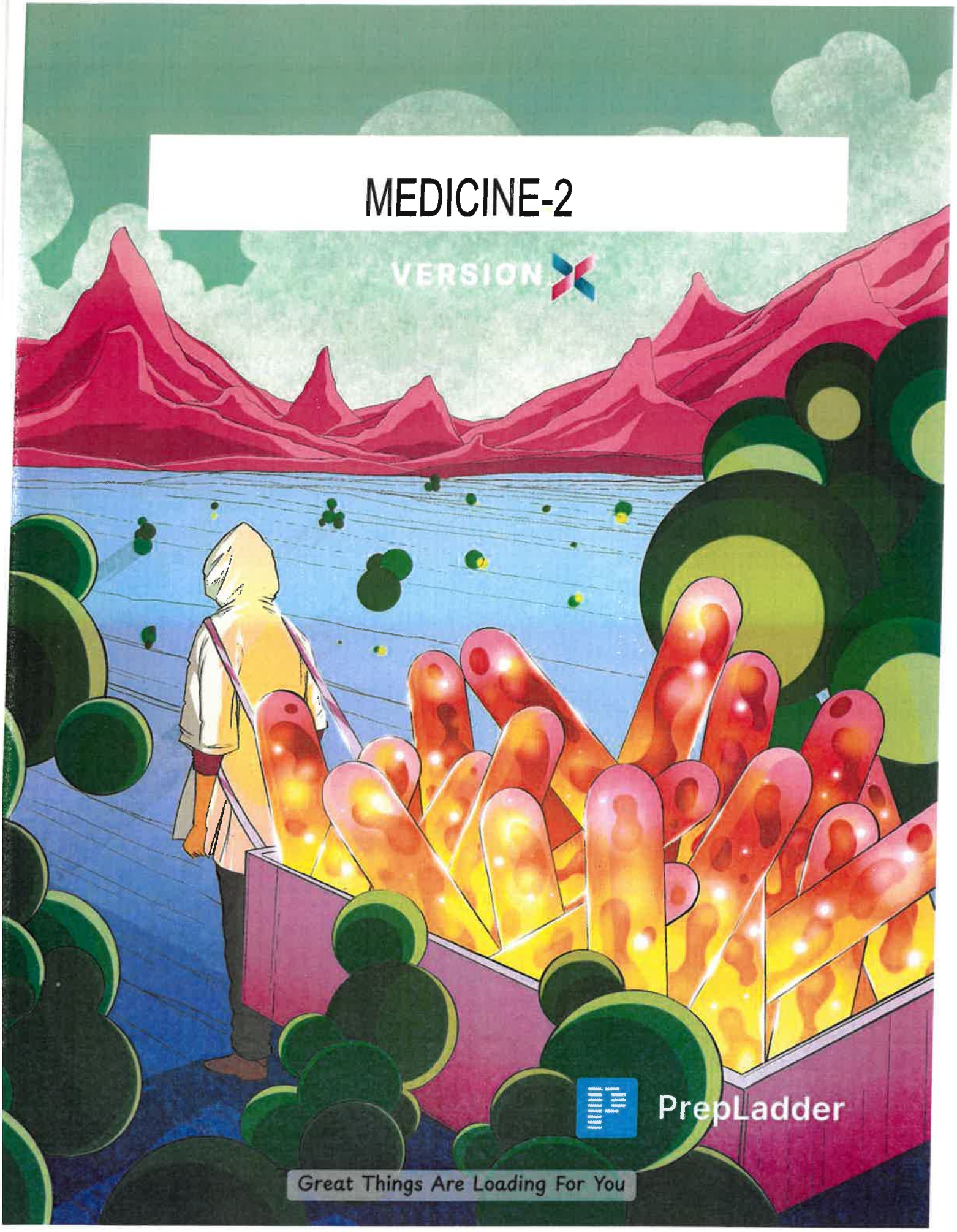
MEDICINE-2

VERSION X



PrepLadder

Great Things Are Loading For You

1. CHRONIC LYMPHOCYTIC LEUKEMIA

CHRONIC LYMPHOCYTIC LEUKEMIA

M/c LEUKEMIA

- In adult/geriatric population: CLL
- In adult population: AML
- In children-ALL

PATHOLOGY

00:01:41

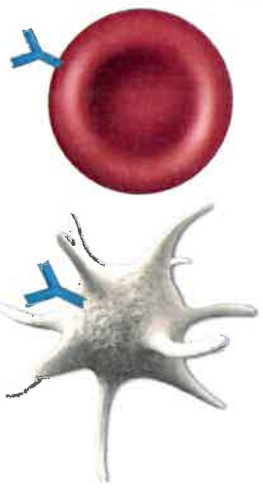
- Tumor of immune competent B cells
- CLL suspected when -
  - Absolute lymphocyte count >5 X 10^9/ ml X 3 months
- If count < threshold, no nodal involvement, no organomegaly and absent cytopenia - Monoclonal B cell lymphocytosis
- Monoclonal Gammopathy of Unknown Significance (MGUS) → Smouldering myeloma →Multiple myeloma → Plasma cell leukemia

Important Information

- Atypical lymphocytosis - seen in EBV (Infectious mononucleosis)

