When you suspect a malignant blood dyscrasia, what do you do until the specialist arrives?

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Disclosures

pleased to be invited to CSHP BC Branch AGM
belonged to VGH Pharmacy and worked in Leukemia/BMT Program of BC since 1995
keen not to bore
no COI

Learning Objectives

By the end of this session, participants will be able to:

- understand the basic pathophysiology of common malignant blood dyscrasias
- appreciate patients are living longer in the community with malignant blood dyscrasias
- identify therapeutic interventions a clinical pharmacists can make in caring for a patient when the diagnosis is suspected and after active treatment is complete

Outline

Review hematopoiesis
Describe common blood cancers
Present cases and interventions
Review treatment options

Blood Cancers in BC*

40 new cases/week

New cases per year

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>600</td>
</tr>
<tr>
<td>Myelodysplasia</td>
<td>200</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1000</td>
</tr>
<tr>
<td>Myeloma</td>
<td>200</td>
</tr>
</tbody>
</table>

BC Cancer Registry (est. 1969)
* Population ~ 4.4 million
Bone Marrow and Blood

Lymph Nodes and Spleen

Bones and Kidneys

Multiple Myeloma

Acute Leukemia

Causation: Genetic/Environmental

Susceptible

General Population

Resistant

Cancer Risk

Exposure

Dr. John Spinelli, BCCA
Acute Leukemia Case

I.G. is a 65 y.o. male
- decreased energy over the last several weeks
- he is sent to the ER

P/E: pale, dyspnea, chest pain, and unexplained bruising on his extremities.

Complete blood count:
- WBC 150 x10⁹/L (range 4-11)
- Platelets 12 x10⁹/L (range 150-400)
- Hemoglobin 90 g/L (range 135-170)

Bone marrow biopsy - acute leukemia

Leukemia Case - Signs and Symptoms

<table>
<thead>
<tr>
<th>Underlying Condition</th>
<th>Signs &amp; Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>Palpitations, dyspnea on exertion, fatigue, malaise, pallor, dizziness, orthostatic hypotension, hypoxemia</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Gingival or mucous membrane bleeding, epistaxis, petechiae, gastrointestinal or urinary tract bleeding, easy bruising</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Fever, severe or prolonged systemic infections, skin abscesses (especially perianal), meningitis, pneumonia</td>
</tr>
<tr>
<td>Tissue infiltration</td>
<td>Adenopathy, splenomegaly, hepatomegaly, gingival hyperplasia, bone pain, cranial nerve deficits</td>
</tr>
<tr>
<td>Hypermetabolic state</td>
<td>Fatigue, night sweats, low-grade fever</td>
</tr>
<tr>
<td>Leukostasis</td>
<td>Alteration in mental status, blurred vision, cranial nerve palsies, priapism, dysuria, pleuritic chest pain due to leukemic embolus in pulmonary vasculature</td>
</tr>
</tbody>
</table>

Leukemia Case - Treatment

Reminder

WBC 250 x10⁹/L
Platelets 12 x10⁹/L
Hemoglobin 90 g/L

What is the most dangerous immediate complication of initiating chemotherapy in this patient?

What measures can you take to minimize this complication?

Leukemia Case - Tumor Lysis Syndrome

- rapid death of malignant cells ↓ release of intracellular contents into systemic circulation
- hyperkalemia, hyperphosphatemia, hypocalcemia and hyperuricemia
- metabolic burden on kidneys which can lead to acute renal failure, EKG changes & death
- 12-24 hours after chemotherapy is initiated

Leukemia Case - Tumor Lysis Syndrome

Large tumor burden
Elevated WBC count
High tumor growth fraction or rapid tumor growth rate
Chemosensitive disease
High serum urate level
Elevated LDH – can be ↓ as a result of cell destruction in patients with a large tumor mass
Presence of volume depletion
Pre-existing renal dysfunction
Concentrated acidic urine pH

Aggressive hydration (3L/m²/24hr) to achieve urine output greater than 100mL/hr – initiate 24-48hr prior to chemo

Electrolyte-free IV solutions

Alkalize urine only if the uric acid is elevated to increase solubility of urate (use NaHCO₃ IV/PO to maintain pH >7)

Allopurinol to ↓ urate formation

If PO₄ becomes elevated, Amphojel® (aluminum hydroxide) 15-30mL q4h. Remove NaHCO₃ if it has been added

