B Cell Malignancies:
Hodgkins Lymphoma
Non Hodgkins Lymphoma
Multiple Myeloma

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Fast Facts of HD, NHL & MM

• 1. Hodgkin’s Disease is highly curable, but has risks of secondary cancers.
• 2. Rituximab has changed Non-Hodgkin’s Lymphoma is treated and causing more focus on co-morbidities.
• 3. Multiple Myeloma is still not curable, but survival has increased greatly due to new therapies.

Hodgkins & Non-Hodgkins

In 2017:
• 8260 new
• 3610- women
• 4650- men
Less than 1% of all malignancies
Survival rates:
5 yr – 88% & up to 94% in people <45 y/o

In 2017:
• 72,240 - new
• 32,160 – women
• 40,080 – men
60% of hematologic malignancies
Survival rates:
5 year – 71% overall

In 2015:
Risk Factors

Hodgkin’s Lymphoma

• History of Mononucleosis
• Hx of Epstein Barr
• HIV
• Familial – esp. in identical twins – younger patients

Non Hodgkin’s Lymphoma

Infection History

• Hx Epstein Barr – Burkitt’s lymphoma
• H. Pylori – Gastric lymphoma
• Human T-cell Lymphotrophic virus

Immunodeficiencies

• HIV
• Solid Organ Transplant
• Severe Autoimmune disorder

Occupational

• Farmers & pesticide exposure
• Radiation exposure - military

Hodgkin’s & Non Hodgkins Pathology

• Reed-Sternberg

Pattern of Spread

Hodgkin’s Lymphoma

• Bimodal age:
  – Average 28 y/o &
  – After 55 y/o
• Chest 4% - outside of nodes
• 40% w/systemic sx
• Orderly progression downward
• Rarely Stage IV

Non Hodgkin’s Lymphoma

• Uncommon under 50 y/o
• Usually after 60 y/o
• Abdomen
• 25% - outside of nodes
• Systemic sx less common
• Less predictable progression
• 40% diagnosed @Stage IV

Comparison of Hodgkin Lymphoma and Non-Hodgkin Lymphoma

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hodgkin Lymphoma</th>
<th>Non-Hodgkin Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodal involvement</td>
<td>Localized to a specific group of nodes</td>
<td>Usually disseminated among &gt; 1 nodal group</td>
</tr>
<tr>
<td>Spread</td>
<td>Tends to spread in an orderly, contiguous fashion</td>
<td>Spreads noncontiguously</td>
</tr>
<tr>
<td>Effect on Waldeyer ring and mesenteric lymph nodes</td>
<td>Usually does not affect</td>
<td>Commonly affects mesenteric nodes May affect Waldeyer ring</td>
</tr>
<tr>
<td>Extravascular involvement</td>
<td>Infrequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Histologic classification in children</td>
<td>Usually one with a favorable prognosis</td>
<td>Usually high grade</td>
</tr>
</tbody>
</table>

Case Study: Kimmer

• Kimmer is 35 year old female, presenting neck lymphadenopathy few weeks postpartum

• She is married, has 4 girls – ages 3 mos, 3 years old and 2 teen age daughters

• Works part time as hostess

Kimmer's labs

• Enlarging left-sided neck mass. CT scan showed multiple bulky cervical lymph nodes. Chest CT – node 3.7 cm. Abdominal CT neg.

• WBC 7.0
• HCT 34.2
• HGB 11.7
• LDH 170
• Creatinine 1.0 & est. GFR 93
• ESR 14
• Denies fever, sweats, wt. loss

Neck CT scan – Pre-treatment

Chest CT – Pre treatment
A chest X-ray showed a large mediastinal mass.

What tests would you anticipate to make an accurate diagnosis?

PET showed mediastinal mass, and positive nodes in neck – no other areas noted.

**Presenting Signs and Symptoms**

- Painless*, enlarged lymph node
  - Cervical lymph node (60-70% of cases)
  - Axillary lymph node (10-15% of cases)
  - Inguinal lymph node (6-12% of cases)

*I. Lymph nodes can become painful with alcohol consumption*
Systemic Symptoms

- Systemic Symptoms (40% of cases)
  - “B symptoms”
    - Fever
    - Night Sweats
    - Unexplained weight loss
- Fatigue
- Itching
- ETOH Intolerance

Diagnostic Evaluation

- History and Physical
- Chest X-ray
- Histologic evaluation, Immunophenotyping – CD20, CD 30
- Laboratory analysis: CBC, ESR, liver function, kidney function, lactate dehydrogenase (LDH), albumin, HIV
- CT scans - neck, chest, abdomen, pelvis
- PET/CT scan
- Bone marrow aspiration & biopsy (anemia and/or “B” symptoms, - only 10% of patients with HD have + BM involvement)
- Ejection fraction, Pulmonary Functions and pregnancy test for treatment planning.
- Fertility counselling

Histology

- Classical Hodgkin’s Disease (95%)
  - Nodular Sclerosis
  - Mixed Cellularity Hodgkin’s Disease (medium prognosis)
- Lymphocyte-depleted Hodgkin’s Disease (worst prognosis)

