Leukemia

Handwritten Note

EduMedWeb

Leukemia / Lymphoma

Leukemia - PB, B.M.

Lymphoma - Lymphnodes, Organs

when tumor load ↑ inter changeable.

WHO Classification

HL

Nodal (LN).

Step-wise.

Rare.

Waldeyer Ring / mesenteric 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 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

CD 15 + 30 +

CD30 > CD15.

(90-100%)

RS cells with different immuno phenotyping

(70%)

Lymphocyte predominant

CD 15 - 30 -

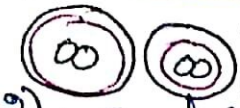
germinal centre of lymphnodes

CD-20 +

CD-45 +

BCL-6 +

1) Nodular Sclerosis



Collagen Band

Lacunar RS

2) mixed Cellularity

m/c - India

mononuclear RS

EBV m/c associated / HIV

3) Lymphocyte poor

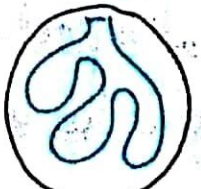
mummified RS, Hodgkin cells. Atypical Large Histiocytes.

4) Lymphocyte Rich.

Mononuclear RS

Popcorn cells

[Lymphocyte, Histiocyte Rich]



RS.

multilobated, polyploid nuclei.

EBV / not associated

Nodular Sclerosis lymphocyte predominant HL.

AIDS defining Cancer:

HIV ⟶ AIDS

CD4 - <200 cells

i) NHL

ii) Kaposi Sarcoma

iii) Cervical Invasive Carcinoma

↓ decreasing order

NHL: DLBCL : m/c - Immunoblastic non Hodgkins lymphoma (60%)

1° CNS lymphoma (20%)

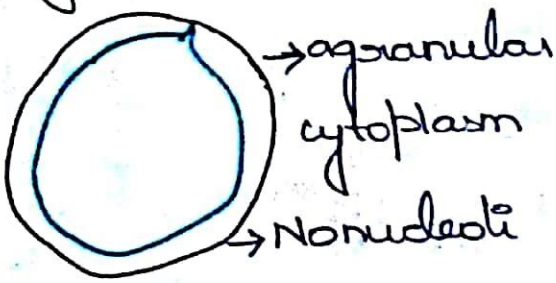
m/c brain tumor in HIV - 1° CNS lymphoma.

Acute Leukemia

- PS | BMT aspirate | bx | cytogenetics

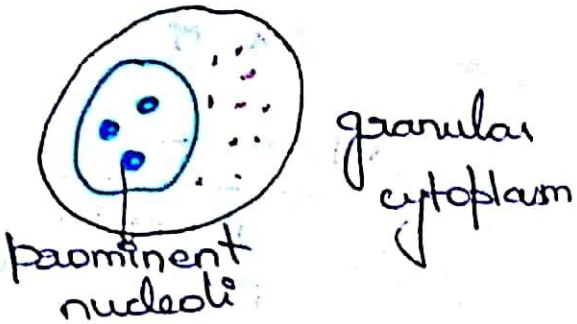
Blast cells - > 20% WHO.

Lymphoblast



PAS +ve

myeloblast



MPO +ve.

Sudan Black B +ve

Both PAS-+ve.

Lymphoblast	Erythroblast
Block positive	Diffuse PAS positivity.

→ Based on pattern of staining

Monocytes (mpo -ve, SBB -ve, NSE (+ve))

M3 M4 M5

Erythroblast - PAS +ve

→ 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.

