Hodgkin’s Disease
Non-Hodgkin’s Lymphoma
Multiple Myeloma

Renee Yanke, ARNP, MN, AOCN
Oncology Advanced Practice Nurse Manager, Oncology Program, Whidbey General Hospital, Coupeville, WA

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.

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
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.

A progressive, malignant disease where collections of abnormal cells replace normal lymphoid tissue. Abnormal cells are thought to be transformed B-cells. Hodgkin’s Disease is characterized by the distinctive binucleate Reed-Sternberg cell, which has the appearance of “owl eyes.”
**Incidence**

- 2014: Estimated 9,190 new cases in US
  - 4,120 women
  - 5,070 men
- Incidence has not changed over time
- Accounts for less than 1% of all malignancies
- Bimodal Incidence
  - Age 15-40 (80%)
  - >55 years (20%)
- Increased incidence in February and March and in higher Socio-Economic Classes (younger patients)

**Etiology**

- No known etiology, although several risk factors have been identified:
  - History of Infectious Mononucleosis infection
  - History of Epstein-Barr virus infection
  - HIV infection
  - Familial risk in sibs esp. identical twins (younger patients)

---

**Hematopoiesis**

**B Cell Action**
Pathophysiology

- A normal lymphocyte undergoes malignant transformation into the Reed-Sternberg cell within a lymphatic structure (lymph nodes or spleen).
- The malignant cells grow and divide uncontrollably and spread from one group of lymph nodes or lymph structure to adjacent groups in a predictable fashion.
- In advanced disease, the malignant cells can invade tissues and organs (bone marrow or liver).

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)

- Systemic symptoms (25% of cases)
  - "B symptoms"
    - Fever
    - Night Sweats
    - Unexplained Weight Loss
  - Fatigue
  - Itching
  - ETOH Intolerance

*I lymph nodes can become painful with alcohol consumption.
Diagnostic Evaluation

- History and Physical
- Chest X-ray
- Histologic evaluation and immunophenotyping - CD20, CD30,
- Laboratory analysis: CBC, ESR, liver function, kidney function, lactate dehydrogenase (LDH), albumin, HIV
- CT scans of neck, chest, abdomen and pelvis
- PET/CT scan
- Bone marrow aspiration and biopsy (recommended for patients with anemia and/or B symptoms, although only 10% of patients with HD have + BM involvement)
- Ejection fraction, Pulmonary function, and pregnancy test for treatment planning.

History and Physical

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

Histology

- Classical Hodgkin’s Disease (95%)
- Nodular Sclerosis Hodgkin’s Disease (>65% of cases, best prognosis)
- Mixed Cellularity Hodgkin’s Disease (medium prognosis)
- Lymphocyte-depleted Hodgkin’s Disease (worst prognosis)
- Lymphocyte-predominant Hodgkin’s Disease (5% of cases, most favorable)

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>I</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>

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

**What does Kimmer’s workup show?**

**What is one other consideration in treatment planning – age? Sex?**

**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

  Overall 5-year survival is 85%.

**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: 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 Classical Hodgkin’s Disease, Subdiaphragmatic presentation
- Chemotherapy + involved field radiation (preferred)
- Inverted Y-field irradiation
- Chemotherapy alone

Therapy: Stage Ia-IIa Lymphocyte-predominant Hodgkin’s Disease
- Early stage w/o B sx: Involved field radiation With B sx: R-CHOP, R-ABVD & possible field radiation
- Advanced stage: R-CHOP x 6 cycles

Therapy: Stage Ib-IIb 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 6-8 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 CD30
- 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: 2-4 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

- 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
Hodgkin’s Disease in younger patients often interferes with school, career, family and financial goals. Long term health impacts.

Hodgkin’s Disease in older adults can raise issues of when therapy is appropriate depending on functional ability and QOL issues and what perceptions older adults have of cancer and cancer treatment.

