Acute → > 20% blasts

Acute leukemia

ALL (Acute Lymphoblastic Leukemia)

- Disease of **children** .
- **Symptoms:**
  - **Fever**
  - **Bone pain**
  - Splenomegaly, hepatomegaly, lymphadenopathy (infiltration by malignant cells)
  - **Headache**, vomiting (meningial spread)
  - May cause bone marrow depression (**anemia**, **thrombocytopenia**, **neutropenia**)

- In **Down syndrome** → Risk of ALL ↑ 10-20x

- **Bone marrow biopsy**: hypercellular with lympho**blast** .
- **Lymphocytes antigens:**
  - T-cell CD1,CD2,CD3,CD4,CD5,CD7,CD8
  - B-cell CD10,CD19,CD20,CD21,CD22,CD23

Pre-B cell ALL :

- Markers: **CD10** "CALLA" , **CD19**, **CD20**
- +ve to **TdT**

B-Cell ALL

- Translocations :
  - **Philadelphia chromosome t(9;22)** … Adults … **poor** prognosis
  - **t(12;21)** … children … **good** prognosis

T-Cell ALL :

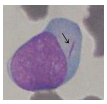
- Common in adolescent males (teens to 20s)
- Makers: CD2,CD3,CD4,CD5,CD7,CD8
- Presents as a mass :
  - Lymphadenopathy
  - Mediastinal mass
  - Anterior with pleural effusions
- Tumor compression may occur :
  - SVC syndrome
  - Tracheal obstruction

- **Treated** with chemotherapy
- In "Sanctuary sites" : Testes and CNS
  - Poor penetration by chemotherapy drugs and relapse may occur in these locations
  - Special treatments (radiation/chemo) used

AML (Acute Myelogenous Leukemia)

- Common in **adults males** (M>F)
- **Symptoms** (symptoms from bone marrow suppression) :
  - **Anemia** : Fatigue, weakness, pallor
  - **Thrombocytopenia**: Bleeding (especially gums)
  - **Neutropenia** : infections
  - Splenomegaly, hepatomegaly, lymphadenopathy (less common than ALL)

- **Peripheral blood smear**: Anemia , thrombocytopenia , Myelo**blast , Auer rods** ... **Hallmark** .
- **Auer rods** (Pathognomonic AML , due to accumulation of MPO , can caus **DIC**).
- So, AML is +ve to **MPO** .



- **FAB** classification system classify AML based on morphological features: **M0-M7**
- A key subtype of AML is **APML (M3)** .
- **Prognostic Factors :**
  - Older age … **poor prognosis**
  - Poor performance status
  - Cytogenetics (**Chr 7 deletion, Chr 5 deletion, trisomy 8**) … **poor prognosis**
  - Molecular mutation
  - 2ary AML … **poor prognosis**
  - Leukocytes count at presentation > 100000 … **poor prognosis**

APML (Acute Promyelocytic Leukemia) (M3)

- Defined by translocation **t(15;17)**
- Creates a **fusion gene**: PML-RARA
  - Promyelocytic leukemia gene (PML) (Chr 15)
  - **Retinoic acid receptor alpha** (RARA) (Chr 17)
    - This abnormal RAR prevents normal maturation of promyelocytes, resulting in the accumulation of a immature cells.
- APML is frequently associated with **DIC**, which can be a **common initial presentation**. The high levels of myeloperoxidase (MPO) in promyelocytes and the release of pro-coagulant factors contribute to this condition.

- **Treatment**
  - **Tretinoin** (**all trans retinoic acid**) → (form of vitamin A)
    - may lead to **ATRA syndrome (Retinoic acid syndrome)**
      - Occurring within the first three weeks of treatment
      - Characterized by fever, dyspnea, chest pain, pulmonary infiltrates, plural and pericardial effusion and hypoxia .

AMML (Acute Myelomonocytic Leukemia) (M4)

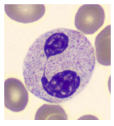
- With **inverted 16** and associated **eosinophilia**
- this is a **good prognostic** category
- Associated with leukemia cutis
- CNS disease may occur

Chronic leukemia

○ CML (Chronic Myelogenous Leukemia)

- Malignant disorder of myeloid progenitor cells
- Classified as a myeloproliferative disorder
- Dysregulated production of **granulocytes** (Neutrophils, basophils, eosinophils)
- **Pathogenesis:**
  The **Philadelphia chromosome** is formed by a **translocation between chromosomes 9 and 22 [t(9,22)],** leading to the creation of the **BCR-ABL fusion gene**. This gene encodes **tyrosine kinases**, which promote increased cell proliferation and reduce apoptosis, resulting in the accumulation of myeloid cells.
- **Lab tests:**
- Peripheral blood (chronic phase):
  - Leukocytosis
  - ↑ neutrophils
  - ↑ myeloblasts, promyelocytes, myeolcytes, bands
  - ↑ **basophils** (rare finding!) → More prominent as the disease progress.
  - ↑ eosinophils
- Mild anemia; normal or **increased** platelets
- All patients should have evidence of the translocation either by **cytogenetics**, **FISH** or **molecularly** **to make a diagnosis** of CML.

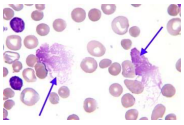
- **CML Phases :**
  - **Chronic phase (usually years)**
    - Can be asymptomatic (↑ WBC on blood testing)
    - Fatigue, malaise, weight loss, **splenomegaly (90% LUQ pain & mass)**
    - Few blasts (usually <5%)
    - More responsive to treatment,especially TKI
  - **Accelerated phase (usually months)**
    - Basophilia, anemia
    - We start seeing immature cells (blasts between 10-20% in blood or BM)
    - Treatment failure (rising WBC)
  - **Blast crisis**
    - Clinically, it behaves like an **acute leukemia** (>20% blasts in periphery or marrow)
    - **Hyposegmented neutrophils** may appear **(Pelger-Huet anomaly)**.
    - Transform to **AML** (more common) or ALL
    - Refractory to treatment



- **Treatment**
  - Imatinib (Tyrosine Kinase Inhibitors) **TKI**
    - Side effects: myelosuppression, Resistance
  - Stem cell transplant (SCT)
  - Bone marrow transplant (BMT) for crisis

CLL (Chronic Lymphocytic Leukemia)

- Disorder of naïve **lymphocytes (lymphocytosis)**
- Characteristic immunophenotype :
    - **CD5**+ B cells
    - "Co-express CD20 and CD5"
- Median age 60
- Patients often **asymptomatic**
- **Clinical Presentation** :
    - Lymphadenopathy, splenomegaly, hepatomegaly
    - **Hypogammaglobulinemia** (↓ IgG, IgA, IgM) → Increased susceptibility to bacterial infections
    - Anemia (Anemia of chronic disease, **autoimmune hemolytic anemia (treated with steroids)**).
    - Thrombocytopenia
- Many patients observed without treatment
- On blood smear : **Smudge cells … Hallmark**



- Patients with **CD38 +ve** , **ZAP +ve** have poor prognosis
- **CLL treatment criteria:**
    - Patient has symptoms
    - Decline in Hb or Plt. (anemia & thrombocytopenia)
    - Lymphadenopathy
    - Hepatosplenomegaly
    - Recurrent infections
- **Treatment :** chemoimmunotherapy

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