiazepines for anxiety, muscle relaxation
- Muscle relaxers

Bisphosphonates

- Potent inhibitors of osteoclast-mediated bone resorption
- Main goal is to stabilize bone and decrease pain
  - Prevent SREs
  - Pain control is not immediate
- Also effective in hypercalcemia
- IV more effective than PO
  - Zoledronic acid
  - Pamidronate

Bisphosphonate Therapy: Side Effects

- Skeletal/bony pain
- Nausea
- Fever
- Anemia
- Hypocalcemia/hypokalemia
- Renal insufficiency
- Osteonecrosis of the jaw (ONJ)
RANK Signaling and Bone Homeostasis

• The binding of RANKL to its receptor, RANK, induces a cascade of signaling events that drives differentiation, function, and survival of osteoclasts
• Essential for osteoclastogenesis
• Osteoclast-induced resorption
• Critical for remodeling
• Denosumab

Hormonal Therapy

• Used in hormonally sensitive tumors such as prostate and breast
• Can improve pain but not the integrity of bone caused by destructive lesions
• Calcitonin

Nurses Play a Pivotal Role

• Identify patients at risk
• Evaluate patient's complaints
• Identify symptoms of bone metastasis
• Help patients understand test results
• Discuss recommended treatment options
• Support, comfort, and palliative care
## References


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## References