Case Study Discussions on the Nurse’s Role in Caring for Patients With Hematologic Malignancies

Welcome and Overview

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www.LLS.org/CE
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Have no affiliations with commercial interests to disclose

Acute Promyelocytic Leukemia (APL) Overview and Case Study

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Outline

- Leukemias and outcomes
- History of APL
- Epidemiology
- Treatment and outcomes in large trials
- What happens outside of a trial
- High mortality outside of a trial
- What is involved in our co-management

Leukemias and Outcomes

**Chronic Leukemias**
- **Chronic myelogenous leukemia (CML)**
  - Imatinib (Gleevec) $\geq 90\%$ survival
- **Chronic lymphocytic leukemia (CLL)**
  - Indolent disease in the elderly
  - Wide array of treatments is available

**Acute Leukemias**
- **Acute lymphoblastic leukemia (ALL)**
  - Generally pediatric disease with $\geq 80\%$ cure rate
  - Cure rates are approximately $40\%$–$50\%$ in adults
- **Acute myelogenous leukemia (AML)**
  - Generally seen in older patients
  - M1 to M7: $50\%$ cure rate across the spectrum
- **M3 – Acute promyelocytic leukemia (APL)**
APL Therapy – History

Discovery t(15;17) in APL
Daunorubicin in APL
In vivo leukemic cell differentiation
Differentiation of APL cells with RA
ATRA therapy
ATRA + CT
ATO in relapse
ATO frontline
ATO + ATO ± GO


HIGHLY FATAL HIGHLY CURABLE

ATO, arsenic trioxide; ATRA, all-trans retinoic acid; CT, chemotherapy; GO, gemtuzumab ozogamicin; RA, retinoic acid.

APL Diagnosis – Pathology

• Pancytopenia – low counts
• DIC common
• Bruising – typical complaint
• Bleeding – quite serious
  – Serious bleeds with normal lab findings
• CNS bleeds – common
  – Most likely reason for patient deaths due to bleeding

CNS, central nervous system; DIC, disseminated intravascular coagulation.
APL – Epidemiology

- APL is an uncommon disease with approximately 1000 new cases per year in the US
- Rare below 10 years of age
- Most common between the ages of 20 and 60 years
- Historically, this is the first disease for which targeted treatment was developed
- Highly effective and curable treatments
  - All-trans retinoic acid (ATRA), arsenic trioxide (ATO), and anthracyclines
APL Survival in Large Cooperative Group Trials

Overall Survival

OS, overall survival.

Australasian APML4 (adding ATO to ATRA/chemo)

CI, confidence interval; DFS, disease-free survival; EFS, event-free survival; HR, hazard ratio; OS, overall survival.
ATRA/ATO vs ATRA/Chemotherapy

What Happens Outside of a Trial

Case Study Discussions on the Nurse’s Role in Caring for Patients With Hematologic Malignancies
Case Study – Real-World Patient

- 56-year-old female; Jehovah’s Witness
- Current diagnosis of flu, normal CBC (early December), treated with Tamiflu; DVT (late December), repeat CBC showing pancytopenia
- Subsequent work-up resulted in a diagnosis of APL
- Refused blood transfusions, so she was supported with cryoprecipitate, Aranesp, Procrit and G-CSF, which was approved by her congregation

CBC, complete blood count; DVT, deep vein thrombosis; G-CSF, granulocyte colony-stimulating factor.

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Population-Wide Survival in the US

- Survival of 90% in multicenter trials is not a reflection of the outcome in the general population. **Death rate of 5% to 10% is an underestimate**
- Recent analysis of US SEER data from 2000–2008 by investigators from MD Anderson showed 71% survival at 1 year and 64% at 5 years
- Current trials that are changing sequence, adding new drugs, and/or withholding maintenance will only have a minimal effect on the survival
- Biggest impact will be made by decreasing early deaths

SEER Data (1975–2008)

Survival Data From SEER Registries

Expected ~95%
## Early Deaths in APL (Days 1 to 30)

<table>
<thead>
<tr>
<th>Study</th>
<th>Total patients</th>
<th>Patients died</th>
<th>Mortality rate</th>
<th>Percentage of patients with hemorrhage in early death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil (2007)</td>
<td>154</td>
<td>43</td>
<td>32%</td>
<td>66%</td>
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<tr>
<td>Anakura &amp; Numaya Turkey (2010)</td>
<td>49</td>
<td>20</td>
<td>40%</td>
<td>65%</td>
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<td>Swedish registry (2011)</td>
<td>105</td>
<td>30</td>
<td>29%</td>
<td>41%</td>
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<tr>
<td>SEER data (2011)</td>
<td>1400</td>
<td>230</td>
<td>13% (24% in 55+ age)</td>
<td>Not discussed</td>
</tr>
<tr>
<td>AHMS, India</td>
<td>33</td>
<td>6</td>
<td>18.1</td>
<td>50% in total patients during induction</td>
</tr>
<tr>
<td>Stanford (2012)</td>
<td>70</td>
<td>19</td>
<td>26%</td>
<td>54%</td>
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<tr>
<td>GRU (new country)</td>
<td>19</td>
<td>7</td>
<td>37%</td>
<td>57%</td>
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<td>ASCO 2012</td>
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</tr>
<tr>
<td>German, &gt;60 years, (2013)</td>
<td>91</td>
<td>24</td>
<td>24%</td>
<td>Not discussed</td>
</tr>
<tr>
<td>Japanese &gt;60 years, Hiroshima (2013)</td>
<td>32</td>
<td>7</td>
<td>21.9%</td>
<td>Not discussed</td>
</tr>
</tbody>
</table>