T.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

2-10years

-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) - MT2 good

b) t(15,17) - MT3 good

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

} AMTL irrespective of Blast count.

d) t(U:11) variable - 11 - Bad prognosis

(karyochromosome no)

2] Associated with NTDS - 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

NTpot
Auer Rods
↓
most definitic myeloid diff

- NT_0 - undifferentiated
- NT_1 - AML without maturation
- NT_2 - AML with maturation
- NT_3 - Acute Promyelocytic Leukemia [Auer Rods - max]
- NT_4 - Acute myelomonocytic NTpot NSE⊕
- NT_5 - Acute monocytic - NSE⊕ NTpo-ve Auer-ve
- NT_6 - Acute erythroblastic - CD71 | glycophorin A
- NT_7 - Acute megakaryocytic - ↑ Synthesis of fibrogenic cytokines
  ↓
  BM fibrosis
  ↓
  Plt | RBC | WBC - ↓

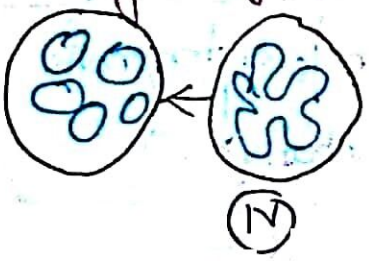
Tissue infiltration (gum hypertrophy)
MT5 > MT4 (monocyte infiltration)

Chloroma – MT2
Myeloblastoma; 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.

Myelodysplastic Syndrome:-
Myeloid stem cells – maturation defect.

- Erythroblasts → Fe^{3+} protoporphyrin → Heme → Fe^{3+} deposits around nucleus in mitochondria → Ringed Sideroblasts
  → MDS, Lead poisoning, Sideroblastic anaemia.
- Myeloid Lineage → Neutrophils → Pseudopelger Huet anomaly → Dohle bodies
  [Pelger Huet (AD)]
- Megakaryocytes → (N) [Largest cell, Nucleus fused & Syncytium 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/mm³

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) Richter's Transformation
(one lymphoma to other)

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

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

P/S - Smudge cells / Paraschute cells / Bare bel cells

Chronic Myeloproliferative disorders.

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

→ all myeloid stem cell proliferation

End Result - Panmyelosis

Due to abnormal Tyrosine kinase activation due to 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 CML with sudden + painful LN enlargement

↓

Blast Crisis

P.S: Neutrophil ↑ immature > mature.

Platelet ↑

Basophilia.

eosinophils ↑.

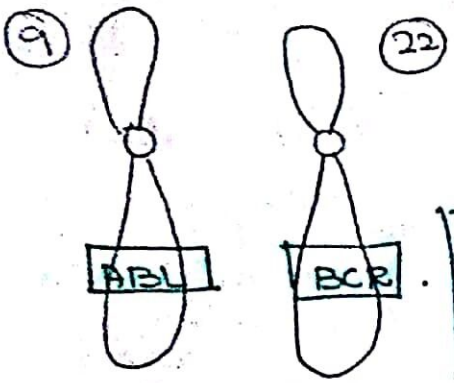
} Presumption.

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 —6 mo.→ III] Blast Crisis

B. MT Biopsy < 10%

cytogenetics
Ph ⊕
confirm

phase

Blast 10-19%

Basophil > 20%

Thrombocytosis/
thrombocytopenia.

Not Responding to Rx

→ Blast > 20%

→ extramedullary
Chloroma
Blast cells

→ Large groups of
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.

↓

Macrophage engulfs them

(foamy macrophages)

+ Small Round cells

Starry Sky appearance

t(8;14) → m/c type of cytogenetics

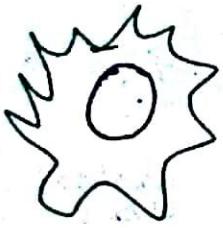
t(8;22)

t(2;8)

Hairy Cell Leukemia

→ B cell lymphoma.

→ bo/m.



