Leukemia / Lymphoma

Leukemia - PB, B.M.

Lymphoma - Lymphnodes, Organs

when tumorload ↑ inter changeable.

WHO Classification

HL

Nodal (LN).

Step-wise.

Rare.

Waldeyer Ring
mesentric LN.

very common

NHL

extranodal (organs)

Random.

m/c involved Lymphnode Cervical.

Hodgkin's Lymphoma:

- EBV → mostly a/w HL (not always)

EBV → B cells. → mirror like nuclei

→ pink/eosinophilic nucleole

Reed-Sternberg cells -

alone is not characteristic of Hodgkins lymphoma.

1) → also present in Infectious mononucleosis.

Downey cells - activated CD8 T cells

2) NHL → Diffuse Large B cell lymphoma.

Immunoblastic

m/c - a/w

1° CNS Ly.

1° effusion lymphoma

Carcinoma / Sarcoma

for Histological diagnosis -

Reed-Stern Berg cells + mixed inflammatory background

Neoplastic + non neoplastic Background

Hodgkins

Classical	RS cells
CD 15+ 30+	with different immuno phenotyping
CD30 > CD15.	
(90-100%)	(70%)

1) Nodular Sclerosis
   - Collagen Band
   - Lacunar RS
2) mixed Cellularity
   - m/c - India
   - mononuclear RS.
   - EBV m/c associated / HIV
3) Lymphocyte poor
   - mummified RS, Hodgkin cells, atypical Large Histiocytes.
4) Lymphocyte Rich
   - mononuclear RS

Lymphocyte predominant

CD 15⁻ 30⁻

germinal centre of lymphnodes

CD-20+

CD-45+

BCL-6+

Popcorn cells

[Lymphocyte, Histiocyte Rich

RS.

multilobated, polyploid nuclei.

EBV / not associated

Nodular Sclerosis lymphocyte predominant HL.

HIV ⟶ AIDS
↓ CD4 T cells

i) NHL
ii) Kaposi Sarcoma
iii) Cervical Invasive Carcinoma

↓ decreasing order

NHL: DLBCL : m/c - Immunoblastic non Hodgkin's lymphoma (60%)

1° CNS lymphoma (20%)

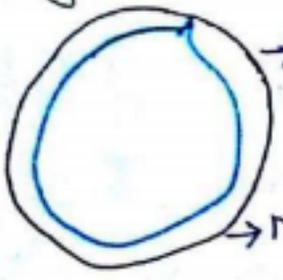
m/c brain tumor in HIV - 1° CNS lymphoma.

Acute Leukemia

- PS | BM aspirate | bx | cytogenetics

Blast cells -> 20% WHO.

Lymphoblast



myeloblast

PAS +ve

Both PAS-+ve.

Lymphoblast	Erythroblast
Block positive.	Diffuse PAS positivity.

MPO +ve.

Sudan Black B +ve

Monocytes (mpo -ve, SBB -ve)

NSE (+ve)

M3 M4 M5

Erythroblast - PAS +ve

→ Based on pattern of staining

→ Auer Rods → abnormal azurophilic granules

ALL - m/c Cancer of childhood.

- all is Common in ALL compared to AML

- CNS
- mediastinum
- Testis

} Bad Prognosis.

B cell (80%)

2-5 years

→ BM involvement

↓ anaemia.

T-cell (15-20%)

Adolescents

mediastinal mass.

NOTCH positive.

I.P.T PAX-5

CD-10 +

CALLA +ve.

↓

Good prognosis.

CD-19 + - 24 +ve.

CD 1-8

CD 28

Even when Blast count is < 20% is

↑ Translocation t(8:21) t(15,17) inv 16

Irrespective of Blast - AML

Good

2-10 years

- White
- female

Bad

<2 years >10 years

- Black
- male

CNS, mediastinal, Testicular

Cytogenetics

Hyperdiploidy (ch>50)

Trisomy, -4, 7, 10

t(9,12)

t(12,21)

CALLA +ve.

B-ALL

(early pre-B-ALL)

Hypodiploidy [ch<50]

t(9,22) BCR-ABL.

t(8,14)

t(1,19)

T-ALL.

Precursor B-ALL.

mature B-ALL.

AMTL:

I Recurrent genetic abnormalities:

a) t(8,21) - MT2 good

b) t(15,17) - MT3 good

c) t(16,16) inv 16. - MT4 Hypereosinophilia.

} AML irrespective of Blast count.

d) t(U:11) variable - 11. Bad prognosis (Karyotheomesome no).

Associated with MDS - poor prognosis.

cytogenetics -

- Monosomy - 5
- Monosomy - 7 - Pediatrics (m/c)
- Deletion - 5 - Adult (m/c) Overall
- Deletion - 7

3) AML Treatment Related - Worse Prognosis

4) Not otherwise Specified

MPO+ Auer Rods → most definitic myeloid diff

- M_0 - undifferentiated
- M_1 - AML without maturation
- M_2 - AML with maturation
- M_3 - Acute Promyelocytic Leukemia [Auer Rods - max]
- M_4 - Acute myelomonocytic MPO+ NSE⊕
- M_5 - Acute monocytic - NSE⊕ MPO-ve Auer-ve
- M_6 - Acute erythroblastic - CD 71 / glycophorin A
- M_7 - Acute megakaryocytic - ↑ Synthesis of fibrogenic cytokines → BM fibrosis → Plt / RBC / WBC - ↓

Tissue infiltration (gum hypertrophy).