- Proliferation of immune-incompetent B- cells with following features
  - Attack self RBC and platelets
    - → COOMBS positive haemolytic anaemia
    - → IgG class of antibodies present for all classes of autoimmune haemolytic anaemia except for Cold agglutinin syndrome
    - → Warm antibody mediated damage
  - Flow cytometry - CD5+ B cell
  - Morphologically mature appearing B- cells
    - → Chronic lymphocytic leukemia (CLL)-monoclonal proliferation of mature B lymphocytes defined by absolute number of malignant cells in blood (5 X 10^4/ml)

ZAP 70	REQUIREMENT OF CHEMOTHERAPY
+	By 3-4 years
-	By 8-12 years



- Cells express ZAP 70 (Zeta associated protein 70) - Intracellular tyrosine kinase
- T/t not started for all cases of CLL, depends on health status of an individual
  - Patient with no co-morbidities → Proceed with chemotherapy
  - Patient with multiple co-morbidities (triple vessel disease, uncontrolled DM) → Person can die with complications of diseases
  - Slow progression of tumor gives window of opportunity to diagnose tumor relatively early

RICHTER TRANSFORMATION

CLL can deteriorate into DLBCL (Diffuse Large B cell Lymphoma)

For demonstration- Excision LN Biopsy

- Hypogammaglobulinemia: ↑ incidence of infections → recurrent pneumonia, UTI, Sepsis and leading cause of death in patients

ETIOLOGY

00:09:27

- Deletion of chromosome 13q
- Trisomy 12
- Deletion of chromosome 17p (Worst prognosis)
- Overexpression -
  - ZAP-70
  - BCL-2 - inhibits apoptosis
- Genes responsible - SF3B1, NOTCH-1
- Chemical - Agent orange in Vietnam war

CLINICAL FEATURES

00:11:03

- Age group - geriatric population
- Male to female ratio-7:1
- 50% cases - asymptomatic
- Category B symptoms
  - Similar to that of TB- evening rise of temperature, weight loss, night sweats

CASE SCENARIO

70-year-old man retired army man presents with early satiety, low grade fever, night sweats and involuntary weight loss for one month. On examination pallor with cervical lymphadenopathy with spleen 6 cm below costal margins is noted. His son tells that last month he had developed herpes zoster lesion on thorax.

WORK UP

CBC	• Hb ↓ • TLC↑ • Thrombocytopenia
PERIPHERAL SMEAR	• Spherocytes - Autoimmune Hemolytic Anemia ○ Normal RBC have central pallor but spherocytes are small and lacking central pallor • Smudge cells
FLOW CYTOMETRY ON PERIPHERAL BLOOD	• IOC
IG LEVELS	• ↓ (hypogammaglobulinemia)

IG LEVELS	• ↓ (hypogammaglobulinemia)
COMPLETE METABOLIC PROFILE	• To identify co-morbidities
LN BIOPSY	• Excision biopsy lymph nodes based on FDG PET/CT report for suspected Richter transformation

CLL	CD 19 +	CD 20 (dim) +		CD 23+	CD 5+
MANTLE CELL LYMPHOMA	CD 19+	CD 20 (bright) +		CD 5+	Cyclin D1+
FOLLICULAR LYMPHOMA	CD 10+	CD 19++	CD 20+	CD 23+ CD 5-	Cyclin D1-

STAGING

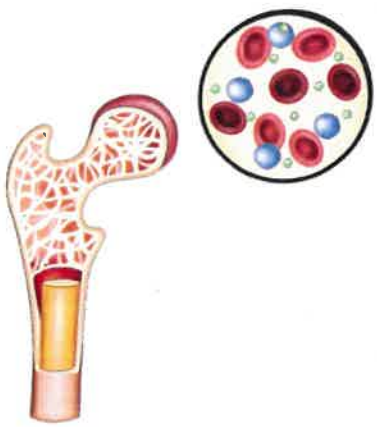
00:18:01

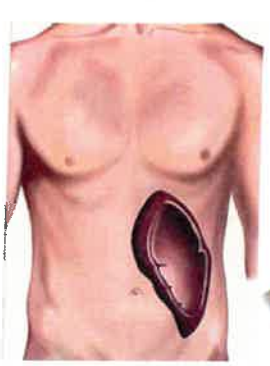
RAI	BINET
Low risk: • Lymphocytosis in blood and marrow	A. <3 lymph node area involvement (Hilar lymphadenopathy, cervical lymphadenopathy, inguinal /axillary group of lymph adenopathy)
Intermediate risk: • Lymphocytosis + cervical lymphadenopathy + hepatosplenomegaly	B. ≥3 lymph node area involved
High risk: • Lymphocytosis + anemia (due to bone marrow involvement)	C. Documentation of presence of anemia - Hb<10 gm/dl, platelet count <1 lac/mm^3

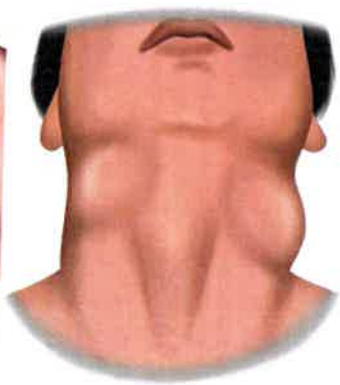
NEED FOR THERAPY IN CLL

00:20:38

- Progressive bone marrow failure
- Massive splenomegaly
- Massive lymphadenopathy
- Autoimmune haemolytic anaemia
- Fever >2 weeks







