ECD and Pain Management

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Background

• Erdheim Chester disease (ECD) is a rare non-Langerhans cell histiocytosis, commonly involving the musculoskeletal system.

• Other tissue can also be involved, including the central nervous system, cardiac, lung resulting in a wide spectrum of clinical features, at times being nonspecific.

• ECD should be considered as a differential diagnosis in patients presenting with bony pain and nonspecific features of multiorgan involvement.
Background

- Clinical presentation can vary from asymptomatic tissue infiltration, bony pains to multiorgan failure

- ECD presents commonly with skeletal symptoms, diabetes insipidus (DI), neurological, and constitutional symptoms

- Bone involvement occurs in about 96% of the cases.

- Classically involves appendicular long bones (distal femur, proximal tibia, and fibula, and less commonly the ulna, radius, and humerus)

- The most common presenting symptom is persistent bone pain (50% of patients) in lower limbs, especially around knees and ankles.
Key Points of Comprehensive Assessment

• Recognize pain and its location, subjective quality, and severity
• Assess not only the type and intensity of pain but how it impacts life of patient
• Use pain assessment to determine the pathophysiology and select treatment strategies
• Determine the best time(s) to assess and reassess the pain
• Establish comfort/function goals with the patient
Pain management

• Pharmacotherapy
  • analgesic ladder
    • opioid analgesics, non-opioid analgesics, adjuvant analgesics

• Adjuvant Techniques
  • Non-invasive
    • Relaxation techniques, distraction techniques, biofeedback, psychosocial interventions
  • Invasive
    • Nerve blocks, surgical or chemical ablation, spinal opioid infusion
Treatment of Bone Pain

- Limited evidence regarding medications for treating bone pain

- Bisphosphonates have shown partial success by reducing bone pain.

- Radiation therapy

- Steroids

- Opioids
Pain Definitions and Pathophysiology

- ...sensory and emotional experience associated with tissue damage or described in terms of such damage –IASP
- Acute / Chronic
- *Nociceptive pain: somatic / visceral*
- Neuropathic pain
- Basal pain / Breakthrough pain
- Psychogenic pain
- Idiopathic pain
Multifactorial Nature of Pain

- Neuropathic Mechanisms
- Somatic or Visceral Nociception
- Psychological State and Traits
- Loss of Work
- Physical Disability
- Fear of Death
- Psychosocial Influences
- Social/Family Functioning
- Financial Concerns

(Adapted from Portenoy, 1988)
Therapeutic Approaches

- Pharmacotherapy
- Rehabilitative
- Psychological
- Anesthesiologic / Surgical
- Complementary and alternative
- Lifestyle changes
Pain Ladder

Step 1: Non-opioids—aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen

Step 2: Mild opioids (e.g., codeine, tramadol) +/- non-opioids

Step 3: Strong opioids (e.g., morphine) +/- non-opioids

Mild to moderate pain

Moderate to severe pain

Severe pain

Mild to moderate pain

Moderate to severe pain

Severe pain
Opioid Therapy: Drug Selection

- Long-acting opioid around-the-clock plus a short-acting opioid rescue dose pm
  - Preferred approach for patients with cancer pain and selected others with chronic pain
  - Rescue dose may or may not be appropriate for all patients, depending on syndrome and ability to use the drug responsibly
  - Rescue is 5%-15% of total daily dose; usually prescribed “q4h pm” when oral

Portenoy, JCO 2014: Principles of Opioid Use in Cancer Pain
# Overview of STRONG Opioids

