Leukemia / Lymphoma

Leukemia - PB, B.M.

Lymphoma - Lymphnodes, Organs

when tumor load ↑ inter changeable.

WHO Classification

HL

Nodal (LN).

Step-wise.

Rare.

NHL

extranodal (organs)

Random.

Waldeyer Ring
mesenteric LN.

→ very common

m/c involved Lymphnode Cervical.

Hodgkin's Lymphoma:

- EBV → mostly a/w HL (not always)

EBV → B cells. → mirror like nuclei

→ pink eosinophilic nucleoli

↓

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

3) Carcinoma / Sarcoma

for Histological diagnosis -

Reed Stern Berg cells + mixed inflammatory background

Neoplastic + non neoplastic Background

Hodgkins

Classical	RS cells	Lymphocyte predominant
CD 15 + 30 +	with different immuno phenotyping	CD 15 - 30 -
CD30 > CD15.		germinal centre of lymphnodes
(90-100%) (70%)		CD-20 +
		CD-45 +
		BCL-6 +

1) Nodular Sclerosis

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

Popcorn cells

[Lymphocyte, Histiocyte Rich]

RS.

multilobated, polyploid nuclei.

EBV / not associated

Nodular Sclerosis lymphocyte predominant HL.

defining Cancer:

HIV ⟶ AIDS

CD4 T cells

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

↓ decreasing order

NHL: DLBCL : m/c - Immunoblastic non Hodgkins lymphoma (40%)

1° CNS lymphoma (20%)

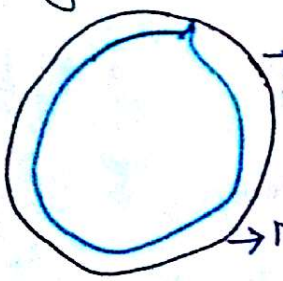
m/c brain tumor in HIV - 1° CNS lymphoma.

Acute Leukemia

- PS | BMT 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))

NT3 NT4 NT5

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% if Translocation t(8:21) t(15,17) inv 16 Irrespective of Blast - AML

Good
2-10years
-white
-female

Bad
<2years >10years
-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) - M2 good
b) t(15,17) - M3 good
c) t(16,16) inv 16 - M4 Hypereosinophilia.
d) t(U:11) variable - 11 - Bad prognosis (aneuploidy no).

} AML irrespective of Blast count.

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 Rod cells (atypical monocytes)

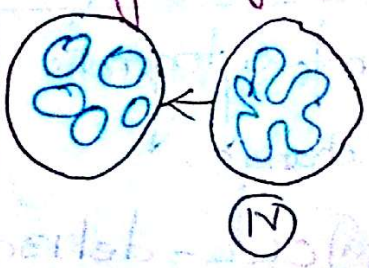
PB, BM } Blast – (N) skin/Tissue } Blast cells

→ predictor for future myeloid Ca.

NTyelodysplastic Syndrome –

NTyeloid stem cells – maturation defect.

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



Chronic Leukemia

Bone marrow biopsy → only prognosis.
never diagnostic.

CLL
boys ⊕
massive Splenomegaly
LN enlargement

SLL
→ peripheral / small lymph node / organ.

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 – mauku – 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
Western world – follicular lymphoma
i) Worst prog
ii) m/c NHL in India World

Smear: Smudge cells / Auer rods / 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 JAK-2 II

End Result - Panmyelosis

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.

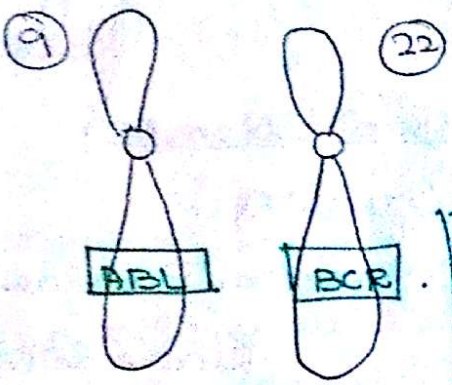
P.S: Neutrophil ↑ immature > mature.
Platelet ↑
Basophilia.
eosinophils ↑.
} Presumption.

