Getting Patients through Therapy: Supportive Care in Multiple Myeloma

Kathleen Colson, RN, BSN, BS

Dana-Farber Cancer Institute
Learning Objectives

Learning objectives:
Upon completion of the program, the participant should be able to:

- Identify the classic clinical presentation and symptoms of multiple myeloma
- Identify nursing interventions to provide supportive care for patients with multiple myeloma
- Outline supportive care strategies for patients with multiple myeloma
Approximately how many Multiple Myeloma patients does your clinic treat on a monthly basis?

1. 1 to 10
2. 10 to 20
3. 20 to 30
4. 30 +

35% 21% 10% 34%
Continuing Evolution of Multiple Myeloma Treatment: Selected New Classes and Targets 2015-2016

1st Generation Novel Agents
- lenalidomide
- carfilzomib
- thalidomide
- bortezomib
- doxorubicin
- pomalidomide
- panobinostat

2nd Generation Novel Therapies/Immunotherapy
- IMiD
- HDAC inhibitor
- Monoclonal antibody
- Vaccines
- Proteasome inhibitor
- Chemotherapy
- Adoptive T cell therapy
- Checkpoint inhibitors

*Not yet FDA-approved for MM; available in clinical trials

IMiD, immunomodulatory drug; HDAC, histone deacetylase

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Supportive Care: Keeping all the Pieces Together
Myeloma Can Result in a Broad Spectrum of Clinical Manifestations

- M Protein
- Immune Deficiency
- Marrow Infiltration
- Destruction of bone

- Renal Compromise (30%)
- Neuropathy (33%)
- Infection (15%)
- Hypercalcemia (15-20%)
- Bone pain (75-80%)
- Lytic lesions (70%)
- Anemia (~70%)

http://myeloma.org/ArticlePage.action?articleId=1044.
DEFINITION OF MULTIPLE MYELOMA (SMOLDERING AND ACTIVE)

Smoldering (Asymptomatic) Myeloma

- Serum monoclonal protein
  - IgG or IgA ≥ 3 g/dL;
  - Or
    - Bence-Jones protein ≥ 500 mg/24 h
    - And/or
  - Clonal bone marrow plasma cells 10%–60%
  - And
  - Absence of myeloma-defining events or amyloidosis
    - If skeletal survey negative, assess for bone disease with whole body MRI or PET/CT

Active (Symptomatic) Myeloma

- Clonal bone marrow plasma cells ≥ 10% or biopsy-proven bony or extramedullary plasmacytoma
  - And
  - Any one or more of the following myeloma-defining events:
    - Calcium > 0.25 mmol/L (> 1 mg/dL) higher than the upper limit of normal or > 2.75 mmol/L (> 11 mg/dL)
    - Renal insufficiency (creatinine > 2 mg/dL) [≥ 177 μmol/L] or creatinine clearance < 40 mL/min
    - Anemia (hemoglobin < 10 g/dL or hemoglobin > 2 g/dL below the lower limit of normal)
    - One or more osteolytic bone lesions on skeletal radiography, CT, or PET/CT
    - Clonal bone marrow plasma cells ≥ 60%
    - Abnormal serum FLC ratio ≥ 100 mg/L (involved kappa) or ≤ 0.01 (involved lambda)
    - > 1 focal lesions on MRI studies ≥ 5 mm

MYEL-A
Bone Disease: Pain

- Accumulation of myeloma cells in bone inhibits normal bone formation
- Increased osteoclast activity (bone resorption)
- Multiple osteolytic lesions in bone
- Supportive therapy
  - Physical therapy, bisphosphonates, radiation, pain medication, kyphoplasty, and vertebroplasty

COMMON SITES OF BONE INVOLVEMENT

Skull (35%)
Spine (49%)
Thoracic Lumbar Vertebrae
Spinal cord compression 2-3%
Pelvis (34%)
Long bones (~20%)

Myeloma Bone Pathology

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Vertebroplasty or Balloon Kyphoplasty
For Tumor-Related Vertebral Compression Fractures

Vertebroplasty and Kyphoplasty stabilize the fracture and correct spinal deformity caused by fractures

Mayo Clinic. www.mayoclinic.org/vertebroplasty
Bisphosphonates Inhibit Bone Destruction

- Bisphosphonates are recommended for all myeloma patients with bone disease
  - Pamidronate
  - Zoledronic acid

- Monitor patients for
  - Renal dysfunction
  - Osteonecrosis of the jaw

Bisphosphonates and Osteonecrosis

- Uncommon complication causing avascular necrosis of the maxilla or mandible

- Suspect with tooth or jaw pain or exposed bone

- May be related to duration of bisphosphonate therapy

How often do you use bisphosphonate therapy (pamidronate or zolendronic acid) with your myeloma patients?

1. Never
2. Monthly
3. Every other month
4. Yearly

- Never: 78%
- Monthly: 5%
- Every other month: 14%
- Yearly: 4%
Renal Dysfunction

- Myeloma proteins are filtered by the kidneys
- Accumulated proteins can cause tubular damage (*Bence Jones* proteins, in particular)
- Not all patients develop renal insufficiency
- Hypercalcemia contributes to renal damage
- Supportive therapy
  - Hydration, avoid NSAIDs, avoid IV contrast

NSAIDS = nonsteroidal anti-inflammatory drugs; IV = intravenous.

Renal: Light Chain Disease
(Bence Jones proteinuria)

- Roughly 30% of patients with MM produce more light chains, which are incomplete immunoglobulins
- Light chains are small enough to pass into urine and block the kidneys
- Also known as kappa [κ] or lambda [λ] light chain myeloma

Renal Health

► Risk Factors
  – Active multiple myeloma
  – High calcium
  – Other medical issues

► Symptoms

► Prevention
  – Avoid certain medications (IV contrast, NSAIDs)
  – DRINK WATER

► Treatment
  – Hydration
  – Treatment for myeloma
  – Dialysis

Anemia

• Common presenting symptom of myeloma
• May also be a result of decreased kidney function, myeloma treatment or other medications.

