Sharing Care in Multiple Myeloma

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Multiple Myeloma
A Different Chronic Disease

• Uncommon, but not rare
  – 20K new diagnoses each year in US
• Needs long-term management
• Always balance psychosocial concerns with goals of therapy
• Potential for high symptom burden, more pain and disability
• Focus on disease control rather than cure
Presentation

• 34% asymptomatic
• **CRAB mnemonic**
  – **Calcium** >11 mg/dL
    • anorexia, somnolence, polydipsia
  – **Renal insufficiency/failure** creatinine >2 mg/dL
    • fatigue, malaise, anorexia
  – **Anemia** (Hgb <10 g/dL)
    • usually normocytic or slightly macrocytic
    • fatigue, weakness, malaise
  – **Bone**
    • pain, lytic lesions, compression fractures, osteoporosis
    • ribs, long bones, vertebra
• **Other**
  – Hyperviscosity, amyloidosis, >2 bacterial infections in last year, carpal tunnel syndrome
When Should I Investigate?

- Bone or back pain and fatigue > 2-4 weeks in an older person
- Differential diagnosis
  - Vitamin D deficiency
  - Hyperparathyroidism
  - Polymyalgia rheumatica
  - Bone metastases
Laboratory

- CBC
- ESR
- Chemistry panel
- Serum and urine protein electrophoresis
- Vitamin D level
- Urine dipsticks insensitive to Bence Jones protein
Imaging

- Skeletal radiograph survey
  - Lytic lesions apparent with >50% trabecular bone loss
- MRI preferred for suspected spinal compression or soft-tissue plasmacytomas
- DEXA has no role
- Nuclear bone scans not indicated
  - Lack of osteoblastic activity
- Avoid studies with contrast media
  - Nephrotoxicity
Treatment of Common Problems

• MM not currently curable
  – Asymptomatic patients do not require treatment

• Hypercalcemia
  – Saline hydration and diuresis
  – Bisphosphonates

• Symptomatic anemia
  – Transfusions and erythropoietin
    • No data on quality of life benefits
    • Increased risk of thrombosis when combined with thalidomide
Pain Management

- Important to treat
  - often undertreated
- May vary in severity
- Need to treat chronic and acute pain
- Easily overlooked source of misery
- Significant impact on coping mechanisms and depression
- Opioids are preferred
- Avoid nonsteroidal anti-inflammatory drugs
  - Adverse renal effects
Bone Disease

- Bisphosphonates
  - Decrease vertebral fractures and pain
  - No change in mortality
  - IV versions preferred
    - Pamidronate
    - Zoledronic acid
  - Jaw osteonecrosis unusual
    - Seen after dental extraction

- Vertebral compression fracture
  - Vertebroplasty and kyphoplasty
  - Radiation generally not required
Immunizations

- Flu vaccine
  - Safe
  - Annual
  - 6 months after transplant

- Pneumococcal vaccine
  - Both PCV13 and PPSV23 now recommended
  - If not previously vaccinated, administer PCV13 first
    - PPSV23 6-12 months after
  - If previously received PPSV23, administer PCV13 ≥12 months after

- Zoster vaccine

- Haemophilus influenzae B
Prophylaxis

- **Trimethoprim/sulfamethoxazole**
  - Recommended for *Pneumocystis carinii*
  - During high-dose steroid therapy

- **Acyclovir or valacyclovir**
  - Recommended for herpes zoster virus
  - During bortezomib-based therapy
Miscellania

- Risk of second malignancies
- Psychosocial stressors
- Physical and occupational therapy
- Support for families with MM
Major Categories of Side Effects for Novel MM Treatments

- Myelosuppression
- Thromboembolic events
- Peripheral neuropathy
- Gastrointestinal side effects
- Steroid side effects
- Challenge for management of emergent side effects
  - Lack of effective practitioner-based guidelines produces a barrier to providing optimal patient care
Myelosuppression: Definition and Symptoms

- **Anemia**
  - Fatigue, malaise and SOB

- **Neutropenia**
  - Increased risk of bacterial, fungal, and viral infections

- **Thrombocytopenia**
  - Bruising and bleeding
Management of Myelosuppression

<table>
<thead>
<tr>
<th></th>
<th>Anemia</th>
<th>Neutropenia</th>
<th>Thrombocytopenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalidomide/Dexamethasone</td>
<td>16%</td>
<td>13%</td>
<td>4%</td>
</tr>
<tr>
<td>Lenalidomide/Dexamethasone</td>
<td>8%</td>
<td>21%</td>
<td>10%</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>12%</td>
<td>14%</td>
<td>32%</td>
</tr>
</tbody>
</table>

- **General recommendations:**
  - Monitor signs and symptoms
  - Monitor CBC
  - Educate on signs and symptoms

- **Myelosuppression management:**
  - Growth factor therapy
  - Dose reduction as appropriate
  - Transfusion as indicated
Overview of Thromboembolic Events

• Cancer patients have a higher risk of TE events (blood clots), which may lead to:
  – Deep vein thrombosis (DVT)
  – Pulmonary embolism (PE)

• MM patients are at an increased risk for blood clots
  – Patients are at increased risk with high-dose dexamethasone treatment
  – The risk for DVT/PE is further increased in patients treated with novel therapies:
    • Thalidomide
    • Lenalidomide

• Measures to prevent novel therapy-associated TE events include:
  – Mechanical
  – Myeloma regimen-related
  – Anticoagulant therapy (clot-preventing)

TE events are serious and potentially life-altering and life-threatening.
DVT/PE: Signs/Symptoms