Rasburicase only in high risk cases (high uric acid and impaired renal function or unable to take allopurinol)
Other pharmaceutical pearls:

- stop all ASA or NSAIDS if thrombocytopenic
- stop heparin or warfarin if platelets <50 x10^9/L
- low threshold to start broad spectrum antibiotics if patient develops fever (T>38°C) if neutropenic (absolute neutrophil count <500) - START IMMEDIATELY
- often present with HSV infections, start acyclovir or valacyclovir

S.H. is a 60 y.o. previously healthy female in Prince George who has progressive back pain over 2 months. She has had repeated urinary tract infections. Blood work revealed anemia, significant kidney dysfunction, increased proteins, IgG monoclonal gammopathy. She is diagnosed with multiple myeloma. Her GP has started dexamethasone and she is scheduled to see a BMT doctor in Vancouver in 6 weeks for a potential transplant. The GP asks you if you know of anything else she should receive in the meantime.

Multiple Myeloma Case

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**Multiple Myeloma Case**

**Lymphoid Malignancy - B-cell neoplasm**

**Presentation**
- Bone Pain - pathologic fractures, vertebral collapse
- Renal Impairment - light chain deposits, hypercalcemia, dehydration
- Infection - lack of normal immunoglobulins
- Neurologic Symptoms - spinal cord compression, polyneuropathy, mental changes (hypercalcermia)

**Pharmaceutical pearls:**
- Fractures: start pamidronate* 90mg IV once monthly for prevention of fractures and reduce bone pain (watch in renal dysfunction), calcium and vitamin D
- Bone pain: analgesics as required
- Renal dysfunction: IV hydration, avoid NSAIDs, avoid IV contrast
- Infection: consider pneumovax and influenza vaccine
  - on high dose dexta: HSV prophylaxis, fungal management, PCP prophylaxis, monitor blood sugars, start H2 blocker or PPI


**Impact of New Drugs on Survival in BC**

<table>
<thead>
<tr>
<th>Date of Diagnosis</th>
<th>% alive at 5 years</th>
</tr>
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<tbody>
<tr>
<td>Before 2003</td>
<td>50%</td>
</tr>
<tr>
<td>2003 and beyond</td>
<td>70%</td>
</tr>
</tbody>
</table>

**Multiple Myeloma Case**

**Supportive therapy with novel agents used in the treatment of multiple myeloma**

- **Prophylaxis against DVTs and PE (thalidomide or lenalidomide)**
  - Anticoagulation recommended with ASA 80mg/day

- **Prophylaxis against HSV (bortezomib)**
  - Acyclovir or Valacyclovir
Interferon vs. Hydroxyurea or Busulfan (1986-1988)

Median Survival (months)

<table>
<thead>
<tr>
<th></th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN</td>
<td>76</td>
</tr>
<tr>
<td>HU or BU</td>
<td>52</td>
</tr>
</tbody>
</table>


Molecular Biology of CML

Numerous investigators, 1982-1990

Imatinib (IRIS, 2000-2001)

Estimated overall survival at 7 years is 86% (94% considering only CML-related deaths)

**New Treatments for Blood Cancer**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatments</th>
</tr>
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<tbody>
<tr>
<td>CML &amp; ALL</td>
<td>Imatinib, Dasatinib, Nilotinib</td>
</tr>
<tr>
<td>AML</td>
<td>Gemtuzumab, Arsenic, DT-IL3</td>
</tr>
<tr>
<td>MDS</td>
<td>Azacitidine, Lenalidomide</td>
</tr>
<tr>
<td>CLL</td>
<td>Alemtuzumab, Rituximab</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Lenalidomide, Bortezomib</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Rituximab, Tositumomab</td>
</tr>
</tbody>
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**Personalized Medicine**

- **Past**
- **Present**
- **Future**

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**Malignant blood cancers**

- constitute 10% of all cancers
- increasing prevalence due to population growth in high risk age group
- patients are living longer often with their disease at presentation, try to prevent complications related to thrombocytopenia +/- kidney dysfunction, immunosuppression and high tumor burden
- long term management includes infection and thrombosis prevention depending on therapy

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**Acknowledgments**

Colleagues

- Dr. Micheal Barnett
- Dr. Kevin Song