Hematology

438 teamwork

Lymphoproliferative disorders

Color index:
Red: Important
Gray: notes
Blue: extra

Editing file

definitions

Lymphoproliferative disorders

characters: -mature lymphocytes (no blasts), -lymphocytosis, -chronic.

Lymphoma

Malignant lymphoid mass involving the lymphoid tissues (± other tissues ie; Extranodal lymphoma, by definition, involves sites other than lymph nodes, spleen, thymus and the pharyngeal lymphatic ring. **e.g : skin ,GIT ,CNS)**

Several clinical conditions in which lymphocytes are produced in excessive quantities (Lymphocytosis)

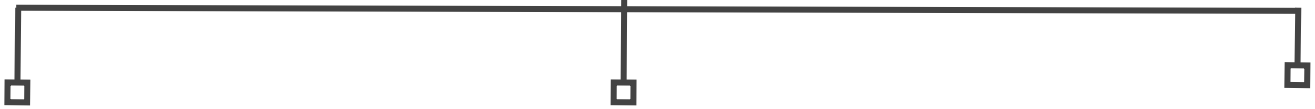
N.B: Lymphoproliferative disorders occur when the normal mechanisms of control of proliferation of lymphocytes break down, resulting in autonomous, uncontrolled proliferation of lymphoid cells and typically leading to lymphocytosis and/or lymphadenopathy, and sometimes to involvement of extranodal sites, e.g. bone marrow.

Lymphoid leukemia

Malignant proliferation of lymphoid cells in Bone marrow and peripheral blood

when the malignancy of lymphocytes reaches the bone marrow or the peripheral blood we call it lymphoid leukemia.

(± other tissues e.g : lymph nodes ,spleen , skin ,GIT ,CNS)



Autoimmune

Infection

Mostly virus

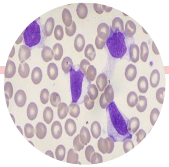
Malignant

Causes of lymphoproliferative disorder:

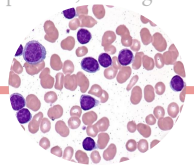
These include (1) malignant—clonal in nature, resulting from the uncontrolled proliferation of a single transformed cell, e.g. lymphoma; (2) nonmalignant—polyclonal lymphoproliferative disorders may result from conditions including (a) infections—lymphocytosis is commonly caused by viral infections, e.g. Epsitein–Barr virus (EBV); lymphadenopathy is a common feature of a very wide variety of infections, (b) reactive—conditions such as systemic lupus erythematosus (SLE) and sarcoidosis frequently cause lymphadenopathy.

Lymphocytosis

Blood film is very important, also Age is very important to expect the cause of lymphocytosis.



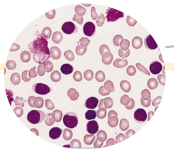
•**Viral infection**
Infectious mononucleosis ,cytomegalovirus ,rubella, hepatitis, adenoviruses, varicella.



•**bacterial infection**
Some bacteria as **Pertussis** ,brucellosis.

•**Immune**
SLE , Allergic drug reactions.

•**Other conditions**
splenectomy,dermatitis, hyperthyroidism, metastatic carcinoma.



Small lymphocytes: in non-infectious causes

•**Chronic lymphocytic leukemia (CLL)** The most important cause of lymphocytosis in adults and aged people is CLL.

•**Other lymphomas**
Mantle cell lymphoma ,Hodgkin lymphoma.

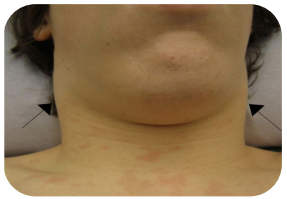
Infectious mononucleosis

An acute, infectious disease, caused by Epstein-Barr virus

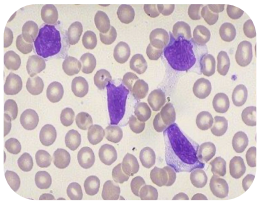
characterized by:

- ➔ fever
- ➔ swollen lymph nodes (painful)
- ➔ Sore throat
- ➔ atypical lymphocyte
- ➔ Affect young people (usually)

it is called kissing disease cuz it is transported via saliva and its common in teenagers.
Sometimes It is very severe to the degree that its differential diagnosis include ALL.