Comparison of NLPHL & Classic HL

<table>
<thead>
<tr>
<th></th>
<th>NLPHL</th>
<th>Classic HL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>5%</td>
<td>95%</td>
</tr>
<tr>
<td>Ages</td>
<td>all ages</td>
<td>Bimodal - 2nd &amp; 3rd decades</td>
</tr>
<tr>
<td>Male</td>
<td>70%</td>
<td>50%</td>
</tr>
<tr>
<td>Sites</td>
<td>lymph nodes/not in mediastinum</td>
<td>Mediastinum, cervical lymph nodes</td>
</tr>
<tr>
<td>Stage at dx</td>
<td>II or III</td>
<td>I or III</td>
</tr>
<tr>
<td>B sx?</td>
<td>&lt;20%</td>
<td>40%</td>
</tr>
<tr>
<td>Clinical sx</td>
<td>indolent, late relapse</td>
<td>aggressive, curable</td>
</tr>
</tbody>
</table>

Staging

A: No systemic sweats
B: Fever, sweats, weight loss > 10% of baseline
E: Involves one extranodal site from known site
X: Nodal mass is > 10 cm or ratio of mediastinal mass to intrathoracic diameter is >1:3

Work-Up Results

• Reed-Sternberg cells present, but atypical in appearance in biopsy of neck node, nodular sclerosing histology. Classical Hodgkins Disease

What does Kimmer’s workup show?

The most common symptom of Hodgkins Lymphoma is:

• A. Sore Throat
• B. Enlarged Axillary lymph nodes
• C. Enlarged Cervical lymph nodes
• D. Sore lymph nodes after going out drinking all night

Prognostic Factors

• “Favorable vs. Unfavorable”: Assigned to those with Stage I or II disease to determine treatment plan. Unfavorable features are:
  – ESR >50
  – Age ≥45
  – Stage IV disease
  – B Symptoms present
  – > 3 sites
  – Male
  – Bulky adenopathy
  – Histology other than nodular sclerosing or LPHL
  – Mediastinal mass > 33% of thoracic cavity or > 10 cm on CT scan

Overall 5-year survival is 90%
Therapy: Stage Ia-IIa
Classical Hodgkin's Disease, Supradiaphragmatic presentation

- No unfavorable factors:
  - Chemotherapy + involved field radiation (preferred)
  - Subtotal lymphoid irradiation alone
  - Mantle irradiation
  - Chemotherapy alone
    - ABVD x 2 & PET/CT
      - Adria,
      - Bleomycin
      - Vinblastine
      - Dacarbazine

- Bulky disease:
  - Chemotherapy + involved field radiation
  - Nonbulky, with unfavorable factors:
    - Chemotherapy + involved field radiation (preferred)
    - Subtotal lymphoid irradiation alone
    - Chemotherapy alone

Therapy: Stage Ia-IIa
Lymphocyte-predominant Hodgkin's Disease

- Early stage w/o B sx: Involved site radiation
- With B sx: R-CHOP & R-ABVD & possible field radiation
- Advanced stage: R-CHOP x 6 cycles
Therapy: Stage Ib-Ilb
Hodgkin’s Disease - All Histologies

- Non-bulky
  - Chemotherapy + involved field radiation (preferred)
  - Chemotherapy alone

- Bulky
  - Chemotherapy + involved field radiation

Therapy: Stage IIIa, IIIb, IV
Classic Hodgkin’s Disease

- Clinical Trial
  - ABVD x 2-6 cycles
  - Radiation if initial mass is still present, but on PET looks negative

Therapy: Relapsed or Primary Refractory Hodgkin’s Disease

- Salvage Therapy:
  - Standard Chemo if previously treated with radiation alone
  - High-dose Chemotherapy
  - Brentuximab vedotin – targets CD-30

- Autologous Hematopoietic Stem Cell Transplant (HSCT)
  - Mobilize stem cells, collect via apheresis, freeze, administer high dose chemotherapy, reinfuse thawed stem cells, engraftment and recovery

Kimmer’s Treatment - Stage II-a

- ABVD & Radiation Therapy
  - Adria – Cardiac – Echo or MUGA – now essential
  - Bleomycin – Pulmonary - PFTs
  - Vincristine
  - Dacarbazine

Plan: 2 cycles with PET-CT after 2 cycles & radiation consolidation
Nursing Considerations: Physical

• Plan for preserving fertility in younger patients
  – Sperm banking for men: Sperm collected over a 2-3 day period, frozen, and stored for up to 10 years.
  – Embryo Freezing – need to allow time for cycle
  – Oocyte freezing – usually clinical trials
  – Ovarian transposition (for inverted-Y radiation)
  – Ovarian tissue freezing: remove and reinsert after tx.

For women: Procedures may not be possible due to time constraints, finances.

