HEME MALIGNANCIES

MYELOID PROLIFERATIVE NEOPLASMS

① Polycythemia Vera

Epidemiology: all populations. All ages. Median age = 60. Men > women.

Etiology: No known cause.

Clinical manifestations: Incidental after ↑ hgb. Others present: headach , dizziness, satiety, visual disturbances.

Lab manifestations: hgb > 18.5. WBC > 10,500. Platelet > 450,000. ↑ LDH. JAK2 mutation. ↓ serum epo level.

Diagnostic Studies: CBC. Bone marrow.

Treatment: not curative but to ↓ symptoms. Phlebotomy. Aspirin if ↑ platelets. Hydroxyurea. Jakify.

② Essential Thrombocytosis

Epidemiology: ↑ prevalence in black people. 2:1 female to male. Median age = 60.

Etiology: Unknown. Most have mutation in Jak2, CALR, MPL → upregulates Jak pathway → ↑ platelets.

Clinical manifestations: Incidental. others present: headache, dizziness, visual changes, thrombosis.
"classic" symptoms = "vasomotor symptoms" → related to microvascular disturbance.

Diagnostic Studies: CBC w/ diff. Peripheral smear. Bone marrow biopsy.

Lab manifestations: Thrombocytosis with platelets of varying size. Normal (or hypercellular) marrow.

Treatment: minimize complications. High risk - hydroxyurea, anticoagulation. Low risk - aspirin.

Prognosis: overall good. Risk of progressing to MDS/AML.

③ Primary Myelofibrosis

Epidemiology: least common MPN. Median age = 67. Some familial links.

Etiology: unknown. Possible link to exposures (radiation)

Clinical manifestations: fatigue. Symptoms due to large spleen, fever, bone pain, night sweats, etc.

Diagnostic Studies: CBC. CMP. Bone marrow biopsy.

Lab manifestations: CD34+ circulating cells. Fibrosis. Genetics.

Treatment: high risk - hydroxyurea, Splenectomy, radiation, chemo

Prognosis: can transform to AML

MYELODYSPLASTIC SYNDROME: pre-leukemia

Epidemiology: Older adults. Median age = 70. Predominatly male. Relatively common.

Etiology: Unknown. Can arise from CHIP (clonal hematopoiesis). Associated with: cytotoxic chemo, radiation, and toxins

Clinical manifestations: fatigue, bruising, cytopenias, infections. OR totally asymptomatic.

Diagnostic Studies: CBC w/ diff. Smear. Bone marrow biopsy.

Lab manifestations: cytopenias. ↑ blasts, ↓ platelets. Dysplasia, hypercellular, impaired myeloid maturation, ineffective erythropoiesis, abnormal megakaryocytes, fibrosis.

Treatment: depends on risk and pt performance. ↓ symptoms, ↑ quality of life, prolong survival.
- GF, transfusion support, azacitidine, other chemotherapies.

LEUKEMIAS

Neoplasms of hematopoietic cells with significant peripheral blood and bone marrow involvement.

B symptoms: fever, chills, night sweats, weight loss, fatigue

CHRONIC MYELOGENOUS LEUKEMIA (CML)

- Classified as a myeloproliferative disorder but STILL CANCER.

Epidemiology: 1 to 2 / 100,000. Median age = 65. 1.4:1 male to female.

Etiology: neoplastic transformation of a hematopoietic myeloid progenitor cell. Risk factor = ionizing radiation

Clinical manifestations: Symptoms - fatigue, sweats, fever, weight loss, fullness/early satiety ("B" symptoms).
OR Asymptomatic
PE findings - splenomegaly and hepatomegaly.

Diagnostic studies: CBC w/ diff. FISH for BCR-Abl = t(9;22) = philedelphia chromosome. BMBx to determine phase.

Lab manifestations: leukocytosis, anemia, thrombocytosis → body using up energy to make WBCs and platelets.
↳ neutrophilia, basophilia, eosinophilia

Treatment: Abl tyrosine kinase inhibitors (Gleevac - imatinib mesylate). Allo SCT for severe cases.
(used to control NOT treat) (↑ mortality but can CURE)

Prognosis: Can transform to acute leukemia

Staging: Chronic → 3-5 yrs. Slow and drawn out.

Advanced → accelerated (6-9 month duration) → blast crisis (3-6 month survival)
↑ WBC, splenomegaly, ↓ response to therapy
worsening symptoms, cytopenias, extramedullary disease
Behaves like acute leukemia.

CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

- malignancy of mature B-cells.
  ↳ Malignant cells are morphologically homogeneous population of mature lymphocytes.