T/t

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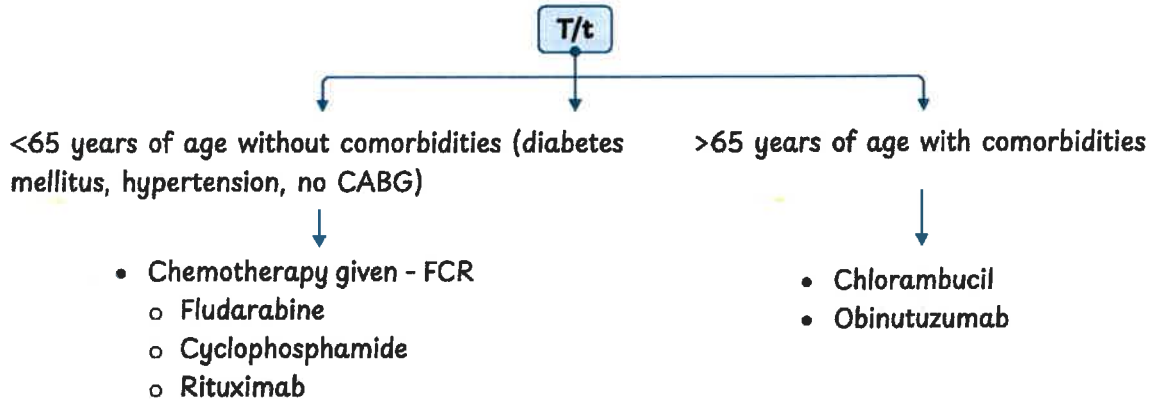


- Anti apoptotic drug - Venetoclax
- Inhibitor of B cell signalling - Ibrutinib, Idelalisib

COMPLICATIONS

00:23:20

- Infection
- Secondary malignancy
  - ↑ risk of skin, prostate cancer
- Autoimmune disorders
  - Autoimmune haemolytic anaemia
  - Autoimmune glomerulonephritis
  - Autoimmune vasculitis

EVAN SYNDROME

- Simultaneous/ sequential appearance of Autoimmune hemolytic anemia and autoimmune thrombocytopenia

MCQ's

Q. A 68-year-old patient presents with early satiety, fatigue and enlarged lymph nodes. Physical examination reveals hepatosplenomegaly. Hb is 8 gm%, TLC is 25000 cells/cumm and absolute lymphocyte count of 8,000/mm^3. peripheral smear is shown below. Which of the following is best test for confirmation of diagnosis?

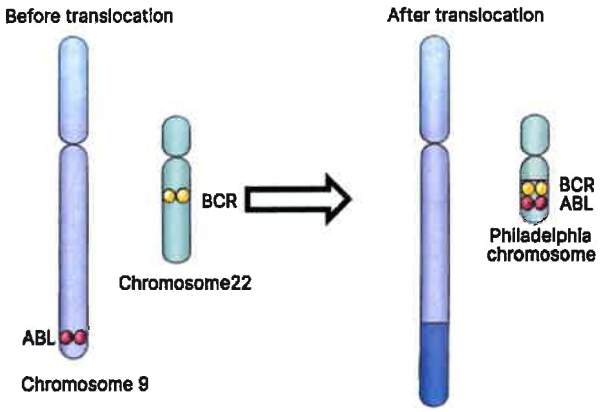
a. Flow cytometry on peripheral blood
b. Bone marrow biopsy
c. FISH
d. Direct coombs test

Ans. *(a)*

2. CHRONIC MYELOID LEUKEMIA

CHRONIC MYELOID LEUKEMIA

- Occurs due to t (9:22) (q34.1, q11.2) → long arm of 9 and long arm of 22
- Example of balanced translocation (no loss of genetic material)



PATHOGENESIS

00:01:50

- Chromosomal swap results in formation of bcr-abl 1 hybrid oncogene
- This produce following novel oncoproteins

$P210^{bcr\text{-}abl}$	M/c fusion protein and levels correlate with diseases activity
$P190^{bcr\text{-}abl}$	Seen in Philadelphia chromosome + ALL
$P230^{bcr\text{-}abl}$	Indolent course

(bcr- breakpoint cluster region, abl- Abelson leukemia)

MANIFESTATIONS CAUSED BY NOVEL PROTEINS

- Inhibition of Apoptosis
- Tyrosine kinase provides unlimited energy to myeloid series and megakaryocyte populations
- Clonal expansion of entire myeloid series (Basophilia)
  - Myeloid series responsible for production of Neutrophils, Basophils and Eosinophils
  - TLC ↑ in Chronic myeloid leukemia → sluggish circulation → risk of Leukostasis
- Neutrophils can survive beyond expiry date, NAP score is low → implies lack of ability to handle infections
- Megakaryoblastic proliferation causes rise of platelet count initially due to stimulated tyrosine kinase activity → platelet count ↑→ risk of thrombotic events
- Progression: Chronic → Accelerated phase → Blast crisis

