PATHOLOGICAL FRACTURES

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Overview of today’s talk

- Introduction
- Incidence
- Mechanism of Metastasis
- Clinical Features
- Investigations / Radiology: salient features
- Evaluation
- Management – Principals
- Prognosis

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Definition:

A *pathological fracture* is one in which a bone is broken, through an area, weakened by pre-existing disease, by a degree of stress, that would have left the normal bone intact.

In other words, a fracture involving “abnormal bone” is a pathological fracture.
Etiology:

Development disorders of bone:

a) Congenital defects of bone tissue:
   - Osteogenesis imperfecta
   - Osteopetrosis

b) Disorder of cartilage growth:
   - Achondroplasia
   - Diaphyseal aclasis (multiple exostosis)
   - Dyschondroplasia (Ollier’s disease)

Nutritional and vitamin deficiencies:

- Scurvy
- Rickets
- Osteomalacia
• **Hormonal imbalance:**
  - Hyperparathyroidism
  - Cushing’s syndrome
  - Pathological fracture from cortisone treatment
  - Frohlich’s syndrome (hypopituitarism)

• **Atrophic conditions of bone:**
  - Disuse osteoporosis
  - Senile osteoporosis

• **Pathological fracture through infected bone:**
  - Osteomyelitis

• **Cystic disorders and fibrous dysplasia of bone:**
  - Unicameral bone cyst
  - Aneurysmal bone cyst
  - Non – osteogenic fibroma of bone
  - Monostotic and polyostotic fibrous dysplasia
Paget’s disease of bone
Primary and secondary tumors of bone:

a) **Primary benign tumors:**
   - Chondroma
   - Benign chondroblastoma
   - Chondromyxoid fibroma
   - Haemangioma of bone
   - Giant cell tumour of bone
   - Disappearing bone disease.

b) **Malignant tumors:**
   - Osteosarcoma
   - Chondrosarcoma
   - Fibrosarcoma
   - Malignant – fibrous histiocytoma
   - Malignant round cell tumour
   - Multiple myelomatosis

c) **Metastatic tumors of bone** – lungs, thyroid, kidney, GI tract, prostate and breast.
Marrow cell disorder:
   Histiocytos
   Gaucher’s disease
Parasitic disease of the bone:
   Hydatid disease
Neurotrophic dystrophies of the bone:
   Tabes dorsalis
   Syringomyelia
   Diabetic neuropathy
Iatrogenic pathological fracture:
   Through screw hole stress protection phenomenon
   Through biopsy
   After removal of infected bone
   Through a donor site for a bone graft

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## Clinical Importance and Prognosis of Bone Metastases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Disease prevalence, U.S. (in thousands)</th>
<th>Bone mets. incidence (%)</th>
<th>Median survival (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myeloma</td>
<td>75 - 100</td>
<td>70 - 95</td>
<td>24</td>
</tr>
<tr>
<td>Renal</td>
<td>198</td>
<td>20 - 25</td>
<td>12</td>
</tr>
<tr>
<td>Melanoma</td>
<td>467</td>
<td>14 - 45</td>
<td>6</td>
</tr>
<tr>
<td>Bladder</td>
<td>582</td>
<td>40</td>
<td>6 - 9</td>
</tr>
<tr>
<td>Thyroid</td>
<td>207</td>
<td>60</td>
<td>48</td>
</tr>
<tr>
<td>Lung</td>
<td>386</td>
<td>30 - 40</td>
<td>7</td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td>1,993</td>
<td>65 - 75</td>
<td>24</td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td>984</td>
<td>65 - 75</td>
<td>36</td>
</tr>
</tbody>
</table>

Pathophysiology of Bone Metastases

- Tumour cells
  - Primary
  - Systemic factors
  - Osteoclast activity
  - Bone secondaries
  - Local factors
  - Osteolysis
  - Direct bone destruction
  - Activated osteoclast
  - Bone
  - Bony complications
  - Growth factors
Cancer and Bone Cell Interactions