## Case Study Discussions on the Nurse’s Role in Caring for Patients With Hematologic Malignancies

Why Is There High Mortality Outside of a Trial?
Possible Reasons

- Selection bias: possible reason
- Delayed treatment
  - Delay in ATRA treatment is commonly cited but not the case
- Decreased supportive care?
  - Probably the biggest reason
    - Prior to ATRA, early deaths in GIMEMA were <10
    - They have a network of treatment centers that follow written guidelines
    - MD Anderson had 5/44 early deaths in their clinical trial but 9/40 after the trial closed

Can We Do Something Different?

[Cartoon: IS THIS THE WAY? WHAT? HEHEHEHE HEHEHEHE
See No Evil Hear No Evil Speak no Evil]

Image used with permission from Bearman Cartoons.
Strategy (at GRU)

- Developed a simple 1.5-page treatment algorithm
- Quick diagnosis
- Ad hoc meeting and treatment planning
- Rapid initiation of therapy
- Aggressive management of coagulopathy
- Prevention of differentiation syndrome; early recognition and management of ATRA syndrome
- Prophylaxis and aggressive treatment of infections
- Implemented in 2010

Methods Used to Decrease Early Deaths

- Reviewed the literature
- Reviewed all patient charts
- Attended national meetings and talked to experts
- Attended the International APL meeting in Rome
- Obtained an external consultant to review our death charts
- Identified the three main causes of death in the first month: BLEEDING, DIFFERENTIATION SYNDROME AND INFECTION
- Implemented a proactive, simple program to decrease early deaths—at a point when the rest of the country did not recognize this as a problem
Case Study Discussions on the Nurse’s Role in Caring for Patients With Hematologic Malignancies

What Is Involved in Our Co-Management

Treatment Outside Our Center

• Co-manage patients
• Text or email has worked very well
• Discuss day-to-day care in case they are more complicated
• Idea is to get them through induction
APL – Workup

- Quick diagnosis
- Rapid initiation of therapy
- Aggressive management of coagulopathy
- Prevention of differentiation syndrome; early recognition and management of ATRA syndrome
- Prophylaxis and aggressive treatment of infections
  (APL IS A MEDICAL EMERGENCY. TREATMENT WITH ATRA SHOULD BE STARTED ASAP)
- Labs, BMBX, ECHO, PICC (no invasive procedures)

Supportive Care

- Tumor lysis prophylaxis
- Antibacterial prophylaxis – Levofloxacin 500 mg QD
- Antifungal prophylaxis – Voriconazole 200 mg PO BID or posaconazole 200 mg PO TID
- Antiviral prophylaxis – Acyclovir 400 mg BID
- Keep hemoglobin in the 8 range

- APL IS A MEDICAL EMERGENCY. TREATMENT WITH ATRA SHOULD BE STARTED ASAP
Treatment of Coagulopathy

- Coagulopathy is a major problem. Procoagulants released by leukemia cells and fibrinolysis
- Intracranial, pulmonary and GI bleeding
- Treatment with ATRA should start ASAP
- Keep platelets above 50,000
- Keep fibrinogen above 150
- If there is clinical evidence of bleeding, give FFP twice a day as you are starting ATRA and chemotherapy until bleeding resolves
- After all clinical and lab coagulopathy resolves, blood product support is like any other leukemia

Differentiation Syndrome

- Dyspnea, unexplained fever, weight gain, ARF, CHF, pleuropericardial effusions and interstitial pulmonary infiltrates
- Meticulous monitoring of intake and output. Daily weights
- Keep I/O matched (SHOULD BE METICULOUS)
- Diuretics should be used if there is evidence of fluid retention and weight gain
- Dexamethasone 10 mg BID should be started as soon as symptoms are noted
- In patients with a WBC >10,000, dexamethasone 10 mg BID could be started before initiating ATRA
- Temporary discontinuation of ATRA or ATO is indicated only in case of severe APL differentiation syndrome

FFP, fresh frozen plasma; GI, gastrointestinal. ARF, acute renal failure; BID, twice daily; CHF, congestive heart failure; WBC, white blood count.
Treatment: AIDA Regimen Example

• Induction
  – **Low-risk patients**
    • WBC <10,000 and platelet count >40,000
    • GIMEMA protocol. ATRA on day 1 followed by idarubicin 12 mg/m² on days 2, 4, 6 and 8 (AIDA)
  – **Intermediate-risk and high-risk patients**
    • WBC >10,000 and platelet count <40,000
    • ATRA to be started as soon as diagnosis is suspected
    • Idarubicin to be started on the same day and given per the GIMEMA protocol on days 1, 3, 5 and 7. Even if genetic results are unavailable, it is reasonable to give anthracycline
    • Older patients (individualized)