NT5 > NT4 (monocyte infiltration)

Chloroma - NT2

NTyeloblastoma; m/c site - Orbital Tissue, skin infiltration

[Granulocytic Sarcoma]

→ Auer rods (atypical monocytes)

PB, BM } Blast - (N) skin/Tissue } Blast cells

→ predictor for future myeloid Ca.

NTyelodysplastic Syndrome -

NTyeloid stem cells - maturation defect.

- ↓ erythroblasts
  - (N) → Fe3+ → protophyrin
  - ↓ Heme.
  - ↓ Fe3+ deposits around nucleus in mitochondria
  - Ringed Sideroblasts
  - → MDS, Lead poisoning
  - Sideroblastic anaemia.
- NTyeloid lineage
  - Neutrophils
  - Pseudopelger Huet anomaly.
  - Dohle bodies
  - [Pelger Huet (AD)]
- NTegakaryocytes
  - (N) [Largest cell, Nucleus fused & Syncitium like]
  - Paven Ball megakaryocytes
  - (N)

Chronic Leukemia

Bone marrow biopsy → only prognosis never diagnostic.

CLL	SLL
boys ⊕	→ peripheral / small lymph node / organ.
massive Splenomegaly	
LN enlargement	

PS/PB: ↑ lymphocyte count.

Absolute lymphocyte count > 5000/mm^3

Ioc → Flowcytometry

B cell > T cell.

Immunophenotyping CD5+ CD23+ Diagnostic.

Mantle cell lymphoma – CD5+ ; CD 23 -ve
B cell type
mantle zone – mauki – CD5+

Bad Prognosis – i) Expression of ZAP-70.
ii) No Somatic Hypermutation.
iii) Trisomy 12.
iv) Richters Transformation (one lymphoma to other)

m/c Cytogenetic change.
a) CLL – del 13q – good.
multiple myeloma – Bad.
Bad prognosis

SLL → DLBL i) Worst prog
ii) m/c NHL in Western world – follicular lymphoma Indian world

Smear: Smudge cells / Parachute cells / Basket cells

Chronic Myeloproliferative Disorders

1) CMTL → I Philadelphia
2) PV
3) Essential Thrombocytosis
4) Progressive myelofibrosis

→ all myeloid stem cell proliferation due to abnormal Tyrosine kinase activation due to I / II

End Result - Primary myelofibrosis

II JAK-2

Essential thrombocytosis - mild / no splenomegaly

Chronic Myeloid Leukemia:

Age - ped, adult, elderly

Peakage - 50-70 yrs

m/c presentation - massive splenomegaly

No lymphnode enlargement

K/C/o CMTL with sudden & painful LN enlargement

↓

Blast Crisis

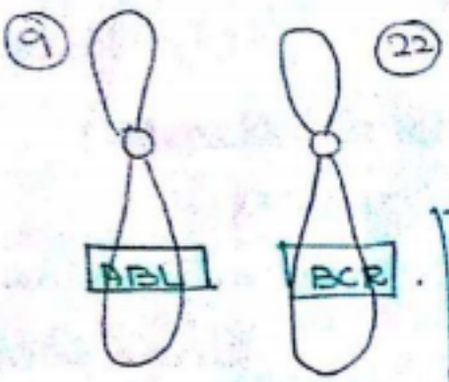
P.S: Neutrophil ↑ (immature > mature)
Platelet ↑
Basophilia
eosinophils ↑
} Presumption

Confirm - Cytogenetics PCR & FISH

FISH - BCR - ABL fusion gene

t(9:22)

Philadelphia chromosome.



long to long arm Translocation

Philadelphia chromosome
22 long arm

Ph chromosome - megakaryocytic - dx of CML.

→ any myeloid lineage.

1) Chronic phase —3 years→ II] Accelerated phase —6 mo.→ III] Blast Crisis

B. MT Biopsy < 10%

cytogenetics
Ph ⊕
confirm

Blast 10-19%
Basophil > 20%
Thrombocytosis / thrombocytopenia.
Not Responding to Rx.

→ Blast > 20%
→ extramedullary Chloroma
Blast cells.
→ Large groups of blast cells in BM Bx

Lymphoma

1) Mantle
→ B cell, 60 years
→ m/c - Cervical LN enlargement
CD5+ CD-23 -ve.
cytogenetics
t(11:14)
cyclin D1 (BCL)

2) Follicular.
→ B cell type
20-30 years
LN Biopsy
i) Centrocytes (Smaller)

- Buttock cells.
2) Centroblasts.
cytogenetics t(14:18)
cyclin D2 (BCL 2)

3) Burkitt lymphoma:
Mature B cell lymphoma.