Osteolytic bone disease

1. Tumour cell
2. PTHrP, prostaglandin E
3. TGF-β, IL-6
4. Unknown

Osteoblastic bone disease

1. Tumour cell
2. PTHrP/IL-6
3. Osteoblast
4. TGF-β
5. Unknown GFs
Consequences of Increased Bone Resorption

- Increased bone resorption
- Hypercalcaemia
- Fracture
- Bone pain
### Common cancers which metastasise to bone

<table>
<thead>
<tr>
<th>Osteoblastic</th>
<th>Osteolytic</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Breast</td>
<td>• RCC</td>
<td>• Breast</td>
</tr>
<tr>
<td>• Prostate</td>
<td>• Thyroid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lung</td>
<td></td>
</tr>
</tbody>
</table>

Endothelin – 1  
ILGF  
Interleukin - 6  
PTHrp

85% of metastases from Breast, Lung, Prostate  
12% From RCC, Thyroid  
3% GIT

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Pathological fracture is suspected when fracture occurs:

- Spontaneously
- After minor trauma
- Unusual fracture pattern
- History of recent several fractures
- Older patient
- History of primary malignancy

Risk factors
INVESTIGATIONS:

RADIOGRAPHY:

PLAIN – X-RAY:

• Study the Fracture
• Don’t ignore the perifracture changes

Other lesions
Alteration in density and architecture
Extra osseous masses or abnormalities
• **Lesion location:**
  Usually eccentric
  Cortical involvement
  Diaphyseometaphyseal junction

• **Densities within the lesion:**
  Bone formation suggests – Osteosarcoma
  Calcification suggests – Chondrosarcoma

• **Reaction (periosteal / endosteal)** should be examined.
• Zone of transition
• Moth eaten or permeative pattern of bone reaction
LABORATORY STUDIES:

✓ Complete haemogram
✓ Peripheral smear
✓ Serum glucose
✓ Serum albumin
✓ Serum calcium, Phosphate
✓ Alkaline phosphatase
✓ LFT
✓ Urine sugar and albumin
✓ Bence-Jones proteins
✓ Serum electrophoresis

Tumor markers: Ca 125, Ca 19.9, CEA

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Search for occult primary carcinoma:

- Breast - Examination
  - Mammography
- Lung – Chest X-ray
- Kidney – Ultrasonography
- Thyroid – Digital palpation
- Prostate – Serum PSA
  - Digital prostate examination
- Myeloma – Bone marrow examination
  - Bence-Jones proteins
  - Serum and urine electrophoresis
  - Skeletal Survey - X-ray skull, spine and pelvis.
- Other organs

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MRI

- Marrow disease
- Epidural and nerve root compression can be detected
- Localize the disease
Bone scan

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Scan pattern

1. Increased accumulation in the bone - hot lesion
2. Defect cold lesion (MULTIPLE MYELOMA some metastases – breast)
   - rare (very fast growing – no bone reaction)
3. Flare phenomenon – increased number of lesions in the case of effective therapy
4. Super-scan - diffusely increased uptake (spread malignancies)
PET Scan

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GOALS OF TREATMENT Metastatic Bone tumors:

To provide pain-free maintenance of normal daily function
Management of Metastatic Bone Tumors

- Management of pain
- Avoiding the fracture
- Bone stabilization

- Conservative measures
- Role of Irradiation
- Role of Surgery

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Pain management

• Non-narcotic analgesics
• Nonsteroidal anti-inflammatory drugs
• Narcotic analgesics
• Interventional anesthetic techniques
Systemic Therapy

- Hormone therapy: Ca breast and prostate
- Chemotherapy
- Bisphosphonates: Zolindronic acid
- Targeted therapy: Denosumab
Mechanism of action – Zolindronic acid

They have affinity for hydroxyapatite crystals in bone.