Older Patients With APL

• Need to individualize
• Maybe begin with single-agent ATRA
• Dose reduction of ATO
• Meticulous supportive care
Nursing Considerations

- Meticulous monitoring of patient during the first 10 days during which 70% of deaths occur
- Primary goal is to decrease early deaths within the first month; three main causes of death in the first month: **BLEEDING, DIFFERENTIATION SYNDROME AND INFECTION**
- Rapid initiation of therapy
- Aggressive management of coagulopathy
- “Normal” laboratory values can still cause bleeding
- Prevention or early recognition and management of ATRA syndrome
- Prophylaxis and aggressive treatment of infections
- Outpatient consolidation, provide calendars, dialogue with patient and family

Consolidation and Maintenance

- Generally depends on induction protocol
- If you pick a regimen, try to stick with the same follow-up treatments
  - Two to three cycles of anthracycline-based consolidation, given along with ATRA
  - ATO-based consolidation
- After completion of consolidation, a bone marrow evaluation should be done to demonstrate molecular remission
  - If molecular remission is achieved, maintenance with 1–2 years of oral ATRA + MTX and 6MP may be beneficial

6MP, 6-mercaptopurine; MTX, methotrexate.
**Algorithm**

- CBC, CMP, and DIC Panel to include Fibrinogen, D-Dimers, PT and PTT twice a day until all laboratory and clinical coagulopathy is completely resolved.
- Supportive care.
- Echocardiogram.
- Baseline chest X-ray.
- PICC Line. Do NOT attempt to put central lines or perform other surgically invasive procedures such as Bronchoscopy or Spinal Tap.
- Supportive care.
- Tumor lysis prophylaxis.
- Antibiotic prophylaxis with Levofloxacin 500 mg po qd or similar antibiotic.
- Antifungal prophylaxis with Posaconazole 200 mg po tid, Voriconazole 200 mg po bid or another agent with similar efficacy.
- Anti-viral prophylaxis with Acyclovir 400 po bid or Valacyclovir 1000 mg PO daily.
- Red cell transfusion is similar to other leukemias and suggested to transfuse at or below 7 g/dl.
- APL IS A MEDICAL EMERGENCY. Treatment with ATRA should be started asap.
- Differentiation syndrome.
- Meticulous monitoring of intake and output.
- Daily weights.
- Diuretics should be used if clinically there is evidence of fluid retention and weight gain.
- Dexamethasone at 10 mg BID should be started as soon as symptoms are noted.
- In patients with a WBC >10,000, Dexamethasone 10 mg bid could be started before initiating ATRA.
- Temporary discontinuation of ATRA or Arsenic Trioxide (ATO) is indicated only in case of severe APL DS.
- Dexamethasone should be maintained until complete disappearance of symptoms and ATRA or ATO should be restarted. Dexamethasone should be stopped 3 days after all DS symptoms have resolved.
- Anthracycline based induction.

**Induction of low risk patients**

(WBC <10,000/ml and Platelets >40,000/ml)

- GIMEMA protocol. ATRA on Day 1 followed by idarubicin 12 mg/m2 on Days 2, 4, 6, and 8.

**Induction of intermediate risk and high risk patients**

(WBC > 10,000 and Platelet count <40,000)

- Idarubicin to be started on the same day and given per the GIMEMA protocol on days 1, 3, 5, and 7. Even if the genetic results are not available, it is reasonable to give the anthracycline.
- Aggressive management of coagulopathy.

**Arsenic trioxide based induction**

Can be considered in the following patient groups:

a) Low and intermediate risk patients (WBC < 10,000/ml)

b) Age >70

c) Not candidates for conventional chemotherapy for any reason.

- Should be restricted to patients with confirmed PML-RAR alpha.
- ATRA at 45 mg/m2 in divided doses twice a day along with Arsenic at 0.15 mg/kg daily, both continued till complete hematologic remission.
- Watch for differentiation syndrome.
- Follow for prolongation of QT interval. Keep Mg above 2.0 and K above 4.0.
- Follow LFTs and for grade 2 to 4 liver dysfunction, HOLD Arsenic.

**Hydroxyurea use for Leukocytosis:**

- NO LEUCOPHERESIS
- WBC 5 - 10k – Hydroxyurea 500 mg qd day
- WBC 10 – 15k Hydroxyurea 500mg BID
- WBC 15 – 20k – Hydroxyurea 500mg TID
- WBC 20 – 50k – Hydroxyurea 500 mg QID
- WBC > 50k – Hydroxyurea 1000 mg QID
- Could also give a dose or two of Idarubicin 12mg/m2 if the Leukocytosis does not resolve or DS does not resolve in spite of using Dexamethasone.

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**Experience in Other Diseases**

- STEMI – Shorter door-to-balloon time improves survival
- In stroke patients, administration of TPA within 3 to 4.5 hours of symptom onset improves survival
- **THE GOAL IS TO STREAMLINE THE PROCESS**

STEMI, ST-segment elevation myocardial infarction; TPA, tissue plasminogen activator.