- massive splenomegaly

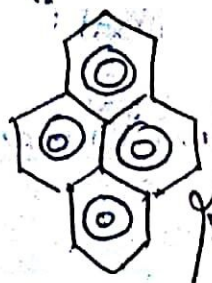
Cytoplasmic Hair like projections (in phase contrast)

(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

NTest-Specific/Best inv:

Annexin A1 +

↑Risk - Atypical mycobacterial infection

>90% - BRAF mutation

NMultiple 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

Perinuclear Hale

Hoff

due to golgi body

NMyeloma kidney - Primary type of Amyloidosis

AL type

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

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

↑ Abnormal Ig synthesis

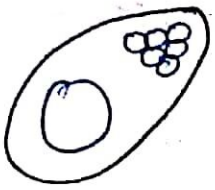
Russell Bodies
Cytoplasm

Dutcher Bodies
Nucleus

Cells

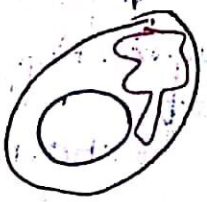
Mott's cells

Bluish cluster of grape like Ig



Flame Cells

Fiery Red cytoplasm due to Ig.



Diagnosis: 1) BMT Biopsy - Plasm cell >10%

2) NT-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 Tumor load
- ↑ Sr. LDH
- ↑ C-R.P.

Best IHC marker : Cyclin - D1

Langerhans Cell Histiocytosis :

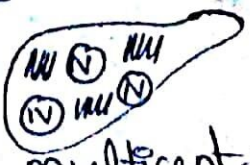
→ 2 - 10 years.

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 - CD1a (Best)

S-100, HLA-DR,

CD-207 (langerin protein)

m/E :

Langerhans cells + eosinophilia.

elongated cells with coffee bean nucleus

Cytoplasmic granules (EM) → Birbeck granules.

Tentalamina Racket

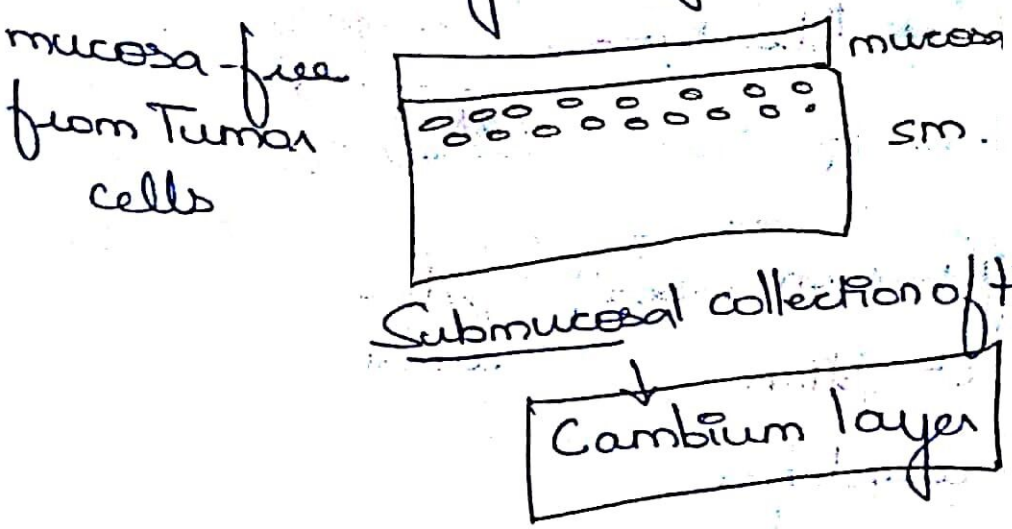
Tennis Racket cells / Strapcells / Tadpole cell

Rhabdomyoblasts (RMTS)

Variant - Lombayonal RMTS -

mucosa - Hollow

Vagina < 5 years Sarcoma Botryoides



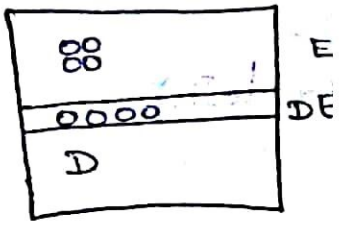
Submucosal collection of tumor

↓

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.