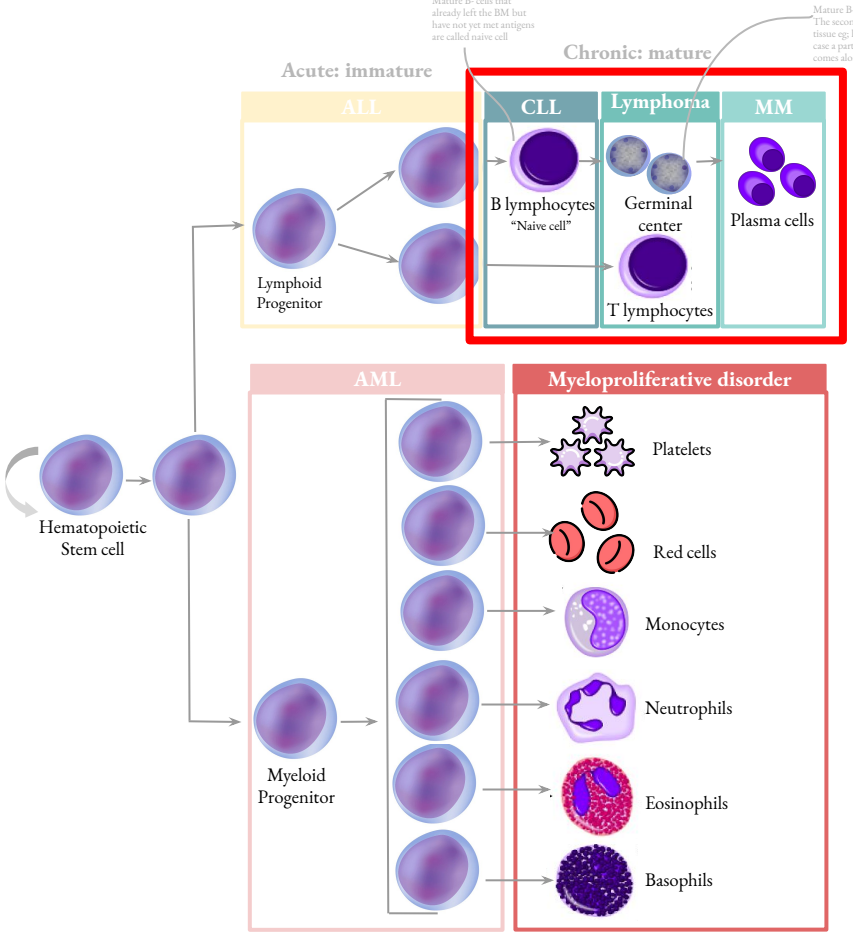
swollen lymph node



atypical lymphocytes:
-very large nucleus.
-abundant cytoplasm.

Malignant Lymphoproliferative Disorder

When there is lymphocytosis, after doing the blood smear send blood to flow cytometry Cuz it is a very imp tool to diagnose.