Symptoms of anemia
• Fatigue, low energy level
• Unable to do regular activities
• Shortness of breath or chest pain with activity
• Pale appearance

Treatment
— Use of red blood cell supplements, with caution
— Possible red blood cell transfusion
— "Energy-sparing" activities
— Reduced dose of medications

Gastrointestinal (GI)

- Constipation, nausea, and diarrhea can occur
- GI symptoms are generally mild
- Nausea
  - Make sure the patient is on PPI
  - Assess for other competing meds that may cause
- Constipation
  - Bowel regimen
- Diarrhea
  - Rule out C.diff or other infection, investigate other causes, loperamide or atropine / diphenoxylate

Recurrent Infection

• May have 15-fold increased risk
• With increased myeloma cells, WBC production ↓
• Normal immune role of plasma cell is lost
• Supportive therapy
  – Antibiotics, IVIG therapy
  – Consider pneumonia and influenza vaccines, and prophylaxis for *Pneumocystis carinii*, herpes zoster, fungal infections

Multiple Myeloma Research Foundation. 2007. www.multiplemyeloma.org
Herpes Zoster

- Herpes Zoster Eruption
Possible Side Effect of Treatment: Peripheral Neuropathy (PN)

- Sensory, motor, autonomic
- Risk
- Symptoms
- Side effect of MM treatment or the disease

Cavaletti et al., 2007; Smith et al., 2013
### Peripheral Neuropathy (PN):
#### Risk Factors and General Considerations

**Non-MM Causes of PN:**
- Endocrine disorders
  - Hypothyroidism
  - Diabetes
- Nutritional disease
  - Vitamin B deficiency
  - ETOH
- Connective tissue disease
- Vascular disease
- Medications
- Herpes zoster
- Most common symptoms
  - Sensory deficits, pain

**MM Disease- and Treatment-Related Hyperviscosity syndrome**
- Hypergammaglobulinemia
- Incidence of PN in untreated pts: 39%
- Incidence of grade 3/4 PN
  - Bortezomib: 26% to 44%
    - ↓ with weekly vs twice weekly dosing
  - Thalidomide: 28% to 41%
    - ↑ with higher doses duration
  - Carfilzomib: overall 14%
  - Pomalidomide: Mild, up to 9%

### Venous Thromboembolic Events: Signs and Symptoms of clot in MM

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>DVT</strong></td>
<td><strong>PE</strong></td>
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<tr>
<td>Slight fever</td>
<td>Anxiety</td>
</tr>
<tr>
<td>Rapid heart rate</td>
<td>Sudden shortness of breath</td>
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<tr>
<td>Unilateral swelling, erythema, warm extremity</td>
<td>Chest discomfort</td>
</tr>
<tr>
<td>Cyanosis/cool skin if blockage</td>
<td>Rapid pulse and heart rate</td>
</tr>
<tr>
<td>Dull ache, pain, tight feeling over area and palpation</td>
<td>Low-grade fever</td>
</tr>
<tr>
<td>Homan’s sign (35% patients)</td>
<td>Pleural friction rub, crackles, diminished breath sounds, wheezing</td>
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</tbody>
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Managing Side Effects of Treatment: Deep Vein Thrombosis and Pulmonary Embolism

• **Strategies to reduce risk of clots:**
  - Anti-embolism stockings (*elastic stockings*)
  - Exercise regimen
  - Low-dose aspirin/anti-coagulation therapy
  - Moving frequently when sitting long periods
  - Travel precautions (Foot/leg exercises, walking, ASA if not already on blood thinner)

• **When taking immunomodulatory medications**
  - Lower drug doses
  - Different dosing schedule
  - Blood thinning with anticoagulation therapy

Targets for monoclonal antibody therapy in myeloma

Adapted from: Anderson KC. J Clin Oncol 2012;30:445-452
Infusion-related reactions (IRRs)

• **IRRs can occur with mAbs**
  – e.g. rituximab causes mild to moderate infusion reactions in most patients\(^1\)

• **Possible signs and symptoms of acute infusion reactions\(^2\)**
  – Allergic reactions/hypersensitivity
  – Skin reactions (itching, rash, urticaria)
  – Systemic reactions (fatigue, fever, sweating, dizziness, myalgia)
  – Respiratory reactions (bronchospam, dyspnea)
  – Cardiovascular symptoms (tachycardia, hypotension)

Infusion-related reactions: SIRIUS trial  (n=106)
(daratumumab monotherapy)

- IRRs in 43%
- Predominantly grade 1 or 2  (5% grade 3; no grade 4)
- Typically during first infusion
- Only 7% had an IRR after the first infusion
- Most common IRRs: nasal congestion (12%), throat irritation (7%), cough, dyspnea, chills, vomiting (6% each)
- No patients discontinued treatment due to IRRs

Lonial et al. ASCO 2015 (Abstract LBA8512); oral presentation
Management of IRRs

• In case of occurrence of IRRs
  – React early to mild signs of symptoms and immediately stop the infusion
  – Look out for upper respiratory tract reactions as early signs
  – Manage symptoms appropriately, consider e.g. antihistamines, corticosteroids
  – Once symptoms have resolved, treatment may be resumed at half the infusion rate
  – In case of grade 4 IRRs permanently discontinue treatment

Summary

• Nurses are positioned to educate patients, identify and intervene side effects
• Knowledge of the drugs and class effects allow for better education, surveillance and continued therapy
• The potential for longer survival exists due to appropriate supportive care measures