Epidemiology: most common adult leukemia. 5/100,000 people. Median age = 70.

Etiology: malignancy of mature B-cells.

Clinical manifestations: Symptoms - B symptoms. Frequent infections. Sometimes incidental.
PE findings - lymphadenopathy, splenomegaly, hepatomegaly.

Diagnostic studies: Flow cytometry and smear - CD5+ CD23+, CD20+, CD19+ and smudge cells. CBC + diff + BMBx.

Lab manifestations: lymphocytosis. Anemia. Thrombocytopenia. Hypogammaglobinemia
↳ mature B-cells aren't becoming plasma cells.
NO plasma cells = no immunoglobulin production

Treatment: Watchful waiting. If worsens → BTK inhibitors, Anti-CD2 monoclonal antibodies, venetoclax.

Prognosis: determined by cytogenetic changes. p53 mutation with 17p deletion = more aggressive.
13q or trisomy 12 = better prognosis.

Staging: CT or PET. 0 = lymphocytosis only. 1 = + lymphadenopathy. 2 = + splenomegaly. 3 = + anemia. 4 = + thrombocytopenia.
↳ look for cytopenias

ACUTE MYELOID LEUKEMIA (AML)

- malignancy of a committed myeloid progenitor → clonal expansion of myeloblasts.
  - malignant cells lose ability to differentiate.

Morphologically homogeneous population of myeloblasts.

Epidemiology: 4.3/100,000. Median age = 69.

Etiology: can arise de novo or as a consequence of underlying disorder (MDS or MPS)

Clinical manifestations:
- SEVERE anemia - fatigue, dspnea.
- SEVERE neutropenia - ↑risk of opportunistic infection
- SEVERE thrombocytopenia - ecchymoses, petechiae, mucocutaneous bleeding
- Hyperleukocytosis - ↑blood viscosity, mental status changes, dysnea, more likely in AML.
- Acute DIC - coagulopathy most commonly seen in acute promyelocytic leukemia.

Diagnostic studies: must have >20% blasts in marrow. CBC w/ diff. Coags. BMBx w/ flow and cytogenetics.

Lab manifestations: increased blasts and auer rods (commonly seen in APL - form of AML)

Treatment: CURABLE. Induction - high dose → clear out marrow → goal is remission. Lower-intensity or combo therapies.
Allogenic stem cell transplant for HIGH-RISK. High morbidity/mortality.

Prognosis: older → worse. GOOD: t(15;17). BAD: deletions of chromosome 5 and 7.
History of MDS/myeloproliferative disorder → BAD. Treatment related → BAD.

ACUTE LYMPHATIC LEUKEMIA (ALL)

- malignancy of a committed lymphoid progenitor cell (pre-T or B cell)
  - malignant cells lose ability to differentiate

Morphologically homogeneous population of lymphoblasts.

Epidemiology: most common cancer in Children. Peak incidence = 2-5 yo. Median age = 15.

Etiology: most commonly of B-cell origin. Less commonly T-cell (mediastinal or soft tissue mass)

Clinical manifestations: Variable. Chronic fatigue. Freaventiy have peripheral blood leukocytosis w/ circulating blasts.
- SEVERE anemia - fatigue, dyspnea
- SEVERE neutropenia - opportunistic infections
- SEVERE thrombocytopenia - ecchymoses, petechiae, mucocutaneous bleeding
- Hepatosplenomegaly - abdominal pain, early satiety.
- Lymph node involvement
- Mediastinal mass - precursor T-cell ALL.
- CNS involvement - prevention is key goal of treatment.
- Testicular involvement - predictor of relapse in men.

Lab manifestations: Peripheral blood leukocytosis with numerous circulating blasts. TLS is EMERGENCY

Treatment: intrathecal chemo or cranial radiation to prevent CNS relapse.

Prognosis: B-cell → generally good especially in kids. T-cell → higher risk. Worse prognosis.
- age: <1 or ≥10 → BAD
- cytogenetics: hyperploidy → GOOD. t(9;22) 11q23 translocation, hypodiploidy → BAD
- high WBC count → BAD

LYMPHOMAS

CD20

Cancer that begins in cells of lymph system

Malignant neoplasm of lymphocytes associated with a solid mass or infiltrate

Differential diagnoses: for lymphadenopathy.

- **Benign reactive lymphadenopathy**: reaction to an immune stimulus.
  - pathalogic pattern relates to type of cell (B or T), not specific as to cause, and normal nodal architecture is preserved.
  - most common cause of enlarged lymph nodes

Lymphoma Epidemiology

- 7th most common cancer in America.
- 92,300 new cases and 21,000 deaths per year.
- Highest incidence: US, Australia, New Zeland, Europe.