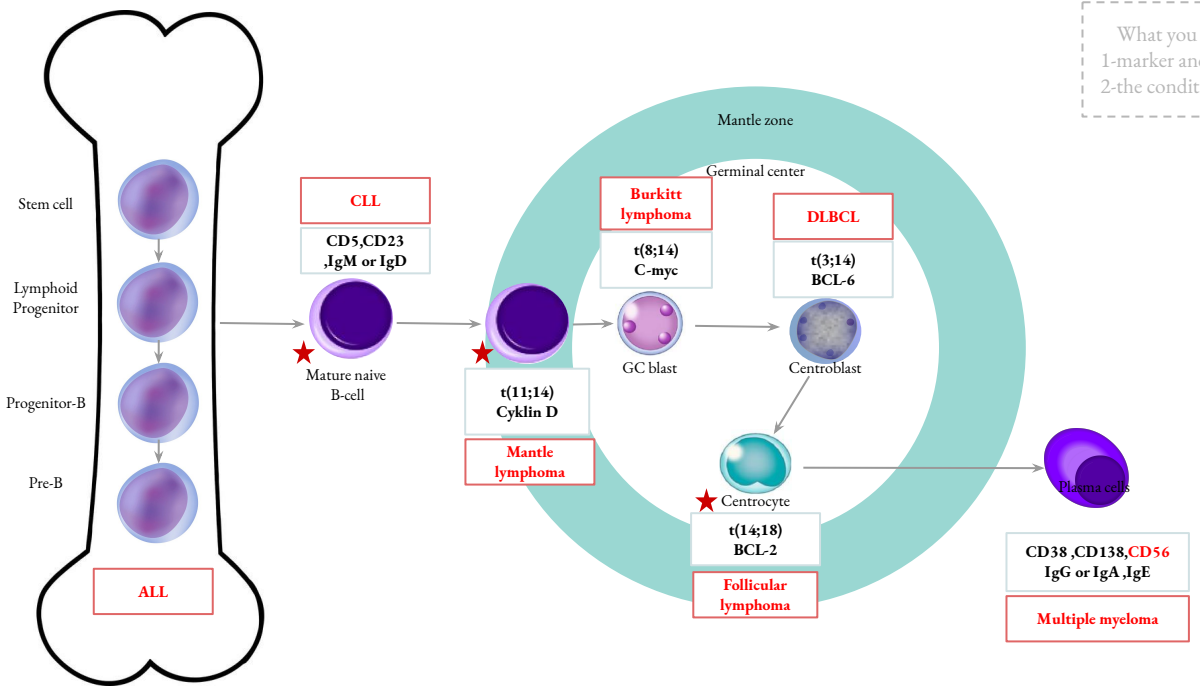


Malignant Lymphoproliferative disorders

- **Immature**
  - ALL
- **Mature**
  - **Lymphoma**
    - Non-Hodgkin Lymphoma
      - **90% B- cell neoplasm**
        - -Burkitt lymphoma
        - -Diffuse large B lymphoma
        - -Follicular lymphoma
        - -Multiple myeloma
      - **10% T- cell neoplasm**
        - -Adult T leukemia lymphoma
        - -Sezary syndrome
        - -Large anaplastic T lymphoma
    - Hodgkin Lymphoma
  - **Lymphoid leukemia**
    - -CLL
    - -Hairy cell leukemia
    - -T- prolymphocytic leukemia
    - -Leukemic phase of lymphoma

Malignant Lymphoproliferative Disorders

CD34 & TDT	Surface immunoglobulin
CD19	
CD20	
CD5	CD10



What you need to know from this diagram?
1-marker and mutation related to each cell.
2-the condition related to each cell.

Chronic Lymphocytic Leukemia

Malignant neoplasm characterized by an increased number of small, mature lymphocytes in the blood (>5,000) and bone marrow (± spleen and lymph node)

The most common adult leukemia (~25% of adult leukemias)

The median age is ~55 to 65 years. (rare < 40 years)

1.5 to 2 times more common in **men** than women

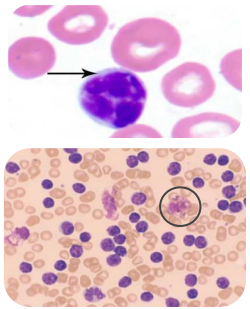
Rai Staging	Prognosis
Stage 0: lymphocytosis only (blood and marrow)	Low risk (Watch & wait)
Stage I: lymphocytosis plus enlarged nodes	
Stage II: lymphocytosis plus enlarged spleen and/or liver, ± nodes	Intermediated (± chemo)
Stage III: lymphocytosis **plus anemia(Hgb<11 g/dL)**,± above	
Stage IV: lymphocytosis **thrombocytopenia** (<10 x 10^9L),± above	High risk (FCR)

Doctor's comment on this table "just know there are stages to CLL", when there is anemia or thrombocytopenia it is a late stage

Features of CLL: ★

- 40% of patients are asymptomatic at diagnosis
- Moderate lymphadenopathy and splenomegaly
- Predisposition to infection
- Autoimmune phenomena (autoimmune hemolytic anemia)
- Transformation to large cell lymphoma (Richter's syndrome)

- **Lymphocytosis (>5,000):**
  - Small mature-appearing lymphocytes
  - Condensed ("soccer ball") nuclear chromatin
  - Numerous "smudge cells"



Fragmented cells (broken)

Smudge cells

Burkitt's lymphoma

01

Definition :

High-grade non-Hodgkin's B-cell lymphoma which is rapidly growing and highly aggressive with extremely short doubling time (24 hrs)

02

Types of Burkitt's lymphoma :

1. Endemic: associated with chronic malaria and EBV In equatorial Africa . It particularly affects the **jaw**, other **facial bone and breast.**
2. Sporadic: occurs throughout the world and affects GIT.
3. Immunodeficiency-associated: associated with HIV infection or the use of immunosuppressive drugs.

03

Genetics of BL :

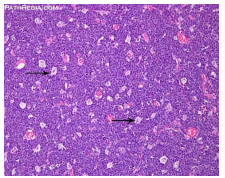
1. Highly associated with t(8;14):Translocation of the c-MYC proto-oncogene at chromosome 8 to immunoglobulin gene at chromosome 14
2. The **c-MYC** is nuclear transcription factor.
3. Burkitt's lymphoma is the fastest growing tumor in humans.