CD34 -ve; Ig ⊕

→ Highest proliferative index among all Human cancers
i) poor prognosis (Brain Tissue involvement)
ii) m/c association with tumor lysis Syndrome.

Bcl 2 -ve. → Germinal Centre BCL-6+ve.

LN Biopsy - Small Round Blue cell tumor
i) Wilms
ii) Neuroblastoma
iii) Ewings.
iv) Lymphoma

Due to high proliferative index

Dead tumour cells

↓

Macrophage engulfwith (foamy macrophages) + Small Round cells

Starry sky appearance

t(8,14) → m/c type of cytogenetics

t(8,22)

t(2,8)

Hairy Cell Leukemia

→ B cell lymphoma.

→ bo/m.

- massive splenomegaly.

Cytoplasmic Hair like projections (in phase contrast)

(Halo/contrast around cells)

TRAP +ve

Δ: BMT aspirate. - Dry Tap.

BMT Biopsy -

Tumor cell pattern

Honey Comb pattern:

Fried egg appearance.

(perinuclear Halo)

Immunophenotyping - CD-11C
CD-25, CD 103

Test Specific/Best inv:

Annexin A1 +

↑Risk - Atypical mycobacterial infection

>90% - BRAF mutation.

Multiple myeloma

plasma cell disorder.

↑IL-6

abnormal plasmablast.
(no perinuclear Hoff)

Light chain Ig.

monoclonal protein - M protein.

Ig G (m/c)
A
M
D (Rare)
E (very Rare)

urine - Bence Jones protein.

50° → clot
100°C → Liquid.

Myeloma kidney - Primary type of Amyloidosis
AL type.

Perinuclear Hale
Hoff
due to golgi body

MT/c Cause of death - Recurrent infection > Renal failure

m/c Cause of Renal failure in MM - Light chain deposition

↑ Abnormal Ig synthesis.

Russell Bodies — Cytoplasm

Dutcher Bodies — Nucleus

Cells

Mott's cells — Bluish cluster of grape like Ig

Flame Cells — Fiery Red cytoplasm due to Ig

Diagnosis: 1) BM Biopsy - Plasma cell >10%

2) MT-protein ↑↑ - Both Serum & Urine

3] Incidence of end organ damage

C - Calcemia

R - Renal damage

A - Anemia

B - Bone lytic lesion

Prognosis

Bad prog

β_2-microglobulin (Tu-load) - Best

↑ Sr. LDH. Tumor load.

↑ C-R.P.

Langerhans Cell Histiocytosis :

→ 2-10 years.

m/c characteristic - Involving all bones of body, simultaneously

→ Seborrheic dermatitis like lesion - Scalp.

Gonadal involvement - Absent / Rare.

1) Letterer - Siwe - multisystem, multifocal, multicentric

2) Eosinophilic granuloma - Scalp defects - multifocal unisystem

3) Hand - Schuller christian

Calvarial defect.

Diabetes insipidus.

Exophthalmus.

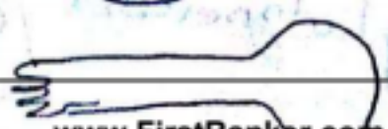
Cytogenetics - Immunophenotyping - CD 1a (Best), S-100, HLA-DR, CD-207 (langerin protein)

m/E:

1. Langerhans cells + eosinophilia.

elongated cells with coffee bean nucleus

Cytoplasmic granules (EM) → Birbeck granules.



Tennis racket / Pentalaminar Racket

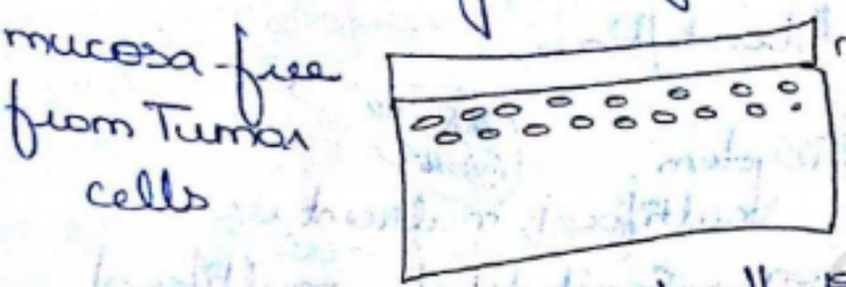
Tennis Racket cells / Birbeck / Tadpole cell

Rhabdomyoblasts (RMTS)

Variant - Lombayonal RMTS -

mucosa - Hollow

Vagina < 5 years Sarcoma Botryoides



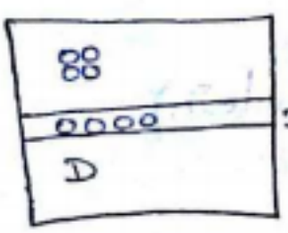
Submucosal collection of tumor

↓

Cambium layer

Mycosis fungoides

Tm/c cutaneous lymphoma



Epidermotrophism

↓

Munro abscess. Pautrier (collection of neoplastic T cells)

Psoriasis

Generalized erythroderma - Sezary Syndrome

Sezary Lutzner cells