1. Inhibit osteoclastic activity.
2. Prevents bone resorption.
3. Induces osteoclastic apoptosis.
4. Increases osteoblastic activity
5. Antiangiogenic properties (animal studies)
Radiotherapy

• External-beam radiotherapy
• Stereotactic Body Radiotherapy (SBRT)
• Radiopharmaceuticals : Unsealed source therapy with bone-seeking radionueclides

**Indication:**

✓ Pain
✓ Impending Fracture/ Fracture (Bone healing)
External RT: Dose and fraction

• 800 cGy in single fraction
• 3000 cGy in 10 fractions
• 2000 cGy in 5 fraction

Multiple painful bony lesion:
• Hemibody irradiation 15-20 Gy given @ 2.5-4Gy/ Fraction
• Radionuclide therapy

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Radionuclides

- Strontium-89, Samarium-153, P-32, Rhenium – 186 are commonly used to treat bone mets

- They get concentrated in highly active site of the bone and emit beta - particles which intern destroy the tumor cells

- It takes 7-14 days to see clinical response and the procedure can be repeated once in 12 weeks

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Surgical management

• Indication: Palliative
• Fracture: Ambulation / Pain relief
• Impending fracture
Impending fractures:

Mirel’s criteria for risk of fracture:

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Upper arm</td>
<td>Lower extremities</td>
<td>Peritrochanteric</td>
</tr>
<tr>
<td>Pain</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Lesion</td>
<td>Blastic</td>
<td>Mixed</td>
<td>Lytic</td>
</tr>
<tr>
<td>Size</td>
<td>&lt;1/3rd diameter of bone</td>
<td>1/3-2/3 diameter of bone</td>
<td>&gt;2/3rd diameter of bone</td>
</tr>
</tbody>
</table>
Mirel’s criteria for risk of fracture:

- **7 or less** – observation

- **8 or more** – prophylactic internal fixation

Most commonly used indication for prophylactic internal fixation of impending fractures are presence of destructive painful lesion 2.5cm in diameter or loss of 50% or more of cortex of long bone.
Prophylactic fixation:

Advantages:
- Decreased morbidity
- Decreased hospital stay
- Easier rehabilitation
- More immediate pain relief
- Faster surgery and less complications
- Less blood loss during surgery

Risks:
- Temporary
- Fixation device may eventually fail
- Loss of fixation is the most significant complication
Prosthetic replacement
Fracture / Impending fracture
Spine

Solitary lesion
Multiple lesion
With / without neurological deficit

Management

• Diagnosis
• Prevention of neurological deficits
Winking Owl Sign
### Assessment of Prognosis in Metastatic Spine Tumors – Tokuhashi 1990

<table>
<thead>
<tr>
<th>Category</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General condition (Performance status)</strong></td>
<td></td>
</tr>
<tr>
<td>Poor (PS 10-40%)</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (PS 50-70%)</td>
<td>1</td>
</tr>
<tr>
<td>Good (PS 80-100%)</td>
<td>2</td>
</tr>
<tr>
<td><strong>No. of extraspinal bone metastases foci</strong></td>
<td></td>
</tr>
<tr>
<td>( \geq 3 )</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>No. of metastases in the vertebral body</strong></td>
<td></td>
</tr>
<tr>
<td>( \geq 3 )</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Metastases to the major internal organs</strong></td>
<td></td>
</tr>
<tr>
<td>Unremovable</td>
<td>0</td>
</tr>
<tr>
<td>Removable</td>
<td>1</td>
</tr>
<tr>
<td>No metastases</td>
<td>2</td>
</tr>
<tr>
<td><strong>Primary site of the cancer</strong></td>
<td></td>
</tr>
<tr>
<td>Lung, stomach, kidney, liver, uterus, thyroid, prostrate, breast, GI, others</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td><strong>Spinal cord palsy</strong></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>0</td>
</tr>
<tr>
<td>Incomplete</td>
<td>1</td>
</tr>
<tr>
<td>None</td>
<td>2</td>
</tr>
</tbody>
</table>
Treatment plan - Harrington