Follow up after Treatment
- H&P w/tests - q 2-4 mos x 2 yrs, q3-6 mos x 3-5 yrs, then annually
- CBC w/diff, CMP, TSH q6 mos, if neck radiated
- CT neck, chest, abd/pelvis q 6-12 months for 2-5 years (involved sites)
- Pneumonia & meningococcal vaccine q6 yrs if spleen radiated
- Influenza vaccine
- Mammogram 8-10 years after tx or at 40 y/o
- Long term f/u late complications - secondary cancers and cardiac effects

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)
Current Research

- New combinations of chemotherapy
- Biologic Therapies 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
- Leukemia and Lymphoma Society
- Lymphoma Information Network
- CureHodgkins.com
- National Marrow Donor Program
- BMT Infonet
- Fertile Hope

Hodgkin’s Disease Pearls

- Focus is to limit the amount of treatment to reduce risk of leukemia and other secondary cancers.
- Discuss Fertility issues or refer to specialist.
- 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
- Consider Survivorship Careplan.

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 1996 for diffuse large cell lymphoma.

---

**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

---

**Incidence - NHL**

- 2014: Estimated 70,800 new cases in US
  - 32,530 – women
  - 38,270 - men
- Accounts for nearly 60% of hematology malignancies
- More common in Caucasians than in African Americans or Asian Americans
- Current lifetime risk is 1:50

- Incidence increasing; currently the 7th most common form of cancer for men and women.
- In 2003, rate was 19.1 per 100,000

---

**Etiology**

- No known etiology, although several risk factors have been identified:
  - Immunodeficiency
    - HIV
    - Post-solid organ transplant
    - Severe autoimmune disorders
  - Infections
    - History of Epstein-Barr virus infection (Burkitt’s Lymphoma)
    - History of Helicobacter Pylori infection (Gastric Lymphoma)
    - History of infection with Human T-cell Lymphotrophic Virus (Rare in US)
  - Occupational
    - Rural farmers & pesticide exposure
    - Radiation exposure - military
Classification

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

- Clinical Classification
  - Indolent Lymphoma *
  - Aggressive Lymphoma

Types of Non Hodgkins Lymphoma

- Diffuse Large B-Cell Lymphoma
- Follicular Lymphoma
- Mucosa Associated Lymphatic Tissue Lymphoma
- Small Lymphocytic Lymphoma/CLL
- Mantle Cell Lymphoma
- Mediastinal Large B-Cell Lymphoma
- Burkitt's Lymphoma
- Lymphoplasmocytic Lymphoma
- Nodal Marginal Zone B-Cell Lymphoma
- Splenic Marginal Zone Lymphoma
- Extramedullary Marginal Zone Lymphoma
- Intravascular Large B-Cell Lymphoma
- Primary Effusion Lymphoma
- Lymphomatoid Granulomatosis
Pathophysiology

- A normal B-lymphocyte or T-lymphocyte undergoes malignant transformation into a lymphoma cell within a lymphatic structure (lymph nodes, spleen, thymus gland, adenoids, tonsils, lymphatic cells in the intestinal tract, or bone marrow).
- The malignant cells grow and divide uncontrollably and spread from one group of lymph nodes or lymph structure to other groups of lymph nodes.
- In advanced disease, the malignant cells can invade tissues and organs (bone marrow, liver, central nervous system).

Presenting Signs and Symptoms

- 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

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

Diagnostic Evaluation

- History and Physical
- Chest X-ray
- Laboratory analysis: CBC-Diff, comprehensive metabolic panel, 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 (examination of cellular markers to determine disease classification) of affected lymph node (complete node should be removed as there may be only a few malignant cells present in the diseased node)
- Endoscopy with biopsy (when indicated by GI lymphoma)
- Lumbar puncture (when indicated by CNS symptoms or HIV+)
- Head MRI (when indicated by CNS symptoms)
### Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<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>
</tbody>
</table>

**Additional Staging Designations:** E - extranodal, N - nodes, S - spleen, L - liver, P - pleura, L - lung, O - bone, M - bone marrow, D - skin, B - B symptoms

### Prognostic Factors

- **International Prognostic Index (NHL):**
  - Age > 60 years
  - Serum LDH > 1X Normal
  - Performance Status 2-4
  - Stage III or IV disease
  - Extranodal involvement > 1 site
  - *Low = 0-1, Low intermediate = 2, High intermediate = 3, High = 4-5*

- **Age-adjusted International Prognostic Index (NHL):**
  - Serum LDH > 1X Normal
  - Performance Status 2-4
  - Stage III or IV disease
  - *Low = 0, Low intermediate = 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**

Score of 5 – high risk for poor outcome

### Rituximab Action

- **Adverse Factor**
  - Yes/No
  - Disease stage III or IV
  - Age > 60 years
  - Elevated LDH
  - ECOG performance status > 2
  - 1 or more extranodal sites