PROGNOSIS OF CML

- Before advent of tyrosine kinase inhibitors, 10-year survival rate: 30%
- After advent of tyrosine kinase inhibitors, 10-year survival rate: >85%
- Allogenic stem cell transplantation used now for blast crisis and accelerated phase

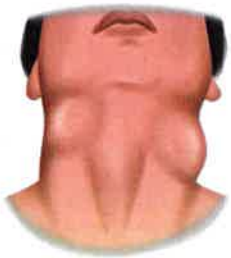
CLINICAL FEATURES

00:09:02

- Age group involved : 55-65 years
- Involuntary weight loss, fatigue & sweating due to Hypercatabolic state
- Pruritus & flushing: Basophilia
- Early satiety & constipation
- On P/A examination: Marked / massive splenomegaly
- Pallor : no multiplication of normoblast →↓ production of RBC
- Initial presentation of diseases: Anaemia with organomegaly
- Enlarged lymph node

THROMBOTIC EVENTS DUE TO

- ↑viscosity - TLC↑
- Leukostasis
- Platelet count ↑



- Due to sluggish circulation - Priapism (involuntary painful erection), blindness, respiratory distress, ↓sensorium, DVT
- Platelet count ↑ initially/ decreased (petechiae) when clonal expansion of entire myeloid series will colonise bone marrow
- Recurrent infections → (Neutrophil Alkaline Phosphate) NAP score ↓

WORK UP

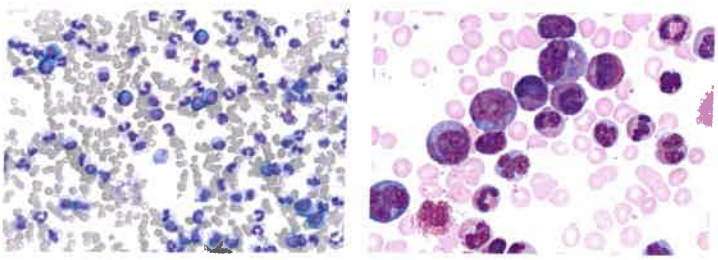
00:13:56

- Haemoglobin↓: Normocytic normochromic anaemia
- TLC↑
- DLC: Basophilia (n: 0-1%)
- Peripheral smear: shift to left: promyelocytes - 8% myelocytes - 20% metamyelocytes - 18%, band neutrophils - 15%, basophils - 10% (illustrative report)
- NAP score ↓
- Vitamin B12↑

VITAMIN B12

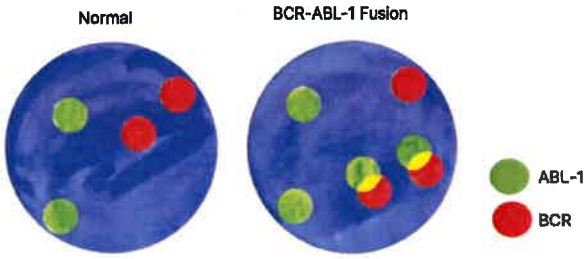
- Vitamin B12 stored in liver and WBCs in body
- WBCs high →↑ Vitamin B12 levels
- WBCs in chronic myeloid leukemia patients, have ↑ levels of transcobalamin receptors → uptake of vitamin B12 ↑ for DNA production

- Platelet count ↑ initially, in subsequent part of diseases → megakaryoblast ↓→ petechiae can occur
- Bone marrow analysis:
  - Hypercellular bone marrow with Myeloid hyperplasia
  - Myeloid: Erythroid= 15-20:1 (normal 2-3:1) → exponential ↑ in myeloid series

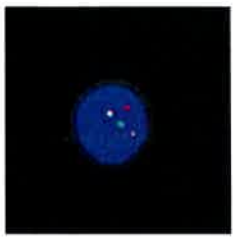


Myeloid Hyperplasia

- Reticulin fibrosis
  → Stain to determine reticulin fibrosis in bone marrow: Snook silver stain
- FISH analysis to quantify Ph+ cells on Peripheral smear/ Bone marrowusing fluorescent probes: **IOC**



- Quantitative PCR for bcr-abl1: best for determining molecular response (total ↓ in cell count of patient)

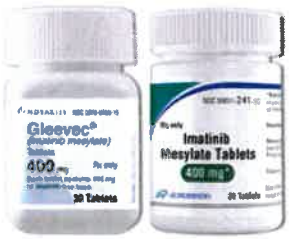


ACCELERATED PHASE	BLAST CRISIS
• Peripheral blood smear (PBS) - >15% blasts • PBS >30% Blasts + promyelocytes • PBS >20% Basophils • Platelet count <1 lak/mm^3	• > 30% blast in peripheral blood or bone marrow • Extramedullary blast proliferation • Start TKI + chemo and SCT (Stem cell transplantation)

T/t 00:21:21

COMPLETE CYTOGENETIC REMISSION	Absence of Ph+ metaphase cells
MOLECULAR REMISSION	>99.9% of cancer cells have been killed and <0.1% of bcr-abl1 transcripts present Or >3 log reduction
MAJOR MOLECULAR REMISSION	<0.0032 % of bcr-abl1 transcripts present/>4.5 log reduction