Strategy to Decrease Early Deaths at Main and Affiliate Sites

- Primary goal: prospectively assess 30-day mortality; Secondary goal: collect survival data
- Widespread education of hematologists, oncologists and nursing staff about early deaths and the need for rapid diagnosis and treatment
- At main sites: Ad hoc meeting at patients’ admission with physicians, residents and nurses and rapid initiation of therapy
- At affiliate sites: An Investigator will help manage patients at affiliate sites using the same algorithm as outlined in the strategy we have used so far
- Decrease induction mortality to 5%–8%

Survival Pre- and Post-Algorithm

- Post algorithm N = 90, Median survival 220 days
  Mortality 6.6% (6/90)
- Pre-algorithm N = 19
  Median Survival 1865 days
  Mortality rate 37%
Planned Coverage on New NCI-ECOG Trial

- Half the population of MN: ~2.5 m
  Sub I: Dr. Mark Litzow

- Half the population of AL: ~2.5 m
- Half of IL: ~5 m
  Dr. Altman
- Half of NC and TN: ~8 m
  Dr. Tallman
- Cover entire population of ~15 m
  Dr. James Foran
- Parts of NY and PA: ~10 m
  Dr. Tallman
  Dr. Luger
- Half of FL: ~10 m
  Dr. Luger

States with Investigators:
ECOG centers:

Resources

- Difficult obtaining patient assistance for drug
- Very expensive
- No patient assistance programs for drug cost
- The Leukemia & Lymphoma Society’s Information Resource Center (refer to support and financial assistance programs)
- Limited pharmaceutical assistance program
- Social work (prescription plans, financial, transportation)
Conclusions

- Early deaths can and **SHOULD** be prevented in APL
- This concept was already validated in Latin America—Brazil, Chile, Uruguay and Mexico. Decreased early deaths from 32% to 15%
- Expedite diagnosis and treatment
- Proactively manage the three main causes of death
- Treating oncologists may be unaware of the problem
- Minimize complications from the presence of thrombocytopenia/bleeding/infection
- APL is a **curable** disease amongst the leukemias


Thank You
Chronic Lymphocytic Leukemia (CLL) Overview and Case Study

Lynn Rich, ANP-BC, OCN
Nurse Practitioner
JP Wilmot Cancer Institute
University of Rochester
Rochester, NY

Outline

- Define disease
- Describe how CLL/SLL is different from leukemia: acute vs chronic leukemia
- Natural history of disease
- Epidemiology
- Rai staging
- Goal of treatment
- Case study
What Is CLL?

- Chronic lymphocytic leukemia (CLL) is a cancer of the lymphocytes that normally work as immune cells to protect against infections.

![Image of blood cells with labels](Image courtesy of JP Wilmot Cancer Institute; Chronic Lymphocytic Leukemia (CLL) Booklet.)

CLL

- CLL is caused when a single B lymphocyte becomes abnormal because of damage (mutation) to its DNA.
- Once this occurs, the body no longer controls this cell, so it continues to divide and lives longer than it should.
- This abnormal cell becomes CLL.
CLL vs SLL

- Small lymphocytic lymphoma (SLL) is a variant of the disease in which there are not a lot of abnormal lymphocytes in the blood
- World Health Organization (WHO) classification considers the two diseases to be identical—one disease at different stages

CLL – Lymphocyte dysfunction is in the bone marrow
SLL – There is more lymph node and lymphoid tissue involvement (vs bone marrow)
CLL vs Acute Leukemia

- Chronic leukemias usually **progress slowly**, and there are a greater number of **mature cells** that can generally carry out normal function.
- Acute leukemias are diseases that **progress rapidly** and affect cells that are **not fully developed**.
How Is CLL Diagnosed?

- Often found on random complete blood count (CBC) by primary
- Notice an elevated white blood count (WBC), specifically elevated lymphocytes

Case Study: Maria S.

- 76-year-old widowed female in reasonably good health; no other comorbidities
- Retired bus driver
- Lived in upstate NY
- March 2011: went to primary
  - Fatigue; “just did not seem right”
- Noted to have elevated WBC: 30 (normal 4–10)
- Was sent to local community oncologist
Normal CBC

- WBC – normal 4–10
- Differential:
  - Neutrophils: 1.8–5.4 K/uL (ANC)
  - Lymphocytes: 1.3–3.6 K/uL (ALC)
  - Monocytes: 0.3–3.6 K/uL
  - Eosinophils: 0–0.5 K/uL
- ALC >5.0 – **criteria to meet CLL** (lymphocytosis) must show clonality on peripheral blood
- 2008 update of the National Cancer Institute guidelines

Natural History of CLL

- Considered indolent (slow-growing) in nature
- Can watch for 5–10 years without intervening
- Life expectancy could be 10–20 years
- However, some patients need treatment quickly and aggressively
- How can we tell?
Further Staging: FISH (fluorescent in situ hybridization)