Nursing Considerations - Physical

• Pregnancy test prior to treatment & Birth control during treatment
• Administer therapy for Hodgkin’s Disease and monitor for/manage side effects
• Nausea/vomiting, fatigue, myelosuppression, mucositis, body image alterations
• Manage oncologic emergencies
• Sepsis
• Superior vena cava syndrome

Nursing Considerations: Psychosocial

• Survivorship Careplan
  www.survivorshipguidelines.org
• Median 8 mos. to regain energy
• Symptom Distress
• Employment
• Health Insurance
• Family & Social Life
• Reproduction, health habits

Post treatment - Kimmer
Follow up after Treatment

- H&P w/ tests – q 3-6 mos x 2 yrs, q6-12 mos x 1yr., then annually
- CBC w/ diff, ESR,CMP, TSH q 12 mos. if neck radiated
- CT neck, chest, abd/pelvis @ 6,12,24 months post tx.& prn.
- PET only if Deauville 4-5
- Pneumonia & meningococcal vaccine q 6 yrs if spleen radiated

Influenza vaccine
Mammogram 8-10 years after tx or at 40 y/o if RT
Long term f/u late complications – secondary cancers and cardiac effects
More frequent echocardiogram
Resume other screenings: low power Lung CT for smoking history, colonoscopy, etc.

What is one other consideration in treatment planning? (consider her age and sex)

A. Family & Fertility Planning
B. Cardiac Function
C. Childcare Needs
D. Completing her move from England

Secondary Malignancy

- Risk for secondary malignancy higher with:
  - Chemotherapy + XRT
  - Younger age at HD diagnosis
  - XRT, especially breast cancer with mantle field irradiation
  - Women
- First 5 years: Acute leukemia (14X), NHL (14X), MM (1.7X)
- Later: Breast (20X), Lung (11X), GI (11X), Sarcoma (6.7X) (increased solid tumors after 10 years.)

Current Research

- Goal: to use as little treatment as possible
- New combinations of chemotherapy
- Biologic Therapies antibodies (Brentuximab, PD-1 antibodies, Rituxan®, I-131, Tositumomab, Velcade®, Zevalin™, others)
- HSCT (standard and non-myeloablative)
- Antiviral therapy (EBV)
- Vaccine
- Long Term F/U – Use of Mammogram MRI
- m-TOR Inhibitors
Patient Resources

- American Cancer Society
- Children's Oncology Group
- Leukemia and Lymphoma Society
- Lymphoma Information Network
- CureHodgkins.com
- National Marrow Donor Program
- BMT Infonet
- Fertile Hope
- National Coalition for Cancer Survivorship
- Livestrong.com

Hodgkin’s Disease Pearls

- Focus is to limit the amount of treatment to reduce risk secondary cancers.
- Discuss Fertility issues or refer to specialist.
- Birthcontrol while on treatment
- Mammograms 8-10 years after treatment or at 40 y/o, whichever comes first!
- Remind patients to return to health maintenance
  - BP, healthy diet, other cancer screenings, skin cancer prevention
- Survivorship Care plan

Given that people are usually younger when diagnosed with Hodgkins – what is one of the key items to monitor long term for women who had radiation?

A. Lung Cancer Screening CTs
B. Fertility and Sexuality
C. Cervical Cancer screening more frequently
D. Mammograms at age 40

Non Hodgkin’s Lymphoma

- A progressive, malignant disease where collections of abnormal cells replace normal lymphoid tissue. Abnormal cells can be transformed B-cells (85%) or T-cells or NK cells (15%).
Case Study: Jeanine

• Jeanine is a 76-year-old female, who was treated in 2003 for diffuse large B cell lymphoma (DLBCL)

Jeanine’s Work Up

• History & Physical – mass x 1 month
• Right neck mass – Biopsy
• Chest x-ray to start – then CT scans
• Labs: uric acid – normal, LDH – normal, – CBC & CMP normal
• CT – enlarged L supraclavicular node & R neck mass
• No fever, chills, weight loss

Classification

• REAL/WHO Classification (>20 sub-classifications)
  – B-Cell Lymphomas (85-90%)
  – T Cell Lymphomas (~10-15%)
  – NK Cell Lymphomas (rare)

• Clinical Classification
  – Indolent Lymphoma *
  – Aggressive Lymphoma

Diagram: Types of Non Hodgkins Lymphoma

- Diffuse Large B-Cell Lymphoma (36%)
- Follicular Lymphoma (12%)
- Burkitt’s Lymphoma (7%)
Presenting Signs and Symptoms

- Painless, enlarged lymph node(s)
- Neck
- Armpit
- Groin
- Abdomen

Systemic symptoms
- “B symptoms”
  - Fever
  - Night sweats
  - Unexplained weight loss
- Itching
- Feeling full, loss of appetite
- Fatigue
- Indigestion, abdominal pain
- Bone pain
- Coughing
- Swelling in the face, neck, chest

Diagnostic Evaluation

- History and Physical
- Chest X-ray
- Laboratory analysis: CBC w/Plts, CMP, liver function, kidney function, lactate dehydrogenase, uric acid, HIV test (when indicated)
- Hepatitis B testing
- PET/CT scans of chest, abdomen and pelvis
- Neck CT (when indicated)
- Bone marrow aspiration and biopsy (bilateral when indicated)
- Histologic evaluation and immunophenotyping (cell markers to determine disease)
- Endoscopy with biopsy (when indicated by GI lymphoma)
- Lumbar Puncture (when indicated by CNS symptoms or HIV+)
- Head MRI (when indicated by CNS symptoms)
- Echo or MUGA pre-chemo

Which of the following is true?