**Class I:** No significant neurological involvement

**Class II:** involvement of bone without collapse or instability and minimal neurological involvement

**Recommended treatment for Class I & II:**
Chemotherapy and hormonal manipulations. If no response, RT.

**Class III:** major neurological impairment without significant involvement of bone

**Recommended treatment for Class III:** usually only RT, if acute onset neurological deficit – add steroids.

**Class IV:** vertebral collapse with pain attributable to mechanical causes or instability but without significant neurological compromise

**Class V:** patients with vertebral collapse or instability with major neurological compromise.

**Recommended treatment for Class IV & V:** surgical management with adjuvant RT.

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Percutaneous Vertebroplasty/Kyphoplasty

PMMA
(Polymethylmethacrylate)

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Spine metastasis: Summary

• Single vertebral metastasis with cord compression: **Surgery**

• Impending fracture, better projected survival – **Surgical fixation and RT**

• Multiple spinal mets : **RT**

• Diffuse skeletal mets with severe pain : **Radionuclide therapy**
Approach to diagnosis of Metastatic lesion
Multiple skeletal lesions
  - Conventional approach

- Basic investigations
- MRI
- CT thorax/Abdomen/Pelvis/PET Scan
- Workup for Myeloma
- Tumor markers
- Endoscopy / Colonoscopy
- Biopsy
Investigations

• S. Alk Phosphatase
• Myeloma profile:
  ESR
  S. Electrophoresis
  Bence Jones Proteins
  Skeletal survey – Skull, pelvis, spine
• True cut core needle biopsy
• Bone marrow aspiration and biopsy

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Cancers of unknown primary site: ESMO Clinical Recommendation for diagnosis, treatment and follow-up

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On behalf of the ESMO Guidelines Working Group*  
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\(^2\)Department of Medical Oncology, Heraklion General Hospital, Heraklion, Greece;  
\(^3\)Medical Oncology Service, Vall d’Hebron University Hospital, Barcelona, Spain

<table>
<thead>
<tr>
<th>Assessment suggested</th>
<th>Target patient population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal standard work-up</td>
<td>All patients</td>
</tr>
<tr>
<td>Thorough medical history and physical examination</td>
<td>All patients</td>
</tr>
<tr>
<td>Basic blood and biochemistry survey</td>
<td>All patients</td>
</tr>
<tr>
<td>Urinalysis and testing for fecal occult blood</td>
<td>All patients</td>
</tr>
<tr>
<td>CT scans thorax, abdomen and pelvis</td>
<td>All patients</td>
</tr>
<tr>
<td>Work-up for clinicopathological subsets</td>
<td></td>
</tr>
<tr>
<td>Mammography or breast MRI (optional)</td>
<td>Female with axillary adenopathy</td>
</tr>
<tr>
<td>Serum aFP and bHCG</td>
<td>Patients with midline metastatic disease</td>
</tr>
<tr>
<td>Serum PSA</td>
<td>Male with adenocarcinoma bone metastases</td>
</tr>
<tr>
<td>Head and neck CT scan or CT/PET scan (optional)</td>
<td>Cervical adenopathies with squamous cell carcinoma</td>
</tr>
<tr>
<td>Endoscopy</td>
<td>Must be sign or symptom oriented</td>
</tr>
</tbody>
</table>

CUP: 3 – 4% of all malignancies
Algorithm for evaluation of a patient with a known history of Cancer

AGGRESSIVE BONE LESION IN A PATIENT WITH A HISTORY OF CANCER

Search for other painful anatomic sites and order plain radiographs or computerized tomography (CT)* scan for each one of them

Total body bone scintigraphy

No other lesions were found in either plain radiographs or bone scintigraphy

Biopsy the diagnosed lesion

Other bone lesions were detected

Order baseline plain radiographs and CT* for all lesions detected

Biopsy the most accessible lesion to establish the diagnosis of metastatic bone disease

* CT is done for lesion of the spine, pelvic girdle, and shoulder girdle
Never ever give up!

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Thank you