- 13 q = favorable (17-year median OS)
- Trisomy 12 and 11 q = less favorable (9–11 years)
- 17p – associated with mutated TP53
  - Poor response rate
  - Short duration of response with standard treatment
  - Most unfavorable prognosis (7-year median OS)

Example: Combined 11q + 17p = more unfavorable

Case Study: CBC at Presentation

- WBC: 30
- ALC: 6.0
- What else is needed when initially diagnosed?
- Obtain CT staging scans
  - Assess for organomegaly, extent of lymphadenopathy
  - Patient did not have
- Obtain bone marrow biopsy
  - Assess for evidence of disease; if so, how much?
  - Patient had 85% CLL in bone marrow
Epidemiology

- In 2013, an estimated 119,386 people in the United States were living with CLL
- 15,720 people were expected to be diagnosed with CLL in 2014

Total CLL expected in 2014: 120,000
New CLL cases in 2014: 15,720

The most common type of leukemia in Western countries
Considered disease of the elderly
Median age at diagnosis is 70 years
However, not unusual to make this diagnosis in younger individuals from 30–39 years of age
### Modified Rai Clinical Staging for CLL

<table>
<thead>
<tr>
<th>Risk</th>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0</td>
<td>Lymphocytosis in blood or bone marrow</td>
</tr>
<tr>
<td>Intermediate</td>
<td>I</td>
<td>Lymphocytosis + enlarged lymph nodes</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Lymphocytosis + enlarged liver or spleen with/without lymphadenopathy</td>
</tr>
<tr>
<td>High</td>
<td>III</td>
<td>Lymphocytosis + anemia (Hgb &lt;11), with/without enlarged liver, spleen or lymph nodes</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>Lymphocytosis + thrombocytopenia (&lt;100) with/without anemia, enlarged liver, spleen or lymph nodes</td>
</tr>
</tbody>
</table>

Hgb, hemoglobin.  

### Case Study: Patient

- March 2011: Presented with intermediate Rai stage  
- August 2011: Rituximab  
- October 2011: Bendamustine/Rituximab  
- January 2012: Increasing WBC, enlarging organomegaly  
- Responded poorly: ALC from 30 to 100  

- Referral made to CLL specialist at University of Rochester: clinical trial options

ALC, absolute lymphocyte count.
Ibrutinib: BTK

- 140-mg oral tablet:
  - CLL dose is 480 mg daily
  - FDA approved in 2014
Case Study: Treatment Course

- Significant lymphocytosis: WBC spikes within first month of treatment
- Usually takes 2–3 months for WBC to return to normal

Other Nursing Considerations

- Reasonably well tolerated
  - Not known to cause nausea
- Important side effect profile
- Bleeding and bruising
  - Should be considered “blood-thinning agent”
  - Hold 5–7 days prior to invasive procedure; restart 7 days after
- Known to cause some diarrhea
  - Typically can treat through; expect 1–2 bouts per day for first week. Patients usually recover quickly
Duration of Response

- Patients attain a complete remission
- How long will this last?
- Patients have been in remission for up to 3 years to date

Survivorship Issues

- Social workers and nursing: necessary to offer extensive emotional support
- During remission: often feel satisfied with response, but fearful of time because they wonder how long remission will last
- Secondly, ibrutinib is an expensive drug
  - Often need social work support to assist with financial assistance
  - Often turn to The Leukemia & Lymphoma Society for assistance with information gathering, as well as financial support
Audience Discussion Question
Many oncologists consider any patient diagnosed with cancer a survivor, what makes a CLL survivor different? What special considerations are required in this population?

Multiple Myeloma Overview and Case Study

Beth Finley-Oliver, RN, BSNc, OCN
Primary Nurse
Moffitt Cancer Center
Tampa, FL

This presentation was recorded in the studio following the ONS symposium
Outline

- Understanding the Disease
  - Staging systems
  - Response criteria
- Case Study
- Treatment Strategy
  - Transplant vs non-transplant candidate
- Treatment Options
  - Newly diagnosed
- Nursing Considerations for Myeloma Patients
  - Bone health
  - Kidney health
  - Anemia
  - Preventing complications
- Multidisciplinary Team
  - Social worker
  - Physical and occupational therapist
    - Financial assistance

What Is Myeloma?

Cancer of plasma cells
- An uncontrolled growth of plasma cells

Myeloma begins in the bone marrow
- Spongy tissue found in the center of bones
“M-spike” – Monoclonal Paraproteins

Myeloma Cell
- Produce Antibodies

Antibody
- Heavy and light chain components

Intact Ig Myeloma
~80% MM
Eg. IgG kappa

Light Chain Myeloma
~15%–20% MM
Eg. kappa

Non-Secretory/Oligosecretory
~0.5%–5% MM
Eg. kappa

Heavy Chain
- IgG > IgA >> IgD & IgE >> IgM

Light Chain
- Kappa (κ) > lambda (λ)

Ig, immunoglobulin; MM, multiple myeloma.