A. NHL is distinguished by HL primarily on the basis of different clinical symptoms
B. Lymphomas are predominantly a malignancy of the lymphocyte.
C. There seems to be a single malignancy for all stages in the developmental process from primitive to mature lymphocytes
D. “B” symptoms (night sweats) indicate a bone marrow biopsy is not necessary.

Stage Description

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Involvement of a single lymph node region or lymphoid structure</td>
</tr>
<tr>
<td>II</td>
<td>Involvement of two or more lymph node regions or structures on the same side of the diaphragm</td>
</tr>
<tr>
<td>III</td>
<td>Involvement of lymph node regions or structures on both sides of the diaphragm</td>
</tr>
<tr>
<td>IV</td>
<td>Disseminated involvement of 1 or more extralymphatic sites, for example, liver or bone marrow</td>
</tr>
<tr>
<td>Additional Staging Designations: E - extranodal, N - nodes, S - spleen, H - liver, P - pleura, L - lung, O - bone, M - bone marrow, D - skin, B - B symptoms</td>
<td></td>
</tr>
</tbody>
</table>

What is Jeanine’s Stage?
Prognostic Factors

- **International Prognostic Index (NHL):**
  - Age > 60 years
  - Serum LDH > Normal
  - Performance Status 2-4
  - Stage III or IV disease
  - Extranodal involvement > 1 site

  * Low = 0, Low intermediate = 2, High intermediate = 3, High= 4-5

- **Age-adjusted International Prognostic Index (NHL):**

  - Serum LDH > Normal
  - Performance Status 2-4
  - Stage III or IV disease

  * Low = 0, Low intermediate risk = 1, High intermediate = 2, High= 3

Overall 5-year survival is 65%

Prognosis?

*What is Jeanne’s prognosis?*

1 for yes, 0 for no

Stage IIe disease
ECOG performance status = 2
LDH normal
One extranodal site
60 years old

<table>
<thead>
<tr>
<th>Adverse Factor</th>
<th>Yes/No</th>
</tr>
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<tbody>
<tr>
<td>Disease stage II or IV</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td></td>
</tr>
<tr>
<td>Elevated LDH</td>
<td></td>
</tr>
<tr>
<td>ECOG performance status &gt; 2</td>
<td></td>
</tr>
<tr>
<td>&gt;2 extranodal sites</td>
<td></td>
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Rituximab Action

Another approach to cancer therapy uses antibodies that have been specially made to recognize specific cancers. When coupled with natural toxins, drugs, or radioactive substances, the antibodies seek out target cancer cells and deliver their lethal load.
Jeanine’s Treatment

- 2003 – R - CHOP for 6 cycles
- Radiation Therapy x 4-6 weeks

What would today’s treatment include?
- Rituximab – Rituxan
- R-CHOP x 6 cycles or
- Bendmustine- Rituxan

Therapy: Aggressive NHL, Diffuse Large B-Cell Lymphoma

- Stage I/II
  - Low IPI Score
    - 3-6 cycles of R-CHOP
    - ± Radiation
  - High IPI Score or Bulky Disease
    - 6 cycles of R-CHOP
    - ± regional radiation

- Stage III/IV
  - Low IPI Score
    - 6 cycles of R-CHOP
  - High IPI Score
    - Clinical trial
    - 6 cycles of R-CHOP
    - Autologous HSCT

**Restage after 2-4 cycles

Therapy: Aggressive NHL, Mantle Cell Lymphoma

- Stage I/II
  - Clinical trial
  - Regional radiation
  - High dose Therapy

Therapy: Aggressive NHL, Burkitt’s Lymphoma

- Clinical Trial
- Combination chemotherapy with high-dose chemotherapy and intrathecal chemotherapy & Rituxan.
  - CHOP is not adequate.
Therapy: Aggressive NHL, Cutaneous T-Cell Lymphoma*

- Excision of single lesion
- Topical Therapy
  - Medicated creams
  - Corticosteroid
  - Mechlorethamine chloride
  - Carmustine bexartene
  - Psoralen plus Ultra Violet A
  - Total-skin electron beam radiation
- Systemic therapy
  - Interferon-A
  - Brentuximab
  - Retinoids
  - H-DAC inhibitors
  - Denileukin difitox (Ontak®)
  - Extracorporeal Photophoresis
  - Gemcitabine
  - Allogeneic HSCT

Lymphoma Challenges: Relapsed Lymphoma

- Salvage Chemotherapy (Rituxan based, ICE, DHAP)
- Autologous HSCT with standard conditioning OR conditioning with chemotherapy + radioimmunotherapy
- Lenalidomide maintenance

Case Study: Jeanine

- 2008 diagnosed with B cell low grade (I) small lymphocytic lymphoma in lacrimal duct. Treated with surgery. Thought to be MALT cell.