**Score of 5 – high risk for poor outcome**
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

- 1996 – 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
    - 3-4 cycles of chemotherapy + Monoclonal Antibody + regional radiation
  - High IPI Score or Bulky Disease
    - 6-8 cycles of chemotherapy + Monoclonal Antibody + regional radiation
- Stage III/IV
  - Low IPI Score
    - 6-8 cycles of chemotherapy + Monoclonal Antibody
  - High IPI Score
    - Clinical trial
    - 6-8 cycles of chemotherapy + Monoclonal Antibody
    - Autologous HSCT

Therapy: Aggressive NHL, Burkitt’s Lymphoma

- Clinical Trial
- Combination chemotherapy with high-dose chemotherapy and intrathecal chemotherapy
Therapy: Aggressive NHL, Mantle Cell Lymphoma

- **Stage I/II**
  - Clinical trial
  - Regional radiation

- **Stage III/IV**
  - Clinical Trial
  - Chemotherapy + Monoclonal Antibody
  - Radioimmunotherapy
  - HSCT

Mycosis Fungoides or Sézary Syndrome

- Excision of single lesion
- Topical Therapy
  - Medicated creams
  - Corticosteroid
  - Mechlorethamine chloride
  - Carmustine bexarotene
  - Psoralen plus Ultra Violet A
  - Total skin electron beam radiation

- Systemic therapy
  - Interferon-A
  - Rituximab
  - Retinoids
  - Bexarotene
  - Denileukin diftitox (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
- Allogeneic HSCT

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...

- 2012 – 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?**

**What about comorbidities?**

### 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 &gt; upper limit of normal</td>
<td>N</td>
</tr>
<tr>
<td>Hemoglobin &lt; 12 g/dl</td>
<td>Y</td>
</tr>
<tr>
<td>≥ 5 extranodal sites</td>
<td>N</td>
</tr>
</tbody>
</table>

Prognosis: Good: 0-1, Intermediate: 2, Poor: ≥3

---

**Jeanine’s Esophagus**

**Jeanine’s Lung**
Maintenance Therapy

- Follicular is not curable, but maintenance can keep it in remission.

**What do you see in practice?**
- Q 3 months
- Q 2 months
- Weekly x 4 q 6 months

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.

Therapy: Indolent NHL, Small Lymphocytic Lymphoma - Grade I

- Stage I/II
  - “Watch and Wait”
  - Q 3 months
  - Local radiation

- Stage III/IV
  - “Watch and Wait”
  - Monoclonal Antibody
  - Single agent chemotherapy
  - Combination chemotherapy
  - Palliative radiation

**Active Monitoring!**

Therapy: Indolent NHL, Follicular Lymphoma

- Stage I/II:
  - Involved field radiation
  - Monoclonal Antibody + chemotherapy followed by involved field radiation
  - Extended field radiation

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

Consider co-morbidities and patient goals
- Administer therapy for Non-Hodgkin’s Lymphoma and monitor for/manage side effects
  - Nausea/vomiting, fatigue, myelosuppression, mucositis, body image alterations, hypersensitivity reactions
- Manage oncologic emergencies
  - Superior Vena Cava Syndrome
  - Tumor Lysis Syndrome
  - Sepsis

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
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.

Definition: A progressive, malignant, incurable disease characterized by a proliferation of abnormal plasma cells in the bone marrow.
In the year 2014, there were an estimated 24,050 new cases of Multiple Myeloma in the US. This condition is more common in men, with 13,500 cases diagnosed in men and 10,550 in women. The mean age at diagnosis is 62 years for men and 61 years for women, with less than 3% of patients diagnosed below the age of 40. African Americans are twice as likely to be diagnosed with Multiple Myeloma compared to other racial groups. This condition accounts for only 1% of all malignancies. The overall 5-year survival rate is 40%.

Since 2004, there have been many improvements in the treatment of Multiple Myeloma. The median overall survival has increased from 71.8 months to 32 months, and the median progression-free survival has increased from 42.8 months to 15.2 months. These improvements are associated with the use of novel agents such as bortezomib, thalidomide, and lenalidomide. The median overall survival has improved significantly, from 9.1 months to 36.7 months.