Diagnosing Myeloma

Blood and urine tests
Bone marrow biopsy or aspiration
Imaging tests
Diagnosis: “CRAB” Criteria

Presentation:
- Hypercalcemia (C)
- Renal Failure (R)
- Anemia (A)
  - Fatigue
- Fractures (B)
  - Bone pain
- Infections (I)


Lytic Lesions

Ca++
**Durie-Salmon Staging System**

**Stage I**
- All of the following:
  - Hemoglobin >10 g/dL
  - Serum calcium normal (<12 mg/dL)
  - Bone X-ray normal or solitary bone plasmacytoma only
  - Low M-protein production (IgG <5 g/dL; IgA <3 g/dL)
  - Bence-Jones protein <4 g/24 hours

**Stage II**
- Fitting neither stage I nor III

**Stage III**
- One or more of the following:
  - Hemoglobin <8.5 g/dL
  - Serum calcium >12 mg/dL
  - Advanced lytic bone lesions
  - High M-protein production rates (IgG >7 g/dL; IgA >5 g/dL; Bence-Jones protein >12 g/24 hours)

**International Staging System (ISS)**

**Stage I**
- Factors: Beta-2 microglobulin <3.5 mg/L
- Albumin ≥3.5 g/dL

**Stage II**
- Factors: Beta-2 microglobulin <3.5 mg/L
- Albumin <3.5 g/dL or Beta-2 microglobulin ≥3.5–<5.5 mg/L

**Stage III**
- Factors: Beta-2 microglobulin ≥5.5 mg/L

**Better Response to Therapy**

**Lesser Response to Therapy**

**Most Favorable Prognosis**

**Less Favorable Prognosis**
**MM Risk Stratification**

<table>
<thead>
<tr>
<th>High Risk (25%)</th>
<th>Standard or Good Risk (75%)</th>
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<tbody>
<tr>
<td>t(4;14) by FISH</td>
<td>Hyperdiploidy</td>
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<tr>
<td>t(14;16) or t(14;20) by FISH</td>
<td>t(11;14) by FISH</td>
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<td>Deletion 17q13 by FISH</td>
<td>t(6;14) by FISH</td>
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<td>Deletion 13 by metaphase analysis</td>
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<tr>
<td>Plasma cell labeling index &gt;3.0</td>
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<tr>
<td>Beta-2 microglobulin &gt;5.5</td>
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<tr>
<td>High-risk MyPRS™</td>
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</tbody>
</table>

FISH, fluorescence in situ hybridization; MM, multiple myeloma; MyPRS, Myeloma Prognostic Risk Signature.

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**Factors Influencing Treatment Choice**

Myeloma Stage  
Age  
Overall Health Status  
Patient Preference  
Cytogenetics

**Response Criteria**

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<thead>
<tr>
<th>Response Type</th>
<th>M Protein</th>
<th>Plasma Cells in Bone Marrow</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stringent complete response (sCR)</td>
<td>None (blood/urine)</td>
<td>No abnormal plasma cells</td>
<td>No free light chains</td>
</tr>
<tr>
<td>Complete response (CR)</td>
<td>None (blood/urine)</td>
<td>&lt;5%</td>
<td>Disappearance of soft tissue plasmacytoma</td>
</tr>
<tr>
<td>Very good partial response (VGPR)</td>
<td>&gt;90% reduction (blood)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>&gt;50% reduction in serum and &gt;90% reduction in urine</td>
<td>NA</td>
<td>&gt;50% reduction in the size of soft tissue plasmacytoma</td>
</tr>
<tr>
<td>Minimal response (MR)</td>
<td>25%–49% reduction in blood and reduction of 50%–89% in urine</td>
<td>NA</td>
<td>25%–49% reduction in the size of soft tissue plasmacytoma</td>
</tr>
<tr>
<td>Stable disease (SD)</td>
<td>Does not meet criteria for response or progressive disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive disease (PD)</td>
<td>&gt;25% increase (blood or urine)</td>
<td>&gt;10%</td>
<td>New bone lesions, soft tissue plasmacytoma, high calcium levels</td>
</tr>
</tbody>
</table>


---

**Case Study**

- **61-year-old male**
- **Presentation**
  - SPEP: 3.6
  - IgG: 6791
  - Serum free light chain - Lambda: 89.56
  - Beta-2 microglobulin: 2.3
  - Albumin: 3.2 g/dL
  - Calcium: 8.2 mg/dL
  - Creatinine: 0.8 mg/dL
  - Hemoglobin: 9.3 g/dL
  - UPEP: 156 mg/24 hours
- **BMBX 70%–80% plasma cells**
- **Survey + lytic lesions**
  - Skull
  - 8th rib fracture
- **FISH results**
  - Hyperdiploidy
  - 13q deletion
  - t(11;14)
  - ISS II
  - Durie-Salmon Stage 2A

BMBX, bone marrow biopsy; FISH, fluorescence in situ hybridization; Ig, immunoglobulin; SPEP, serum protein electrophoresis; UPEP, urine protein electrophoresis.
Treatment Options for Transplant-Eligible Patient

• Transplant
  • Avoid melphalan
  – RVD
    • Lenalidomide 25 mg, days 1–14
    • Bortezomib 1.3 mg/m², days 1, 4, 8, and 11
    • Dexamethasone 20 mg PO, days 1, 2, 4, 5, 8, 9, 11, and 12
  – VDC
    • Bortezomib 1.3 mg/m², days 1, 4, 8, and 11
    • Cyclophosphamide 500 mg PO, days 1, 2, 4, 5, 8, 9, 11, and 12

Bisphosphonate Monthly

RVD, lenalidomide, bortezomib, and dexamethasone; VDC, bortezomib, dexamethasone, and cyclophosphamide.