A Third Primary Lymphoma...

- 2016 – Large cluster lymph nodes in chest with obstructive pneumonitis. Mediastinoscopy with biopsy showing grade II Follicular cell lymphoma – possibly showing transition to large cell lymphoma.
- Symptoms: Marginally able to eat solid food due to esophageal obstruction. Moves very little air in left lung.

What treatment would you expect to use?
At this point, Jeanine’s comorbidities might affect treatment. Which is the most likely concern in choosing treatment?

A. Functional Status
B. Kidney function
C. Cardiomyopathy
D. Hepatitis B

FLIPI Calculation

Calculate Jeanine’s score:
Stage III Hgb: 11
Age 77 Extranodal sites: 3
LDH normal

<table>
<thead>
<tr>
<th>Adverse Factor</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease stage III or IV</td>
<td>Y</td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>Y</td>
</tr>
<tr>
<td>LDH = upper limit of normal</td>
<td>N</td>
</tr>
<tr>
<td>Hemoglobin &lt; 12 g/dl</td>
<td>Y</td>
</tr>
<tr>
<td>&gt; 3 extranodal sites</td>
<td>N</td>
</tr>
</tbody>
</table>

Prognosis: Good: 0 - Intermediate: 2, Poor: > 3
Therapy: Indolent NHL, Small Lymphocytic Lymphoma - Grade I
- Stage I/II:
  - “Watch and Wait” Q 3 months
  - Local radiation

Maintenance Therapy:
Follicular is not curable, but maintenance can keep it in remission. What do you see in practice?

A. Q 3 months
B. Weekly x 4 q 6 months
C. Q 2 months
D. None of these

Therapy: Indolent NHL, Follicular Lymphoma
- Stage I/II:
  - Involved field radiation
  - Monoclonal Antibody
  - Single agent chemotherapy
  - Combination chemotherapy
  - Palliative radiation

- Stage III/IV:
  - “Watch and Wait”
  - Local radiation for palliation of symptoms
  - Chemotherapy +/- Monoclonal Antibody
  - Monoclonal Antibody
  - Clinical trial
  - Autologous HSCT

Hepatitis B
- Growing concern – Testing for Hepatitis B surface antigen (HBsAg) and Hepatitis B core antibody (HBCAb) for anyone receiving CD20 agents
  - If HBsAG positive – treat with Entacavir instead of Lamivudine due to risk of developing resistance
  - Treat through treatment and for 12 months after completion of tx.
  - Monitor during treatment and q 3 months afterwards
A day after treatment, Jeanine called to report having cloudy urine, feeling very achey, and kind of shaking – her pulse is irregular. You suspect she has symptoms of:

A. Urinary Tract Infection  
B. Tumor Lysis Syndrome  
C. Dehydration  
D. Atrial Fibrillation

What is TLS?

- Tumor Lysis Syndrome
  - Hyperkalemia
  - Hyperphosphatemia
  - Hyperuricemia
  - Hyperuricosuria
  - Hypocalcemia
  - Leading to Acute Renal Failure

Signs & Symptoms TLS

- Nausea/vomiting
- Dyspnea
- Irregular Heartbeat
- Cloudy urine
- Lethargy &/or joint pain

Treatment for TLS

- Anticipate and start treatment before chemo!
- Allopurinal – Inhibits uric acid production
  - 2-3 d prior times 10-14 d
- Rasburicase (Uricase) – degrades uric acid – single dose adequate
- Fluids – Fluids – Fluids!
MoAb Infusion Reactions

- Monoclonal antibody binds to site – that can cause cell death. Cytokines released are thought to be cause of reaction.
- Dependent on cytokines
- Occurs during or within 24 hours
- Decreases in frequency and intensity with subsequent infusions

Management: premeds, slowing or interruption of infusion & supportive care (steroids, antihistamine, O2)

A Monoclonal Antibody (MAB) infusion reaction is different from an allergic reaction in the following ways:

A. They are both due to cytokine release
B. Allergic reactions occur after repeated exposures to agent
C. Reactions to MABs usually decrease after the first exposure
D. B & C

Infusion Related Reactions

<table>
<thead>
<tr>
<th>Cytokine-related infusion reaction</th>
<th>Allergic (hypersensitivity) reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depends on cytokines</td>
<td>IgE related</td>
</tr>
<tr>
<td>Common with MOABs</td>
<td>Uncommon with MOABs</td>
</tr>
<tr>
<td>Usually occurs in first 24 hours</td>
<td>Occurs during infusion or up to 2-3 weeks later - &amp; with add’l exposure</td>
</tr>
<tr>
<td>Decreases in frequency and severity with additional doses</td>
<td>Stays the same or increases with additional doses</td>
</tr>
</tbody>
</table>

Use premeds, slow or interrupt infusion, and supportive care

Supportive care

Nursing Considerations: Psychosocial

- Non-Hodgkin’s Lymphoma in younger patients often interferes with career, family and financial goals.
- Non-Hodgkin’s Lymphoma associated with a diagnosis of HIV can intensify the burden of the disease and treatment.
Nursing Pearls: Physical

- Consider co-morbidities and patient goals
- Consider checking Hepatitis B and C testing, & CMV
- Ask about antiviral and/or antibiotic treatment
- Monitor for infusion reactions with monoclonal antibodies
- Manage oncologic emergencies
  - Superior Vena Cava Syndrome
  - Tumor Lysis Syndrome

The best treatment options for a MAB reaction include:

A. B, C & D
B. Stop the infusion & request help from your peers
C. Follow Monoclonal Antibody Infusion Reaction Procedure/Protocol
D. Restart infusion when patient is stable at previous rate and increase according to the prior protocol and remember to breathe yourself!