- 1st generation tyrosine kinase inhibitors: Imatinib → 1st generation tyrosine kinase inhibitor, now showing resistance
- 2nd generation tyrosine kinase inhibitors:
  - Dasatinib, Nilotinib, Bosutinib
- 3rd generation tyrosine kinase Inhibitors used in T315I (≥ tyrosine kinase inhibitor drug failure present) mutation
  - Asciminib> Ponatinib
- Another drug (protein synthesis inhibitor used in T315I mutation): Omacetaxine



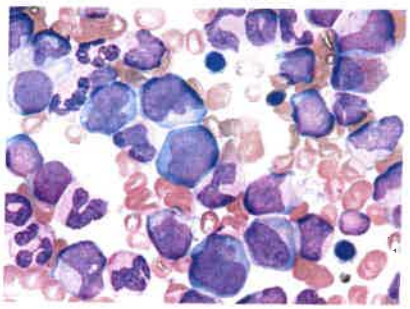
ATYPICAL CML/Bcr-abl1 NEGATIVE MYELODYSPLASTIC/MYELOPROLIFERATIVE NEOPLASM

- BCR-ABL-1 negative
- Chromosome 20 mutation

- Diagnostic clue: Left shift but no basophilia seen
- Median survival of only 2 years (contrast with 10+ years of TKI treated CML)
- T/t: Allogenic SCT (↑ relapse)

JUVENILE CHRONIC MYELOMONOCYTIC LEUKEMIA

- <4 year of age
- Left shift plus monocytosis
- Fetal haemoglobin levels ↑ due to defective proteins that affect hemoglobin switching



MCQ

00:28:25

Q. A 62-year-old male patient with CML diagnosis is found to have a T315I mutation in BCR-ABL1. Which of the following drug will be initiated in this patient?

a. Bosutinib
b. Tofacitinib
c. Ponatinib
d. Nilotinib

Ans. c

3. ACUTE MYELOID LEUKEMIA

ACUTE MYELOID LEUKEMIA

00:00:37

- 5-year survival rate: 25%
- Problems encountered during management:
  - Leukostasis (M/c in AML > CML): ↑ Viscosity → sluggish circulation causing
    → Respiratory distress d/t lung involvement (M/c organ involved) – SPO_2 ↓
    → Drop in Glasgow coma scale
    → Priapism
    → Retinal blindness
  - ↑Risk of DIC

ETIOLOGY

- **Idiopathic**
- **Bone marrow failure**
  - Fanconi anemia
  - Diamond Blackfan syndrome: AML → Aplastic anemia
  - Shwachman-Diamond syndrome → Pancreatic exocrine insufficiency
- **Defective DNA repair**
  - Bloom syndrome and Ataxia telangiectasia
- **Down Syndrome (children < 4 years)**
  - M_7 AML d/t GATA1 gene
    - Acute megakaryoblastic leukemia
- **Secondary malignancy**

EXPOSURE TO	INCUBATION BEFORE AML	ASSOCIATED WITH
Alkylating agents	4–6 yrs	Monosomy 5, 7
Topoisomerase II inhibitors	1–3 yrs	Chromosome 11

- **Radiation exposure**
- **Benzene**
- **Drugs like Phenylbutazone and Chloramphenicol**
- **Chromosomal Translocation**
  - M_3 AML: t(15;17) → PML-RARA fusion gene sequence
    - Differentiation block / maturational arrest at Promyelocytes stage

- M3 AML → ↑ DIC risk
- t(8;21) → RUNX1-RUNX1T1
  - Associated with granulocytic sarcoma / chloroma
- Inversion 16 and t(16;16)
- FLT3-ITD activation mutation (M/c genetic mutation in AML)

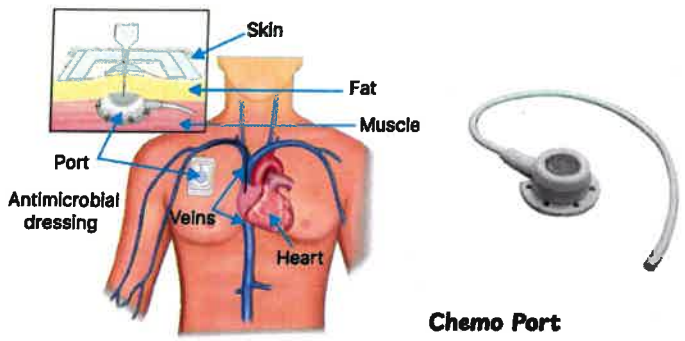
FAVOURABLE PROGNOSIS

FLT3-ITD	t(8;21)
EBPA	Inversion of chromosome 16
NPM1	t(16;16)

- FLT3-ITD^{high} → Poor Prognosis

Important Information

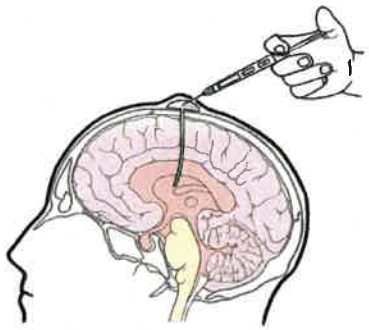
CHEMOPORT



Chemo Port

- Chemoport helps deliver medications directly into **superior vena cava**

OMAYA RESERVOIR



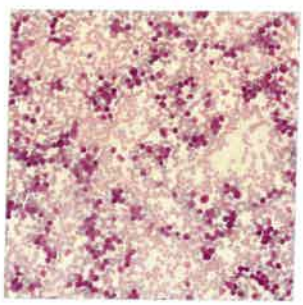
OMAYA RESERVOIR

- An Ommaya reservoir used to deliver medication directly into CSF

CLINICAL FEATURES

00:13:08

- 65 years with fast progression of symptoms over 3 months
- Fatigue/Weight loss
- Fever → Infections (e.g. Pneumonia)
- TLC ↑↑ > 1 lac/mm^3, leukostasis
  - Organs involved in decreasing order:
    - → Lung (M/c)
    - → Brain
    - → Priapism
    - → Blindness