Response: VGPR

BMT evaluation: PR, 2 more cycles

BMT, bone marrow transplant; Ig, immunoglobulin.
### Disease Course

<table>
<thead>
<tr>
<th>Date</th>
<th>M spike (g/dL)</th>
<th>IgG (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/11/2012</td>
<td>0</td>
<td>1000</td>
</tr>
<tr>
<td>02/04/2013</td>
<td>0</td>
<td>2000</td>
</tr>
<tr>
<td>02/22/2013</td>
<td>0</td>
<td>3000</td>
</tr>
<tr>
<td>03/15/2013</td>
<td>0</td>
<td>4000</td>
</tr>
<tr>
<td>04/05/2013</td>
<td>0</td>
<td>5000</td>
</tr>
<tr>
<td>04/26/2013</td>
<td>0</td>
<td>6000</td>
</tr>
<tr>
<td>05/13/2013</td>
<td>0</td>
<td>7000</td>
</tr>
<tr>
<td>08/09/2013</td>
<td>0</td>
<td>8000</td>
</tr>
</tbody>
</table>

**High-dose melphalan and autologous transplant 6/5/2013**

---

Ig, immunoglobulin.

---

### Case Study Discussions on the Nurse’s Role in Caring for Patients With Hematologic Malignancies

### Nursing Considerations
Managing Side Effects

Immunomodulatory Drugs (IMiDs)

<table>
<thead>
<tr>
<th></th>
<th>Thalidomide</th>
<th>Lenalidomide</th>
<th>Pomalidomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelosuppression</td>
<td>Minimal</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>VTE</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>GI</td>
<td>Constipation</td>
<td>Diarrhea</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Rash</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Sedation</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Teratogens!

GI, gastrointestinal; VTE, venous thromboembolism.
Proteasome Inhibitors

<table>
<thead>
<tr>
<th></th>
<th>Bortezomib</th>
<th>Carfilzomib</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Schedule</strong></td>
<td>Days 1, 4, 8, and 11 every 21 days</td>
<td>Days 1, 2, 8, 9, 15, and 16 every 28 days</td>
</tr>
<tr>
<td><strong>Modes of administration</strong></td>
<td>IV/SC</td>
<td>IV</td>
</tr>
<tr>
<td><strong>Myelosuppression/thrombocytopenia</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Neuropathy</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Zoster</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Dyspnea</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Fatigue</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>GI</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Cardiac/pulmonary (RARE)</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

GI, gastrointestinal; IV, intravenous; SC, subcutaneous.

Steroids (Dexamethasone/Prednisone)

- Mood Swings
- Insomnia
- Irritability
- Hyperactivity
- Edema
- Flushing
- Fatigue
- Blurry vision
- Cataracts
- Dyspepsia
  - PPI
- Muscle atrophy
- Hyperglycemia
- Acne
- Muscle cramping
- Taste changes
- Ulcer
- Weight gain
- Hair loss

PPI, proton pump inhibitor.
Nurse’s Role

- Education and support
  - Oral adherence to complex regimens
- Improving quality of life by helping to manage side effects
- Navigating patients and their caregivers throughout the disease process

Bone Health

- Bisphosphonates
  - Avoid invasive dental procedures
  - Prevent pathological fractures
    - Orthopedist
    - Neurosurgeon
- Pain control
  - Avoid NSAIDs
  - Narcotic education

NSAID, non-steroidal anti-inflammatory drugs.
Renal Health

- Cast nephropathy (myeloma kidney)
- Hypercalcemia
  - Aggressive hydration and treatment
- Dehydration
  - IV fluids
- NSAIDS
- IV contrast
- Aminoglycoside antibiotics
  - Gentamycin, tobramycin, etc.
- Bisphosphonates

IV, intravenous; NSAID, non-steroidal anti-inflammatory drugs.

Anemia

- Due to disease or treatment
- Supportive care
  - Erythropoietin-stimulating agents
    - Epoetin alfa
    - Darbepoetin alfa
  - PRBC transfusions
  - Fatigue
    - Treatment
    - Disease
    - Physical therapy

PRBC, packed red blood cell.
Safety and Mobility

- Exercise
  - Physical/Occupational therapy
- Nutrition and hydration
  - Consult from nutritionist
- Psychosocial well-being
  - Support system
  - Fatigue
  - Sleep disturbances
  - Anxiety
  - Depression

Multidisciplinary Team Approach

- Social workers
  - Financial assistance programs
    - Non-profit organizations
      - The Leukemia & Lymphoma Society
      - Chronic Disease Fund
      - Patient Network Access
    - Pharmaceutical companies
- Physical and occupational therapists
- Dietician
- Pharmacist
- Dentist