Risk factors: Usually no known cause.

- age, infection, autoimmune, immunocompromised, exposures.

WHO Classification

- Non-hodgkin: B-cell (85%) or T-cell (15%)
- Hodgkin

Staging

1. single node OR single site
2. Two + nodes OR extra site on same side of diaphragm.
3. Lymphatic involvement on both sides of diaphragm.
4. Liver or bone marrow involvement OR extensive involvement of another organ.

Classification based on nature of lymphoma

Low Grade → Intermediate grade → High grade

Asymptomatic

B symptoms
- fevers
- night sweats
- weight loss

Follicular Lymphoma

Epidemiology: middle age - elderly.

Clinical manifestations: variable

Diagnostic: excision lymph node biopsy, imaging, BMBx (if localized)

Lab results: Small cleaved cells, CD10, CD20, BCL2 +, t(14;18)

Prognosis: median survival = 10 years
- incurable with conventional chemo.
- Typically present with high stage.
- Many progress to diffuse large cell

Treatment: Bendamustine + Rituximab

Treatable but NOT curable

Diffuse Large B-Cell Lymphoma

Epidemiology: most common NHL
Occurs in children and adults
1/3 of cases are extranodal

Etiology: Immune dysfunction

Presentation: nodal mass or B symptoms

Diagnosis: excision lymph node biopsy, PET

Lab results: CD20+, BCL-6+ can be CD5, CD10, MYC, BCL-2 positive also

Treatment: goal is to cure.

Front line - R-CHOP with curative intent
- If relapse → SCT or CAR-T therapy

Burkitt Lymphoma

Epidemiology: endemic → Africa (95% EBV +)
Non-endemic → worldwide (15-20% EBV +)
Predominantly in children

Presentation: quite symptomatic w/ B symptoms

Diagnosis: excisional lymph node biopsy
PET/CT. LP/MRI to make sure its not in CNS.

Lab findings: t(8;14) most common.
- c-myc proto-oncogene downstream IgH gene.

Mature B-cell phenotype (CD20+, MYC+)

"Starry Sky"

Prognosis: Very curable

Treatment: no agreed front line. Need CNS-directed therapy

HODGKIN LYMPHOMA

Epidemiology: EBV present in 40% of cases. Peak = 20. No extranodal involvement. Spreads along adjacent nodes.

Clinical manifestations: Symptoms typically due to location of nodal mass in neck/chest.

Diagnostic studies: Excisional lymph node biopsy. PET/CT to pick up marrow involvement.

Lab manifestations: CD30+. Reed-Sternberg cell = pathonomonic.

Prognosis: Very curable. Consider STC or other regimens if relapse.

Treatment: Front line = ABVD

- PET/CT after two cycles is prognostic and dictates course of further treatment.

PLASMA CELL DYSCRASIAS

Diseases associated with monoclonal proliferation of immunoglobulin producing plasma cells.

Epidemiology: Mean age = 69. 2:1 AA to Caucasian. Men > women. 10-15% of heme malignancies

Clinical presentation: Organ dysfunction. Lytic lesions or fractures.

Diagnosis: monoclonal protein? SPEP, serum IFE, Ig levels, UPEP/IFE.
Organ damage? HP, CBC, skeletal survey, PET, MRI.

CD138

Normal Plasma Cells → **MGUS** → **Smoldering myeloma** → **Multiple Myeloma**

MGUS
- Benign
- M protein: <3g/dL
- Plasma cells: <10%
- NO CRABS
- Older adults
- Watch and wait

Smoldering myeloma
- Asymptomatic
- M protein = ≥3 g/dL
- Plasma cells = ≥10%
- NO CRABS
- Continued monitoring
- Higher risk for developing MM

Diagnostic criteria:
1. M-protein in serum or urine. (≥3g/dL)
2. Clonal plasma cells in marrow OR plasmacytoma (>10%)
3. CRAB - relate organ damage
   - C = hypercalcemia
   - R = renal insufficiency
   - A = anemia
   - B = bone lesions
4. SLiM criteria

Epidemiology: peak 65-70. Males > females. AA > white > Asian

Etiology: family Hx. Radiation. Chronic antigenic stimulation

Tests: CBC, BUN/Cr (renal function), Smear, Skeletal survey (Rouleaux - Stacked)

Treatment: not curable. Chemo.

Prognosis: Cytogenetic studies

Staging: B_2 microglobulin and albumin.