Hyperleukocytosis in Acute Myeloid Leukemia

- Platelets ↓
  - Petechiae, Epistaxis, Purpura
- Lymphadenopathy and hepatosplenomegaly
- Gingival involvement seen in M_5 AML (Acute monocytic leukemia)

Important Information

Acute Lymphoblastic Leukemia (ALL)

- Typically affects children
- Presents with -
  - Rapid onset of anemia, bleeding, petechiae
  - Organomegaly - Hepatosplenomegaly, lymphadenopathy
  - CNS involvement

Acute Myeloid Leukemia (AML)

- More common in older adults (usually >65 years)
- Presents with -
  - Rapid development of anemia, bleeding, petechiae
  - Organomegaly - Hepatosplenomegaly, lymphadenopathy
  - Gingival hypertrophy/ U/L proptosis

- Chloroma/Granulocytic sarcoma
  - U/L proptosis
  - Paraplegia (Spinal cord)
- ↑DIC: t(15:17)
  - M_3 APML

Important Information

AML Subtypes Key Points

- M_3: APML → t(15:17), ↑ risk of DIC
- M_5: Gingival involvement
- M_7: Down syndrome (< 4 yrs)

DIAGNOSTIC CRITERIA FOR AML

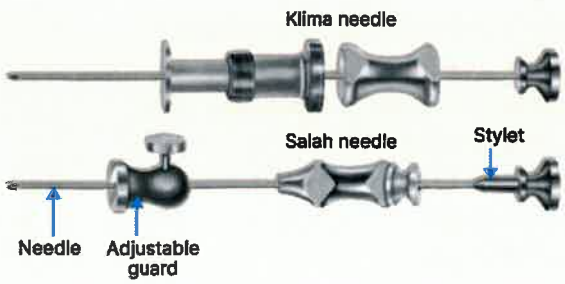
00:18:59

- Bone Marrow Aspiration -
  - Percentage of myeloblasts >20%
  - If chromosomal abnormalities are present, diagnosis of AML is made even if blast count <20%
    → t(15;17), t(8;21), Inv 16, t(16;16)

Important Information

Bone Marrow biopsy needle

- Salah needle, Klima needle



- Jamshidi needle

Bone marrow biopsy needle: Jamshidi needle

WORKUP OF AML

00:23:01

- Lab Findings -
  - Hb ↓, TLC ↓/↑↑, Platelets ↓
- IOC - Bone Marrow Aspiration (>20% myeloblast)
  - Morphology/Cytogenetics/Flow cytometry analysis
    → Markers - CD13, CD117
    → M7 variety - CD41, CD61
- Molecular Studies -
  - FLT3 (M/c), CEBPA, NPM1
- CXR to identify LN groups
- Echo to detect Ejection fraction of heart
- HLA Typing as part of plan for Allogenic SCT
- KFT and serum uric acid for evaluation for risk of Tumor Lysis Syndrome

Important Information

- Tumor Lysis Syndrome (TLS)
  - K↑, Hyperphosphatemia, Hypocalcemia
  - Uric Acid ↑→ ATN
  - T/t - I/V Fluids + Rasburicase (DOC)

WHO 2016 CLASSIFICATION OF AML

00:26:34

- AML with Recurrent Genetic Abnormalities -
  - t(8;21)
  - Inv(16)
- APML with PML-RARA
- AML with MDS-Related Changes
- AML with NOS
- Myeloid Sarcoma
- Myeloproliferative Disorder Associated with Down Syndrome -
  - Transient Abnormal Myelopoiesis

SUBTYPES OF AML WITH NOS

- M0: AML with minimal differentiation.
- M1: AML without maturation
- M2 (M/c): AML with maturation
- M4: Acute myelomonocytic leukemia

- M5: Acute monocytic leukemia
- M6: Pure erythroid leukemia
- M7: Acute megakaryoblastic leukemia (a/w Down's syndrome)
- Acute basophilic leukemia
- Panmyelosis with myelofibrosis

T/t OF AML

00:27:53

- Chemotherapy - Cytarabine + Anthracyclines
  - Daunorubicin, Idarubicin
- M3 AML (APML) Specific Therapy -
  - ATRA (All-Trans Retinoic Acid) + ATO (Arsenic Trioxide)
  - MOA -
    → ATRA - Differentiates neoplastic cells → senescence of leukemia cells
    → ATO - Induces apoptosis
  - Complication - Differentiation syndrome (pulmonary endothelial damage → severe SOB)
    → Management - Supplemental O_2 + steroids
- Allogenic stem cell transplantation - Relapse prevention strategy in AML