Current Research

- Novel agents
- New chemotherapy drugs, new combinations of chemotherapy and new dosing schedules
- Monoclonal antibodies
- HSCT
- Autologous Cytotoxic T-cell Transplants
- Antisense therapy (induces apoptosis)
- Vaccinations
- Arsenic Trioxide
- Examining genetic diagnostic/prognostic indicators

Patient Resources

- Leukemia and Lymphoma Society
- Lymphoma Research Foundation
- National Marrow Donor Program
- BMT Infonet
- American Cancer Society
- Lymphomaresources.com
Case Study: Janice

• Janice is a 61 y/o woman w/ recent onset of Raynaud’s phenomenon in fingers. In Rheumatoid workup, serum electropheresis was done, showing monoclonal paraprotein. Denies bone pain, except for arthritic pain. Does c/o fatigue/weakness.

Multiple Myeloma

– Definition: A progressive, malignant, incurable disease characterized by a proliferation of abnormal plasma cells in the bone marrow.

Incidence

• 2017: Estimated 30,280 new cases in US
  – 12,790 women
  – 17,490 men
• Mean age at diagnosis is 62 for men and 61 for women (less than 3% of patients are <40 years of age)
• African Americans are 2X as likely to be diagnosed with Multiple Myeloma
• Accounts for only 1% of all malignancies
• Overall 5 year survival is 40%.
**Novel Therapy Impact**

- Many improvements since 2004:
  - Median OS 32 mos. Vs 71.8 mos
  - Median PFS: 15.2 mos vs. 42.8 mos

- Improvement correlates with use of novel agents – bortezomib, thalidomide & lenalidomide
  - Median 36.7 mos. Vs 9.1 mos.

[http://www.peerviewpress.com/o1/d17](http://www.peerviewpress.com/o1/d17)

**Etiology**

- No known etiology, although several risk factors have been identified:
  - Exposure to ionizing radiation and pesticides
  - Family – *sibs or child of person* – 4x more likely
  - Exposure to petroleum products
  - Employment as farmer or wood or leather worker
  - Exposure to Agent Orange
  - HIV infection

**Pathophysiology**

- Malignant myeloma cells accumulate in bone marrow disrupting production of RBCs, WBCs and Platelets.

- Invasion & destruction of bone around the bone marrow cavity

- Release of monoclonal protein (M-protein) into blood stream resulting in Immunosuppression

**“Punched out” lesion of Myeloma**

![Image of a medical scan showing a “punched out” lesion of myeloma](image_url)
Plasma Cells in Myeloma

Hypercalcemia

- Excessive thirst and urination
- Sleepiness
- Confusion
- Constipation
- Nausea/vomiting
- Loss of appetite

Renal

- Renal Insufficiency (50% of cases)
  - Elevated serum creatinine
  - Hydronephrosis
  - Renal obstruction
Presenting Signs and Symptoms:

**Anemia**
- Pancytopenia
  - Anemia (67% of cases)
  - Thrombocytopenia
  - Neutropenia
  - Infections (especially pneumonia and UTI)
  - Immunoglobulinopathy
- Hyperviscosity (4-10% of cases)
- Parasthesias
- Bleeding
- Blurred vision
- Dizziness
- Stroke symptoms

**Bone**
- Bone pain (58%)
  - Pathologic fractures (30% of cases)
  - Osteolytic lesions
- Spinal cord compression (15-20% of patients)
  - Back pain
  - Paresthesias
  - Sensory loss

In what month is Myeloma most likely to be diagnosed?

Diagnostic Evaluation

**Laboratory Analysis:**
- CBC-DP, Renal function,
- Lytes, Calcium, Albumin,
- Quantitative immunoglobulins, SPEP,
- Beta₂-microglobulin level,
- CRP, LDH, serum viscosity,
- 24-hour urine - Bence-Jones quantitation
- Urine protein electrophoresis & immunofixation

**History and Physical**
- Skeletal Survey
- Unilateral Bone Marrow Biopsy
- MRI or CT (when plasmacytoma or SCC suspected)
- Tissue biopsy to confirm presence of plasmacytomas (prn)

Presenting Symptoms of Multiple Myeloma may include the following:

A. Hypercalcemia, bone pain
B. Hyperglycemia, chest pain
C. Pancytopenia, DVT
D. A & C
E. B & C
Not Just Bone Marrow Anymore-

- Chromosomal Changes
  - Cytogenetics
  - FISH (Fluorescent in situ hybridization)
    - Deletion of chromosome 13
    - Deletion of chromosome 17p13

Diagnostic Criteria:

- > 10% monoclonal plasma cells in bone marrow &/or documented plasmacytoma
- M component in serum and/or urine
- One or more of the following (CRAB)
  - Calcium elevated – serum Ca++ > 11.5 mg/dl
  - Renal insufficiency (serum creatinine > 2 mg/dl)
  - Anemia (hgb < 10 g/dl or 2 g/dl below normal)
  - Bone disease (lytic lesions or osteopenia)

A difficult diagnosis

- What symptoms could be related to multiple myeloma?
- Which of these symptoms could be related to a multitude of other causes?