There is no known etiology for Multiple Myeloma, although several risk factors have been identified. These include exposure to ionizing radiation and pesticides, exposure to petroleum products, employment as a farmer, wood, or leather worker, exposure to Agent Orange, and HIV infection. A normal plasma cell undergoes malignant transformation into a myeloma cell within the bone marrow. Myeloma cells establish themselves in the bone marrow by binding to fibronectin and to stromal cells and create plasmacytomas, or small myeloma cell tumors. The malignant cells grow and divide uncontrollably and, in most cases, overproduce immunoglobulins. Myeloma cells continue to grow, proliferate, and spread, producing physiologic alterations that lead to the signs and symptoms of Multiple 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

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
Presenting Signs and 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?

“Punched out” lesion of Myeloma

Diagnostic Evaluation

- Laboratory Analysis:
  - CBC-DP
  - Renal function
  - Electrolytes
  - Calcium
  - Albumin
  - Quantitative immunoglobulins, SPEP
  - Beta-microglobulin level
  - CRP
  - Lactic dehydrogenase, serum viscosity
  - 24-hour urine for Bence-Jones quantitation and
  - Urine protein electrophoresis and 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 (when indicated)
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?

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 Indolent) Multiple Myeloma
  - Low concentrations of 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
Favorable Prognostic Factors:
- Beta₂-microglobulin < 2.5mg/l
- CRP < 4mg/dl
- No chromosomal translocations
- Plasma Cell Labeling Index (PCLI) < 1%
- No plasmablastic morphology
- Normal lactic dehydrogenase

Overall 5-year survival is 30%

Labs:
- Hct: 30%
- 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
- Bisphosphonates
- High-dose chemotherapy
- Thalidomide
- Combination chemotherapy: vincristine, doxorubicin, dexamethasone (VAD)
- Stem-cell transplantation
- Bortezomib
- Lenalidomide
- Carfilzomib
- Pomalidomide

Therapy: Solitary Plasmacytoma

- Osseous
  - Radiation therapy to involved field. Continue surveillance, and if plasmacytoma is refractory to treatment or progresses following an initial response, restage with a full work-up and treat as indicated for smoldering or systemic myeloma.
- Extrasosseous
  - Radiation therapy to involved field and/or surgery. Continue surveillance, and if plasmacytoma is refractory to treatment or progresses following an initial response, restage with a full work-up and treat as indicated for smoldering 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 w/CBC, CMP, Immunglobulins and M protein
Skeletal survey, MRI, Bone marrow based on clinical picture

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)

First-line Therapy:
Multiple Myeloma – Transplant Eligible

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

- Bisphosphonate – Zometa, Pamidronate

First Line Therapy
Multiple Myeloma – Transplant Ineligible

- Lenalidomide/low dose dex (1)
- Melphalan + prednisone + bortezomib (1)
- Melphalan + prednisone + lenalidomide (1)
- Melphalan + prednexitone + thalidomide (1)
- Bortezomib + dex (1)
- Melphalan + prednisone (2)
- Dexamethasone (2)
- Liposomal doxorubicin + VCR + dex (2)
- Thalidomide + dex (2)
- VCR + doxorubicin + dex (2)
Second-line or Salvage Therapy: Systemic Multiple Myeloma

- Salvage Therapy
  - Combination chemotherapy (if single-agent used prior)
  - High-dose chemotherapy
  - Thalidomide & dex
  - Bortezomib & dex
  - Lenalidomide & dex
  - VMP
  - Bisphosphonate

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

- 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

**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.

- Bortezomib:
  - Burning, numbness, tingling – hyper- and hypoesthesias
- Thalidomide:
  - Numbness & tingling – hyper- and paresthesias

**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

**Neurotoxicity Assessment Tool May Help to Identify PN Symptoms**

<table>
<thead>
<tr>
<th></th>
<th>Not at All</th>
<th>A Little</th>
<th>Some-what</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have numbness or tingling in my hands</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel moderate tingling in my feet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel discomfort in my hands</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have joint pain or muscle cramps</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel weak all over</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have trouble hearing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I get a ringing or buzzing in my ears</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have trouble buttoning buttons</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have trouble fitting the shape of small objects when they are in my hand</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have trouble writing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</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?"
Nursing Considerations: Psychosocial

- Assist patient and families in coping with:
  - Survivorship
  - an incurable disease
  - the “Watch and Wait” approach to MGUS and Smoldering Myeloma

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

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

On the count of three – everyone say water.... 1, 2, 3