MCQs

Q. A 67-year-old male presented with clinical features of Acute Myeloid Leukemia. Which of the following organs is most commonly involved in leukostasis?

a. Liver
b. Heart
c. Kidney
d. Lung

Ans. (d)

4. ACUTE LYMPHOBLASTIC LEUKEMIA

ACUTE LYMPHOBLASTIC LEUKEMIA

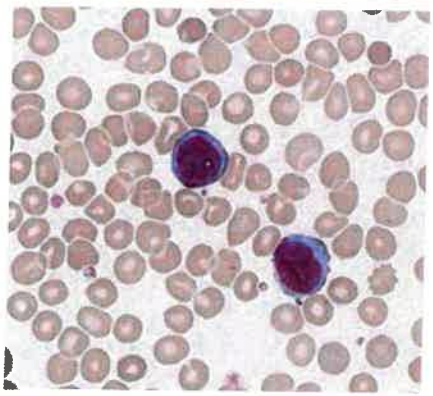
00:00:18

SUBTYPE	PERCENTAGE OF ALL CASES	SPECIFIC FEATURES
B-cell ALL	70%	• M/c subtype seen - Common B cell ALL • Marker: CD 10+ • T (9:22)
T- cell ALL (HTLV 1 associated)	25%	• Can cross blood testis barrier - testicular involvement • Mediastinal involvement (pressure on adjoining tissues like trachea, bronchi, superior vena cava syndrome)
Biphenotypic	5%	• Mixed lineage • MLL gene/KMT 2A involvement • Now called as-Mixed Phenotypic associated Leukemia (MPAL)

BONE MARROW ASPIRATION DONE AND SLIDES STAINED WITH WRIGHT GIEMSA STAIN

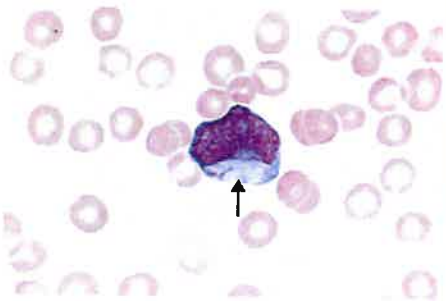
- Large cell with dark nucleus
- Nuclear cytoplasmic ratio ↑ (↑N:C)
- Scanty cytoplasm, Fine chromatin
- Lymphoblast concentration in bone marrow >20% - Acute Lymphoblastic Leukemia

LYMPHOBLAST



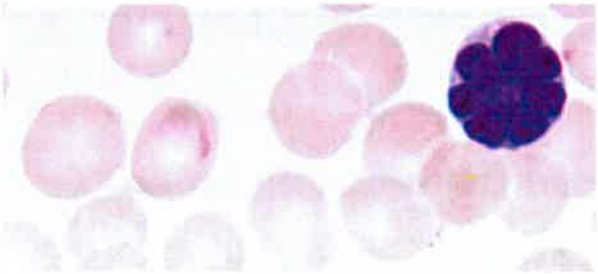
- ↑ N:C ratio
- Auer rods/Myeloblast present
- If percentage of cells >20% myeloblast-Acute Myeloid Leukemia

MYELOBLAST



- ↑ N:C
- Indentation in nucleus gives appearance of flower - Flower cells
- Adult T cell Leukemia caused due to association with HTLV-1

ADULT T-CELL LEUKEMIA



ETIOLOGY

00:05:52

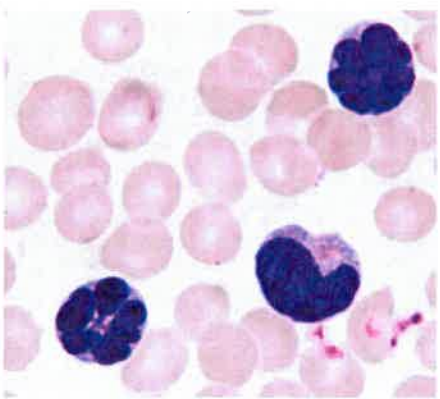
A	• Ataxia Telangiectasia
B	• Bloom Syndrome (defective DNA repair)
C	• Chemotherapy induced secondary malignancy • Drugs responsible - alkylating agents like Cyclophosphamide, Topoisomerase II inhibitor ○ Drugs used in T/t of AML, Myelodysplastic Syndrome, Carcinoma breast
D	• Down syndrome
I	• Ionizing radiation, Infection- HTLV
F	• Fanconi anemia
K	• Klinefelter syndrome
N	• Neurofibromatosis type 1

- Philadelphia chromosome, t(9:22)
- Other causes
  - t(8:14) → Burkitt's Lymphoma
  - t(4:11)
  - t(1:19)

HTLV-1

00:10:50

- Adult T cell Leukemia
- Flower cell or clover leaf



CNS LEUKEMIA

00:11:19

- ALL > AML
- Raised ICP/Meningismus
- Cell Count >5 cells/mm^3
  - Lumbar puncture → breech of blood vessels → blood can enter CSF → cancer cells introduced → intrathecal methotrexate given after lumbar puncture to minimize chances of accidental inoculation of cancer cells into CSF
- CT - Leptomeningeal metastasis
- Intrathecal methotrexate should be given after LP