What tests will be needed to confirm a diagnosis of multiple myeloma?

A. Serum Protein Electropheresis/Urine Protein Electropheresis
B. Immune globulins – IgA, IgE, IgM
C. All of these
D. Skeletal Survey
Classification

- **Solitary Plasmacytoma**: Single collection of myeloma cells in bone or soft tissue
- **Monoclonal gammopathy of undetermined significance, or MGUS**
  - Serum M Protein <3g/dl
  - <10% plasma cells in marrow
  - Asymptomatic
- **Smoldering (or Asymptomatic) Multiple Myeloma**
  - >3g/dl M Protein
  - 10%–20% plasma cells in marrow
  - Asymptomatic (no anemia, renal failure, hypercalcemia, or lytic lesions)
- **Systemic Multiple Myeloma**
  - Positive serum/urine M Protein
  - Marrow plasmacytosis
  - Anemia
  - Renal dysfunction
  - Lytic bone lesions

Prognostic Factors

- **Favorable Prognostic Factors**:
  - Beta₂ microglobulin < 2.5mg/l
  - CRP < 4mg/dl
  - No chromosomal translocations
  - Some translocations have better prognoses
  - Plasma Cell Labeling Index (PCLI) < 1%
  - No plasmablastic morphology
  - Normal lactic dehydrogenase

  *Overall 5-year survival is 40%*

The Work-up - Janice

- **Labs**:
  - Hgb: 11.9
  - Creatinine 1.0
  - Beta-2 microglobulin 3.8
  - ESR 111
  - Flow cytometry
  - 13% plasma cells
  - IGM spike 1.9

- **Urine** for light chains (sub-unit of immunoglobulins)
- **60% Plasma cells in Bone Marrow**
- **Skeletal survey negative**

Multiple Myeloma Therapies Are Continuously Evolving

- Glucocorticoids
- High-dose chemotherapy
- Bisphosphonates
- Thalidomide
- Lenalidomide
- Carfilzomib
- Pomalidomide
- Melphalan
- Doxorubicin
- Stem-cell transplant
- Daratumumab
- Ikazomab
- Elotuzomab
Combination of Therapies:

- **Steroids**
- **Immunomodulators**
  - Thalidomide
  - Lenalidomide
  - Pomalidomide
- **Proteosome Inhibitors**
  - Bortezomib - injection
  - Ixazomib - oral
  - Carfilzomib - infusion
- **Histone deacetylase inhibitor**
  - Farydak - oral
- **Monoclonal antibody**
  - Daratumumab – CD-38 infusion

Therapy: Solitary Plasmacytoma

- **Osseous**
  - Radiation therapy to involved field.
  - Continue surveillance
  - If refractory to treatment or progresses following initial response
  - Restage with full work-up
  - Treat as indicated for smoldering or systemic myeloma.
- **Extraosseous**
  - Radiation therapy to involved field and/or surgery.
  - Continue surveillance
  - If refractory to treatment or progresses following an initial response
  - Restage with full work-up
  - Treat as indicated for moldering or systemic myeloma.

Therapy: MGUS and Smoldering MM

- “Watch and wait”
- Continue surveillance, and when there is progression, treat as indicated for systemic myeloma.

**What would you want to watch?**

Q 3 – 6 month visit: CBC, CMP, LDH, beta-2 macroglobulin, Immunoglobulins and M protein. Skeletal survey, MRI, Bone marrow based on clinical picture

First-line Therapy: Multiple Myeloma – Transplant Eligible

- Bortezomib + Dexamethasone (1)
- Bortezomib + doxorubicin + dex (1)
- Bortezomib + lenalidomide + dex (1)
- Bortezomib + thalidomide + dex (1)
- Dexamethasone (2)
- Bortezomib + cyclophosphamide + dex (2)
- Lenalidomide + dex (1)
- Vincristine + liposomal doxorubicin + dex (2)
- Thalidomide + dex (2B)
- Carfilzomib/lenalidomide/ dex (2)
- Liposomal doxorubicin/vcr/dex (2)
- Ixazomib/lenalidomide/dex (2B)

Bisphosphonate – Zometa, Pamidronate
Factors for Successful Transplant

- No abnormal chromosomes/ no translocations
- Low serum β₂ microglobulin level
- Low serum C-reactive protein level
- Less than 12 months of treatment
- Use of non-TBI prep
- < 60-65 years old
- Serum creatinine ≤ 1.0 mg/dl
- CR response to treatment