- Swelling, erythema, warm extremity
- Cyanosis/cool skin
- Distension of superficial venous collateral vessels
- Anxiety
- Sudden dyspnea
- Chest discomfort
- Tachycardia
- Tachypnea
- Low-grade fever

PE IS AN EMERGENCY!
Peripheral Neuropathy: Definition, Signs, and Symptoms

Damage to the peripheral nervous system, including any injury, inflammation, or degeneration of peripheral nerve fibers

- Signs/symptoms:
  - Temporary Numbness
  - Tingling
  - Parasthesias
  - Sensitivity to touch
  - Muscle weakness

- Severe symptoms:
  - Burning pain
  - Muscle wasting
  - Paralysis
  - Organ dysfunction

Thalidomide/bortezomib can cause peripheral neuropathy
### Table 2. National Cancer Institute: Grading of Peripheral Neuropathy

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral motor neuropathy</td>
<td>Asymptomatic; clinical or diagnostic observations only; intervention not indicated</td>
<td>Moderate symptoms; limiting instrumental ADL</td>
<td>Severe symptoms; limiting self-care ADL; assistive device indicated</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>Asymptomatic; loss of deep tendon reflexes or paresthesia</td>
<td>Moderate symptoms; limiting instrumental ADL</td>
<td>Severe symptoms; limiting self-care ADL</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
</tr>
</tbody>
</table>

**Definition:** A disorder characterized by inflammation or degeneration of the peripheral motor nerves

**Definition:** A disorder characterized by inflammation or degeneration of the peripheral sensory nerves

*ADL = activities of daily living.*

*US Department of Health and Human Services.*

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General Strategic Recommendations for the Management of PN

- Ongoing evaluation
- *Dose and schedule modifications*
- Pharmacological interventions
- Non-pharmacological interventions
- Patient education

**Pharmaceutical**
- For all patients prior to therapy:
  - B-complex vitamins including B1, B6, B12 (at least 400 mcg)
  - Folic acid 1 mg daily
- For grades 2 or higher
  - Tricyclic antidepressants
  - Amino acids on an empty stomach
  - Neurontin®, Lyrica®, Cymbalta®
  - Lidoderm® patch 5% to affected area every 12 hours

**Non-Pharmaceutical**
- Gentle massage of affected areas with cocoa butter, capsaicin cream
- Home health referral to review safety at home
- Assistance with ADL
- Referrals: pain management, neurology, physical/occupational therapy
# Gastrointestinal Side Effects of Novel Therapies

<table>
<thead>
<tr>
<th>Drug</th>
<th>Constipation</th>
<th>Diarrhea</th>
<th>Nausea</th>
<th>Vomiting</th>
</tr>
</thead>
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<tr>
<td>Lenalidomide/Dexamethasone</td>
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<td>Thalidomide/Dexamethasone</td>
<td>55%</td>
<td>12%</td>
<td>28%</td>
<td>12%</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>42%</td>
<td>57%</td>
<td>57%</td>
<td>35%</td>
</tr>
</tbody>
</table>
Management of Diarrhea

• **Non-pharmacologic**
  – Increase fluid intake
  – Avoid caffeinated, carbonated, or heavily sugared drinks
  – Dietary changes: avoid fiber

• **Pharmacologic**
  – Caution concerning medications or herbal supplements, which can cause diarrhea
  – Antidiarrheal agents:
    • Imodium®
    • Lomotil®
    • Tincture of opium
    • Sandostatin®
  – Intravenous hydration to correct electrolyte imbalance
Management of Nausea and Vomiting

- **Non-pharmacologic**
  - Dietary intolerance and restrictions
  - Avoid exercise and do not lie flat for 2 hrs after eating
  - Fresh air and loose clothing
  - Relaxation, guided imagery, biofeedback, acupuncture

- **Pharmacologic**
  - Select anti-emetics based on how strongly the novel agents stimulate N/V and consider type of N/V.
    - **Nausea**: Ativan®, Compazine®, Decadron®, Pepcid®, Phenergan®, Reglan®, or Zantac®
    - **Vomiting**: Emend®, Zofran®, Kytril®, Anzemet®, or Aloxi®
  - Intravenous hydration to correct electrolyte imbalance
Overview of Steroid Side Effects

• Steroid classes:
  – Glucocorticosteroids
  – Corticosteroids
  – Used as single agents and in combos
    • Dexamethasone
    • Prednisone
    • Prednisolone
Steroid Side Effects

- Insomnia
- Psychiatric illness
- Personality changes
- Infections
- Osteoporosis
- Cataracts

- Diabetes
- Fluid retention
- Sexual dysfunction
- Rash
- Hypertension
- Epigastric pain
- Gastric ulcers
Management of Steroid-Dependent Side Effects: Constitutional

- Steroids affect every system
- Psychological:
  - Mood alterations, let-down effect, insomnia
- GI: flatulence/hiccoughs
- Musculoskeletal: proximal myopathy and muscle cramping
- Bone: osteonecrosis, osteoporosis
- Endocrine: hyperglycemia, hypogonadism, sexual dysfunction
- CV: edema
Management of Side Effects

• Effective management includes:
  – Monitoring patients carefully
  – Educating patients and caregivers about what to expect during treatment
  – Appropriate prophylaxis
  – Pharmacologic and non-pharmacologic interventions

• Effective management leads to:
  – Increased adherence to therapy
  – Improved quality of life
  – Prevention of serious adverse events that can lead to prolonged hospitalization, and increased morbidity and mortality