04

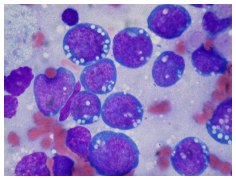
Morphology:

BMA: Homogenous medium size cells with round nuclei and deeply basophilic and vacuolated cytoplasm
Biopsy: Diffuse infiltration with "**starry sky**" (Macrophages engulfing the apoptotic cells)

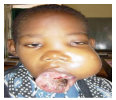
Biopsy :



BMA :



Clinical presentation:



The patient before and after 25 Day of intensive chemotherapy

- Burkitt's lymphoma has cure rate:
1. 90% at early phase
2. 70% at advance disease

Follicular lymphoma

01

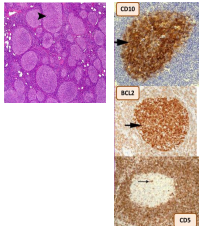
Definition :

FL is malignant proliferation of germinal center B cells centrocyte which has at least a partially follicular pattern , Most common type of “indolent” lymphoma (25%), Indolent but incurable (some exceptions)

02

Pathogenesis and diagnosis:

- Pathogenesis : Due to overexpression o f Bcl2 caused by t(14;18) .
- Diagnosis: Immunophenotyping: Positive for CD10, CD20 and Bcl2, Negative for CD5 (in most cases)



03

Clinical presentation:

- Lymphadenopathy (100)
- Splenomegaly (80%)
- BM involvement (60%)
- blood involvement (40%).

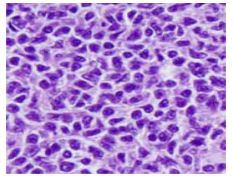
04

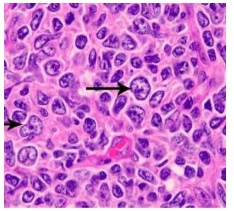
Prognosis of FL :

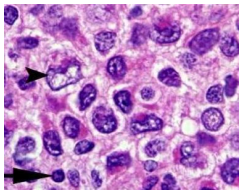
- Median survival is around 10 years.
- Transformation to aggressive lymphoma (DLBCL) can occur.

Management of FL:

Stage :	Management :
Low grade FL	Watch and wait
FL in transformation	Chemotherapy
Aggressive transformation (DLBCL)	Aggressive Chemotherapy(± SCT)





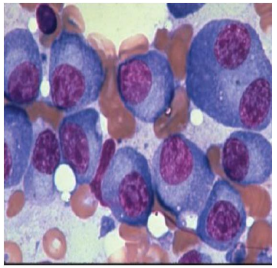


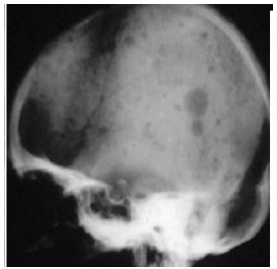
Multiple Myeloma :

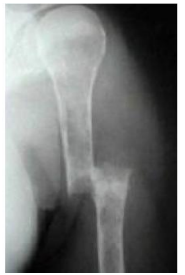
Malignant B neoplasm characterized by a triad of abnormalities:

Accumulation of plasma cells in the bone marrow **Lytic Bone lesions**

Production of a **monoclonal** immunoglobulin (Ig) or Ig fragments







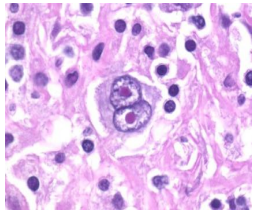
Classical Hodgkin Lymphoma

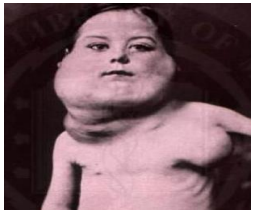
Indolent malignant lymphoma.

characterized by:

presence of few large binucleated cells (Reed-Sternberg) surrounded by reactive cells (lymphocytes, plasma cells ,eosinophils)

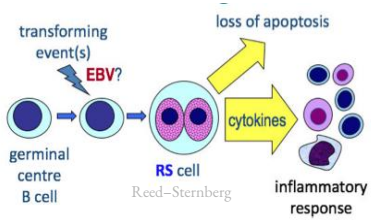
Involving cervical lymph nodes in young adults (most often)





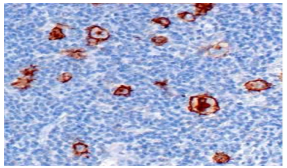
Binucleated cells

pathogenesis:

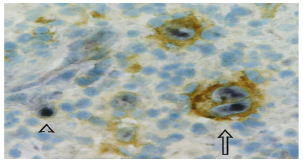


Diagnosis:

CD 30 and CD15 Should be positive



CD30

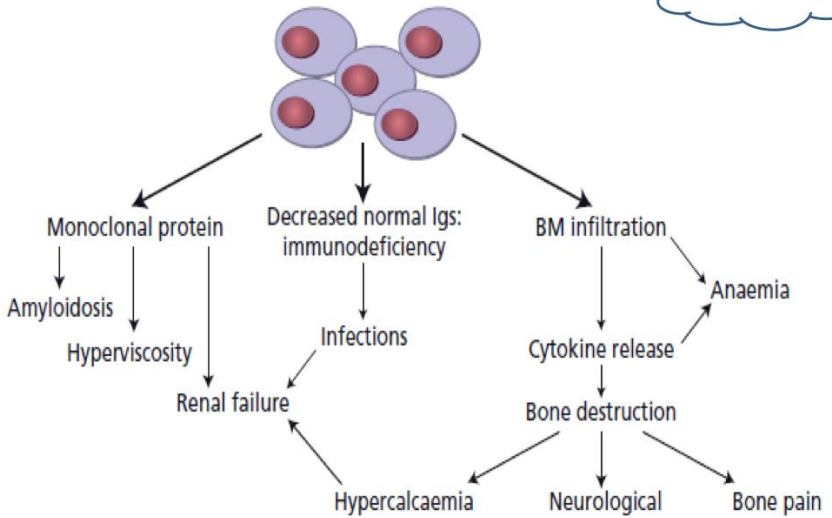


CD15

For reading :

Pathogenesis of MM

For reading



For reading

Immunophenotype of Small B-Cell Neoplasms

Marker	CLL/ SLL	Mantle Cell Lymphoma	Follicular Lymphoma	Hairy Cell Leukemia	Marginal Zone Lymphoma
CD5	+	+	–	–	–
CD10 (cALLA)	–	–	+	–	–
CD20	Dim	+	+	+	+
CD23	+	–	+/–	+/–	–
FMC-7	–	+	+	+/–	+
Surface Ig*	Dim	Moderate or bright	+	+	+
Other				CD11c, CD25, and CD103	

Dr. Notes

1-Lymphoma can happen at any stage of B cell maturation even in plasma cells
2-IgM antibodies are released from native B cells and that's why they are usually elevated during early stages of infection
3-A patient with lymphocytosis is not given chemotherapy directly, rather we (watch and wait)
4-In multiple myeloma we will have paraneoplastic syndrome marked by large amount of immunoglobulins and cytokines
5-The excessive abnormal immunoglobulins and cytokines will stimulate osteoclasts leading to lytic bone lesion

Quiz

Key answers:
1-A 2-B 3-C 4-C 5-B
6-B

1- which of the following diseases is associated with lymphocytosis?

A. EBV
B. HIV
C. TB
D. HBV

2- one of the most important feature of CLL. ***(from dr.notes)***

A. Less than 5,000 lymphocytes
B. More than 5,000 lymphocytes
C. Less than 10,000 lymphocytes
D. More than 5,000 neutrophils

3- one of the most important feature of multiple myeloma ***(from dr.notes)***

A. Splenomegaly
B. Smudge cells
C. Lytic bone lesions
D. Large cells lymphoma

4-Burkitt's lymphoma cytogenetic abnormality? ***(from dr.notes)***

A. t(8;16)
B. t(5;18)
C. t(8;14)
D. t(8;21)

5- 12 years old male presented to ER with enlarged lymph nodes involving the cervical nodes, present of Reed–Sternberg cells under the microscope. What's the diagnosis?

A. Multiple myeloma
B. Hodgkin's lymphoma
C. Follicular lymphoma
D. Burkitt's lymphoma

6-Which of these cells is associated with Follicular lymphoma?

A. GC cell
B. Centrocyte
C. Plasma cell
D. Centroblast

THANKS

| TEAM LEADERS

- | Abdulaziz Alghamdi
- | Elaf Almusahel

= Done by

= Editor مدقق

= Note taker

= Textbooks note taker

| TEAM MEMBERS

- *Amirah Alzahrani*
- Deema Almaziad
- Jude Alotaibi
- *Njoud Almutairi*
- *Nouf Albraikan*
- Noura Almazrou
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