Butturini, A et al. (2009)

Course of Action in Myeloma

**Induction**
- VD
- Rev/IDa
- Cyt/Borti/Dex
- VTD
- VRD

**Consolidation**
- Stem Cell Transplant

**Maintenance**
- Nothing
- Thalidomide
- Bortezomb
- Lenalidomide

**Relapse**
- Bortezomb
- Lenalidomide
- Thalidomide
- Carfilzomb
- Pencobezset
- Daratumumab
- Ixazomib
- Elotuzumab

Maintenance Therapy

- **Preferred Regimens:**
  - Bortezomb
  - Lenalidomide
  - Thalidomide

- **Other Regimens:**
  - Bortezomb & prednisone
  - Bortezomb & thalidomide
  - Interferon
  - Steroids
  - Thalidomide & Prednisone

First Line Therapy

Multiple Myeloma – Transplant

Preferred Regimens
- Lenalidomide/low dose dex (1)
- Bortezomb/cyclophosphamide/dex
- Bortezomb/lenalidomide/dex (1)

Other Regimens
- Bortezomb + dex (1)
- Ixazomib/lenalidomide/dex
- Carfilzomb/lenalidomide/dex (2B)
Second-line or Salvage Therapy: Systemic Multiple Myeloma

- Repeat Induction TX (if >6 months)
- Combination chemotherapy (if single-agent used prior)
- Bortezomib & dex
- Lenalidomide & dex
- Carfilzomib/lenalidomide/dex
- Ixazomib/lenalidomide/dex
- Pomalidomide/dex
- Daratumumab
- ............

Bisphosphonates

- Use in all myeloma patients from time of diagnosis
  - Smoldering – only if symptomatic – yearly bone survey
  - Monitor renal function
  - Monitor for osteonecrosis of jaw
    - Dental exam prior to use
- Zometa – 30 minute infusion
- Pamidronate – 2 hour infusion

Therapy

- What would be the likely treatment for Janice’s cancer?

- What supportive therapies need to be initiated as well?

For the future...

- If Janice’s disease fails to respond to treatment, or if she initially responds and then relapses, what are key considerations when planning her care & therapy?
Nursing Considerations: Physical

- Oral Adherence
- Monitor and manage complications
  - Renal failure, pain, infections
- Manage side effects:
  - Neuropathy, hypercoagulability, myelosuppression, viral infections.
- Maintain safe environment (Fall Precautions)
- Manage oncologic emergencies
  - Spinal cord compression, sepsis, hypercalcemia

Peripheral Neuropathy

- Bortezomib:
  - Burning, numbness, tingling – hyper- and hypoesthesias

- Thalidomide:
  - Numbness & tingling – hyper- and paresthesias

Peripheral Neuropathy: Sensation terms

- Anesthesia – absent touch sensation
- Hyperesthesia – increased touch
- Hypoesthesia – decreased touch
- Paresthesia – abnormal touch sensation – burning, prickling, formication (bugs crawling) often in absence of anything touching the skin to cause this.

Assessment

- Report Changes in sensation to your healthcare provider – MD/nursing
  - Numbness/tingling
  - Change in pain, touch, temperature and/or position sensation
- Difficulty with ADLs – buttoning shirt, writing, etc
- Different tools available
  - Survey
  - Skin test (like with Diabetes)
  - Electrical stimulation test
You noticed that Janice’s handwriting has been getting worse and it looks like she is walking on pins and needles – You suspect, and will:

A. She has Peripheral Neuropathy due to her treatment
B. Assess her hands – type of neuropathy, duration, skin condition/temperature
C. Instruct her about safety precautions – prevent burns, avoid tripping due to difficulty walking, etc.
D. A, B & C

Nursing Considerations: Psychosocial

• Assist patient and families in coping with:
  – Survivorship
  – an incurable disease
  – What is important to patient?

Myeloma Pearls of Wisdom

– Protect kidneys – No NSAIDS!!
– Drink 2 liters fluid every day
– No IV contrast with CT scans
– Protect Bones – use caution when lifting > 5 lbs
– Avoid deep tissue massage and chiropractor visits
– Exercise to increase muscle mass
– Monitor bone density
– Biphosphonate q month
– Watch for infection/neutropenic precautions
– Fall Precautions

Neurotoxicity Assessment Tool
May Help to Identify PN Symptoms

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<th>Symptom</th>
<th>Not at All</th>
<th>A Little</th>
<th>Some What</th>
<th>Quite a Bit</th>
<th>Very Much</th>
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<td>Numbness tingling in my hands</td>
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<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Numbness tingling in my feet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
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</tr>
</tbody>
</table>

Consider asking your patient additional questions:

– “If you reach into the freezer to get something, does your hand feel uncomfortable?”
– “If you hold a mug of hot coffee, is it uncomfortable?”
– “Have you been having any trouble buttoning your shirts?”
Patient Resources

- Multiple Myeloma Research Foundation
- International Myeloma Foundation
- Multiple Myeloma Education Network
- Leukemia and Lymphoma Society
- National Marrow Donor Program
- BMT Infonet
- American Cancer Society