Confirm - Cytogenetics PCR < FISH

+ISH - 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 granular
blast cells in
BMT 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.
ii) 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 + Small Round cells

↓

Macrophage engulfwith (foamy macrophages) → Starry Sky appearance

t(8,14) → m/c type of Cytogenetics

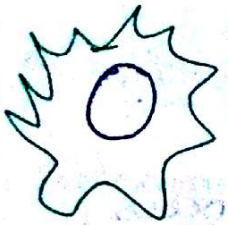
t(8,22)

t(2,8)

Hairy Cell Leukemia

→ B cell lymphoma.

→ bo/m.



- massive splenomegaly.

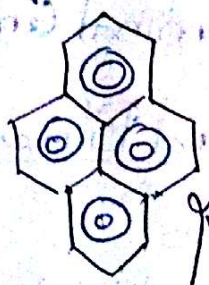
Cytoplasmic Hair like projections (in phase contrast)

(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

NTest-Specific/Best inv:

Annexin A1 +

↑Risk - Atypical mycobacterial infection

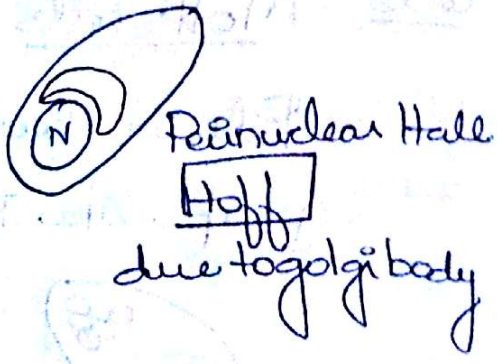
>90% - BRAF mutation.

NTultiple myeloma

plasma cell disorder.

↑IL-6

abnormal plasmablast.
(no perinuclear Hoff)



Light chain Ig.

monoclonal protein - Mprotein.

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

urine - Bence Jones protein.

50° → clot
100C → Liquid.

Nyeloma kidney - Primary type of Amyloidosis
AL type.

MM 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 - Plasm cell >10%

2) MM - 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.

Protein - D,

Langerhan's 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.

Tentalamina Racket

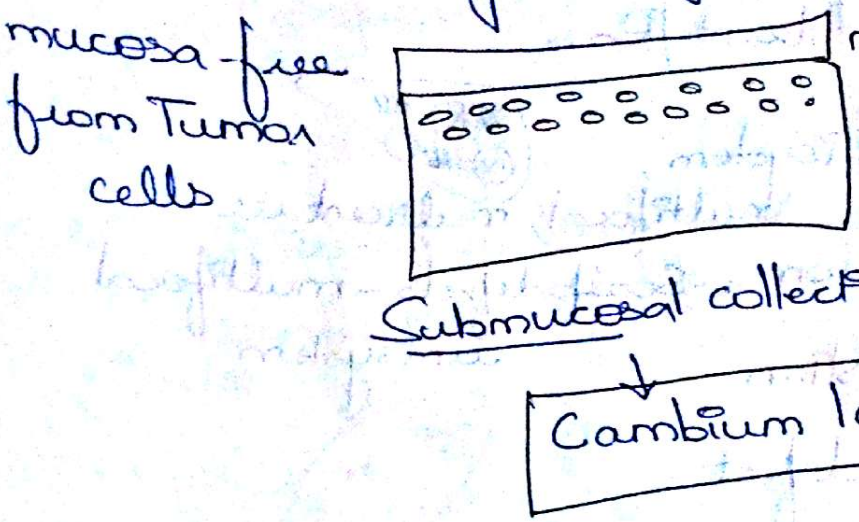
Tennis Racket cells / Bipolar / Tadpole cell

Rhabdomyoblasts (RMTS)

Variant - Lombayonal RMTS -

mucosa - Hollow

Vagina < 5 years Sarcoma Botryoides



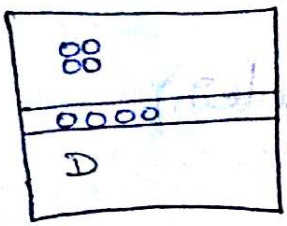
Submucosal collection of tumor

↓

Cambium layer

Mycosis fungoides

T/c cutaneous lymphoma.



Epidermotrophism

↓

Munro abscess. Pautrier (collection of neoplastic T cells)

Psoriasis

Generalized erythroderma - Sezary Syndrome

Sezary Lutzner cells.