CLINICAL PRESENTATION

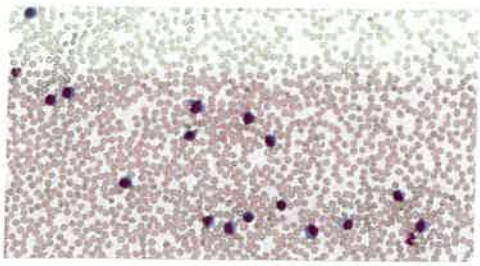
00:13:25

- Age group of presentation - 2-8 years, > 50 years
- Progressive Pallor and Anemia
- Bleeding - Epistaxis
- Infection - Recurrent Pneumonia
- Petechia, purpura, bleeding
- Hepatosplenomegaly, Lymphadenopathy
- CNS leukemia → ↑ ICP → 6th nerve palsy
- Bony/Sternal Tenderness

WORK UP

00:18:00

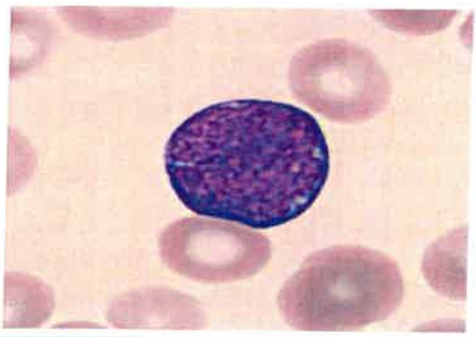
- CBC and Peripheral smear
  - Hb ↓
  - TLC Normal/↓/↑↑
  - Leukostasis (AML>ALL) → initially low neutrophil count → recurrent pneumonia
  - Platelet count ↓
- IOC - Bone Marrow Aspiration/Biopsy



Bone marrow smear: ALL

BONE MARROW ASPIRATION/BIOPSY

- Salah and Klima needles used
- Site-Posterior Superior Iliac Spine



- Lymphoblasts count >20% with ↑ N:C ratio, fine chromatin

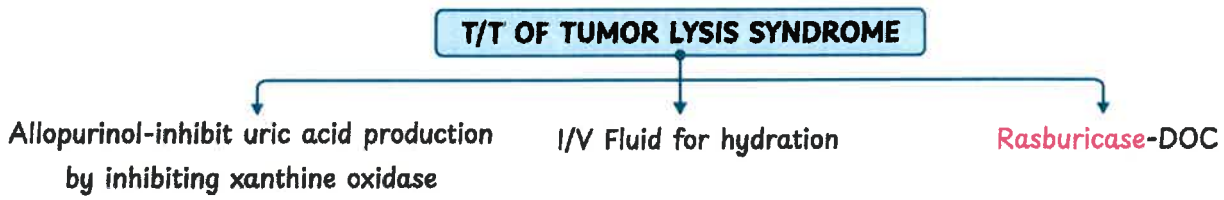
TEST DONE ON BONE MARROW SAMPLE

CELL MORPHOLOGY EVALUATED IN SMEARS USING WRIGHT AND GIEMSA STAIN

- L1 (M/c)
- L2
- L3 -
  - Burkitt's leukemia and associated with t(8:14)
  - Mature B cell ALL
  - CD10 ⊕ with S. Ig ⊕

IMMUNOPHENOTYPING USING FLOW CYTOMETRY	• B cell ALL: CD19 CD22 CD79A CD10 • T cell ALL: CD2 CD3 CD7 • Biphenotypic variety: combining both B cell ALL and T cell ALL
CYTOGENETICS: FISH (FLUORESCENT IN SITU HYBRIDISATION)	• t (9:22) • t (8:14) • t (4:11) • t (1:19)
CYTOCHEMISTRY (DIFFERENTIATE MYELOBLAST FROM LYMPHOBLAST)	• MPO- negative • PAS- Positive • Terminal deoxynucleotidyl transferase (TdT)- Positive

- Serum electrolytes and uric acid to get baseline values due to risk of Tumor Lysis syndrome
  - Tumor lysis syndrome - chemotherapy → death of large number of cancer cells → ATP breakdown to produce phosphates → hyperphosphatemia → chelation with cancer → calcium ↓
    → Potassium ↑
    → Uric acid ↑→ blockage of kidney tubules by uric acid crystals → acute tubular necrosis



  - Lumbar puncture - to check CSF for leukemia cells
  - HLA testing as patient subsequently sent for stem cell transplantation

HIGH-RISK ALL FEATURES

00:26:20

- Age group: <1 year and >10 years (extreme age)
- ↑ WBC count: >50,000/mm^3
- Lymphadenopathy/ Hepatosplenomegaly/ Mediastinal mass (organomegaly)
- Mature-B Cells
- Hypoploidy
- t(9:22), t(8:14), t(4:11), t(1:19)
- Blasts: >1,000/cumm in peripheral smear after 14 days of chemotherapy
- Absence of CD_{10} and presence of MLL rearrangement
- T/t - Allogenic stem cell transplantation in 1st remission with chemotherapy

LOW RISK ALL

- Age group: 1-9 years
- WBC count <50,000/mm^3
- Pre-B cell ALL
- Hyperploidy

STANDARD RISK	VERY HIGH RISK
• Same as high risk +normal cytogenetics	• Induction failure • t(9:22)