In the Name of God

“Hematologic Malignancies”
Definition & Classification

- Arising from hematopoietic cells & lymphoid tissues
- Myeloid: granulocytes, monocytes, erythrocytes, platelets
- Lymphoid: B & T lymphocytes
Hematopoietic stem cell

**ALL**

- Lymphoid progenitor
  - naïve
  - B-lymphocytes
  - T-lymphocytes
  - Plasma cells

**AML**

- Myeloid progenitor
  - Neutrophils
  - Eosinophils
  - Basophils
  - Monocytes
  - Platelets
  - Red cells

*Plasma cells*
Classification

- Leukemia
- Lymphoma
- Plasma Cell Disorders

- Uncommon < 10% of all cancers
- Chemotherapy
- Surgery and/or radiation is not used
- Growth rate; Rapid
Leukemia

- Myeloid or lymphocytic
- Acute (immature) or chronic (mature)

Acute Myeloid Leukemia (AML)
- Adults
  - Appear suddenly; progress rapidly

Acute lymphocytic Leukemia (ALL)
- Children
  - Death due to infection or bleeding within weeks to months
Classification of acute leukemias

**ALL**
- mainly children
- M > F
- curable in 70% of children
- curable in minority of adults

**AML**
- mainly adults
- M > F
- curable in minority of adults
Leukemia

<table>
<thead>
<tr>
<th>CLL</th>
<th>Chronic Lymphocytic Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>CML</td>
<td>Chronic Myeloid Leukemia</td>
</tr>
<tr>
<td>Survive for Years</td>
<td>Curable in only a fraction</td>
</tr>
</tbody>
</table>
Lymphoma

- Two major types
- Hodgkin disease (HD)
- Non- Hodgkin Lymphoma (NHL)
- NHL seven times more than HD
Plasma Cell Disorders

- Antibody-secreting B cells
- Most common form;
  - Multiple Myeloma (IgG & IgA)
  - Waldenstrom Macroglobulinemia (IgM)
Leukemia
Acute Myeloid Leukemia

1. Signs & Symptoms; Increasing fatigue, fever, anemia, ↓plt

2. Poor prognostic signs; Age>60 yo, pre-existing hematologic disorder, prior exposure to chemotherapy, poor baseline performance

3. FAB Classification System; French-American-British M₀-M₇

4. ↑WBC; Incapable of fighting infection; stroke, blindness, headache
Treatment

• **First decrease WBC count;**
  – Hydroxyurea 2-4 g Po or Leukapheresis
  – 7+3; idarubicin on days 1-3 + cytarabine on days 1-7

• **Exception;** AML-M3: ATRA or tretinoin starting 2 days before

• **ATRA ADR;** Retinoic acid syndrome (RAS); fever, weight gain, respiratory distress, lung infiltrates, pleural effusion, hypotension, ARF

• Dexe 10 mg BD for 3d
Treatment

• Other ADRs of ATRA: dryness of mouth/skin, hair loss, skin rash, conjunctivitis, muscle weakness, depression, elevated liver enzymes, high cholesterol but patients may alive for 3-5 years

• Arsenic trioxide (ATO): QT prolongation, RAS, N/V, rash, hypokalemia, hyperglycemia
Complication

• Tumor Lysis Syndrome (TLS);
  – Hyperuricemia, hyperphosphatemia, hypocalcemia, uremia => arrhythmia & ARF

• Allopurinol; before chemotherapy 300-600 mg/d

• Rasburicase; catalyst in enzymatic oxidation of uric acid to allantoin - effect within 4 hours; expensive
Complications

- Myelosuppression;
  - Filgrastim
  - Sargramostim esp. in older > 55 yo

- Thrombocytopenia;
  - Plt < 10000/mm3 ; transfusion
  - premenopause; ocp or medroxyprogesterone 10-20 mg/d
Postremission Therapy

• High-Dose Cytarabine, low dose in elderly
  ➢ Cerebellar
  ➢ Ocular (artificial tears, corticosteroid eye drops in case of conjunctivitis)
  ➢ Dermatologic Toxicity
Refractory or resistant AML

- Gemtuzumab; anti CD33 antibody
• Signs & Symptoms; 30-40% asymptomatic, splenomegaly

• Initial treatment; Reduce WBC; Hydroxyurea to WBC <20000/mm$^3$

• Curative therapy; Allogeneic HCT; best result in young patients within 1 year of diagnosis

• Complete response; WBC<10000/mm$^3$ and Plt<450000/mm$^3$
Treatment

- Imatinib mesylate (Gleevec); max 400 mg BD
- Most common toxicities; superficial edema, nausea, muscle cramps, rash
- Refractory or intolerant of Imatinib; Dasatinib 70 mg BD
ALL (Acute lymphocytic Leukemia)

- Poor prognostic factors; ↑WBC, very old or very young
- Treatment for children; vincristine, prednisone, asparginase ± anthracycline
- Treatment for adults; vincristin, prednisone, anthracycline ± asparginase
- Prophylactic therapy to prevent CNS disease (HD/IT/ cranial irradiation)
- Long term MD for 2-3 years; MTX/ MP
CLL (Chronic Lymphocytic Leukemia)

• Signs and symptoms; Lymphocytosis > 5000 lymph/mm3 with the absence of fever or signs of infection

• Most common type of leukemia in adults
• In 90% cases; age > 50 yo
• 40% asymptomatic
Indications for treatment

- Significant anemia and/or thrombocytopenia
- Lymphadenopathy, hepatomegaly, splenomegaly, \( L^x2<6\text{mo} \)
- Recurrent Infections
Initial Therapy

- Elderly; Chlorambucil
- Fludarabine; ADR; fever, myelosuppression, immunosuppression
- Cladribine
- Rituximab; anti-CD20; pretreatment with acetaminophen & diphenhydramine
- Prophylaxis; pcp, herpes simplex/ zoster, IVIg
- Alemtuzumab; anti- CD52 monoclonal Ab
Lymphomas
Non- Hodgkin Lymphoma

- Signs and symptoms; LAP, extranodal involvement; fever (>38°C), night sweats, weight loss (>10% body weight over 6mo) : B symptoms
- Indolent vs aggressive
- CHOP; cyclophosphamide, doxorubicin, vincristine, prednisone
- R-CHOP; Rituximab
- Antiemetic, bowel regimen, GCSF
Non- Hodgkin Lymphoma

• Radioimmunotherapy
• If Plt > 100,000/mm³

• For preservation of thyroid what do you suggest?
• 2 drops of KI PO TID 24h before the first dose for 14d after therapy
• Avoid social contact up to 7 days
• Hematologic toxicity up to 9 wks
Hodgkin Lymphoma

- Curable even in advanced stages
- Painless lymph node, most commonly neck (cervical or supraclavicular)
- **ABVD**: doxorubicin, bleomycin, vinblastine, dacarbazine
- **ADR**: Pulmonary complication
Plasma cell Disorders
Multiple Myeloma

- Prevalent in men and older; >40yo
- Bone pain & skeletal disease
- Hypercalcemia, renal dysfunction
- Treatment;
  - Thalidomide; immunomodulator, antiangiogenic, 200-800 mg/d
    ✓ ADR; sedation, constipation, thrombotic events and neuropathy
  - Dexamethasone or a combination
• HCT (Hematopoietic Cell Transplantation)
• What about significant bone loss?
  – Pamidronate 90 mg over 2 hours
  – Zoledronic acid 4 mg over 15 min
• Bisphosphonates can precipitate renal failure
• Osteonecrosis of jaw (ONJ); rare but serious
• More common with Zoledronic acid
• Discontinue after 2 years
Thank you For your Attention