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Onset (minutes)</th>
<th>Peak effect (hours)</th>
<th>Duration (hours)</th>
<th>Initial scheduled dose</th>
<th>Available Oral/TD Formulation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone/Acetaminophen Hydrocodone ER</td>
<td>PO: 30</td>
<td>1-1.5</td>
<td>IR: 4</td>
<td>5/325 mg po q4h</td>
<td>Tablet, Liquid, Tablet</td>
<td>Co-ingestion with alcohol increases peak concentration</td>
</tr>
<tr>
<td></td>
<td>PO: 60</td>
<td></td>
<td>LA: 12</td>
<td>10mg po q12h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>PO: 30</td>
<td>0.5-1</td>
<td>IR: 3-6</td>
<td>LA: 15 mg po q12h, IR: 7.5mg po q 4 hrs prn</td>
<td>Tablet, cap, liquid</td>
<td>Kadian® can be given via PEG tube (16Fr or larger)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>PO: 10-15</td>
<td>0.5-1</td>
<td>IR: 3-6</td>
<td>LA:10 mg po q12h, IR: 2.5-5mg po q 4 h prn</td>
<td>Tablet, Liquid</td>
<td>Long acting formulation reformulated to minimize drug abuse</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>PO: 15-30</td>
<td>0.5-1</td>
<td>IR: 3-5</td>
<td>LA: 8mg po once daily, IR: 1-2 mg po q4h</td>
<td>Tablet, Liquid</td>
<td>ER Hydromorphone available in 8mg, 12mg, 16mg, 32mg</td>
</tr>
<tr>
<td>Methadone</td>
<td>PO: 30-60</td>
<td>1-7.5</td>
<td>Variable</td>
<td>PO: 2.5 mg po q12h</td>
<td>Tablet, Liquid</td>
<td>Multiple drug interactions, monitor electrolytes, QTc</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>PO: 10-15</td>
<td>0.5</td>
<td>8 (IR) 12 (ER)</td>
<td>ER: 10 mg po q12h, IR: 5mg po q 6-8h prn</td>
<td>Tablet</td>
<td>Co-ingestion with alcohol and food increases peak concentration</td>
</tr>
<tr>
<td>Fentanyl Transdermal</td>
<td>TD: variable, typically takes &gt;5 hours</td>
<td>24-48</td>
<td>72</td>
<td>12meg patch Q 72 hours</td>
<td>patch</td>
<td>Adjust dose after 3 days. May take up to 2 applications to reach steady state</td>
</tr>
</tbody>
</table>
Pain score ≥ 4

Opioid Naive
  - Oral Route
  - Dose 5-15mg po short acting Morphine or equivalent

Opioid Tolerant
  - Oral Route
  - Dose 2-5mg IV Morphine or equivalent
  - Calculate previous 24 hr total PO requirement and administer 10-20%
  - Calculate previous 24 hr total PO requirement and convert to total IV equivalent and administer 10-20%
Opioid Management

• Opioids are the preferred medications to treat cancer related pain

• Challenges still exist
  - Inadequate pain control
  - Common side effects like nausea and constipation
  - Opioid induced neurotoxicity
Opioid Induced Neurotoxicity (OIN)

- Caused by accumulation of the parent opioid and its metabolites
  - Excessive sedation
  - Hallucination
  - Confusion
  - Myoclonus
  - Seizures
Opioid Rotation (OR)

• Substituting one opioid with another using equianalgesic ratios

• Indications
  ➢ Uncontrolled pain
  ➢ Opioid induced neurotoxicity
  ➢ Common side effects
  ➢ Route of administration
  ➢ Opioid availability
Treatment of OIN

- Opioid rotation
- Dose reduction or discontinuation
- Hydration
- Discontinuation of other contributing drugs
- Symptomatic treatment with neuroleptics
Opioid Rotation for Uncontrolled Pain

- Balance between analgesia and side effects to allow dose escalation
- Large individual variation in response to different mu-agonists
- Incomplete cross tolerance between opioids
- Higher cross tolerance to adverse effects than to analgesic effects
• 31% of cancer outpatients and 34% of cancer inpatients required OR by the palliative care team
• Uncontrolled pain most common indication for OR in outpatients and adverse effects such as OIN most common indication in inpatients
• 65% of cancer outpatients had successful OR
• 81% of cancer inpatients had a successful OR
• MEDD significantly decreased in patients with successful OR and also in patients with OIN as reason for OR
Neuropathic pain

- Tricyclic antidepressants
- Anticonvulsants
- Clonidine
- Corticosteroids
- Local anesthetics
# Non Pharmacological Methods of Pain Management

- Distraction
- Hypnosis
- Meditation
- Relaxation
- Exercise
- Biofeedback
- Guided Imagery
- Acupuncture
- Pet Therapy
- Art Therapy
- Music Therapy
- Reiki