Summary

• Multiple myeloma is most often a chronic and complex disease
• Treatment decisions are individualized to the patient
• Managing side effects helps patients maintain quality of life
• A multidisciplinary team approach helps support patients and caregivers
Follicular Lymphoma Overview and Case Study

Lynn Rich, ANP-BC, OCN
Nurse Practitioner
JP Wilmot Cancer Institute
University of Rochester
Rochester, NY

Outline

• Define disease
• Epidemiology
• Natural history of disease
  – Indolent vs curable
• Approved treatment options
  – Rituxan maintenance vs observation
• Use of idelalisib
• Communication strategies: support of social workers
• Resources: survivorship challenges
Lymphoma

General name given to a group of cancers that affect the lymphatic system
- Includes:
  - Lymph nodes
  - Plasma cells
  - Spleen
  - Lymphatic vessels
  - Bone marrow
  - Immunoglobulins
- Immune system helps protect against disease and infection


Lymphoma

Two distinct types:
- Non-Hodgkin lymphoma (NHL)
  - Approx. 50 different subtypes
- Hodgkin lymphoma (HL)
  - Approx. 5 different subtypes
Follicular Lymphoma (FL)

- B-cell NHL (vs T/NK-cell NHL)
- Damage to DNA of one of the parent B cells causes a malignant transformation resulting in uncontrolled and exaggerated growth of the lymphocyte

Image courtesy of JP Wilmot Cancer Institute; Chronic Lymphocytic Leukemia (CLL) Booklet.

Follicular Lymphoma (FL)

- 2nd most common subtype of NHL
- Average age at diagnosis is 60 years
- Indolent: slow-growing disease
- Treatable, but not curable
  - Impact of deciding treatment

NHL: Epidemiology

Approximately 70,800 new cases of NHL in 2014

Case Study: MB

- 57-year-old married female
  - 3rd-grade elementary teacher
  - Symptom profile
    - Abdominal fullness
    - Sweats
    - Fatigue
    - Lymphadenopathy
  - Next step, stage?

DLBCL, diffuse large B-cell lymphoma.
Ann Arbor Staging System

**Case Study: MB**

- Stage III
  - Bilateral axillary – small
  - Abdominal – 10-cm mass
  - Small inguinal node (groin node)
  - Bone marrow negative
    (would have been stage IV)
**Treatment**

- Watch and wait?
- Grade 1, 2, or 3?

---

**Ready to Treat**

- Criteria includes:
  - >3 sites of disease, 3 cm or more
  - 1 node measuring 7 cm
  - Cytopenias – refractory thrombocytopenia disease
  - Effusions
  - Symptoms of disease, or B symptoms
  - Threatened organ involvement
  - Elevated LDH

*LDH, lactate dehydrogenase.*
Case Study: MB

• Treated with R-CHOP – completed 2007
  – Attained complete remission
• Consider maintenance with rituximab vs observation
  – Upfront vs consolidation
  – Things to consider:
    • Expected response
    • Impact on overall survival
    • Quality of life
    • Financial impact

R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Case Study: MB

• No maintenance rituximab
• Relapsed in 5/2008
  – Concerning?

• What we did:
  – Salvage RICE × 2, then autologous stem cell transplant
  – Complete remission 9/2008

RICE, rituximab, ifosfamide, carboplatin, and etoposide.
Case Study: MB

- Relapsed 12/2014
  - Essentially asymptomatic – mild abdominal fullness
  - However, CT of abdomen showed increased disease
- Is she ready for treatment?
  - What are the treatment options?

CT, computed tomography.

Idelalisib – What Is It?

- PI3K inhibitor
  - Phosphoinositide 3-kinase delta
**Idelalisib**

- Oral agent
- FDA approved in 2014
- Used for CLL/SLL or FL
- In relapsed setting

**Side Effect Profile**

- Concern for pneumonitis or colitis
  - What to look for
  - When concerned
  - How to follow
- Concern for evolution of liver function abnormalities
  - What to look for
  - When concerned
  - How to follow

CLL/SLL, chronic lymphocytic leukemia/small lymphocytic lymphoma.
Things to Consider

- Is this patient a good candidate?
  - Why wouldn’t she be?
  - Why would she be?

- Bring in social worker
  - Help to assess medical literacy (implications)
  - Help with financial assistance
    - What are potential sources of assistance?

Communication Strategies

- Create a calendar with details
  - When to take pills, get blood drawn, etc.

- Dialogue with patient
  - Check in by phone
    - At least weekly initially
    - Consider MyChart®

- Eventually evolve to monthly visits, if tolerated
What Happened to MB?

- Began idelalisib 150 mg BID
- Well tolerated
- Held after 2 months for elevated LFTs
- Update to date…

Resources – Survivorship Issues

- The Leukemia & Lymphoma Society
  - www.LLS.org
  - Explore local chapter support groups
- YMCA – Exercise program
  - Explain cancer survivor
  - Describe health and fitness programs
- Look for specific related survivor support groups
  - www.LLS.org/survivorship
Case Study Discussions on the Nurse’s Role in Caring for Patients With Hematologic Malignancies

Thank You