Leukemia

Basis of classification

Stem cell: CD34 & TDT	Myeloid: MPO, CD13, CD33, CD14, CD64, CD41 (M7) & CD235a (M6)	B-lymphoid: CD10, CD19, CD22, CD79a T-lymphoid: CD3, CD4, CD5, CD7, CD8

Acute leukemia

Immature cells | >20% blasts | Auer rods | | T-ALL: mediastinal & CNS lesions | AML: adults | ALL: child

AML		ALL	
Karyotype	Molecular	Karyotype	Molecular
t (8;21) (M2) (Granulated blasts often with Auer rods)	AML1-ETO	t (9;22) Hypodiploidy (worse prognosis)	BCR-ABL1
t (15;17) (M3) (Promyelocytic leukaemia) Rx: ATRA or arsenic.	PML-RARA (DIC)	t (4;11)	AF4-MLL
t (16;16) or inv. (16) (M4) (Myelomonocytic leukaemia)	CBFB-MYH11 (Gum hyperplasia)	t (12;21) Hyperdiploidy (better prognosis)	ETV6-RUNX1
t (9;11) (M5) (Monocytic leukaemia)	MLLT1-MLL (Gum hyperplasia)	t (5;14)	IL3-IGH

Chronic leukemia

Adults (old) | Mature cells (granulocytes) | Lymphoid (LPN-CLL) | Myeloid (MPN (CML) \ MDS)

MPN features:	- Cytoses, splenomegaly, high uric acid, hypercellular BM, progress to acute leukemia (mainly AML) (CML belongs to MPN)

CML

- Stem cell MPN.
- Predominant granulocytic cells.
- Associated w\ BCR-ABL1 in the Philadelphia (Ph) chromosome → t (9;22) → ↑ tyrosin kinase activity. → treated w\ Imatinib.

Clinical presentation	- 20-40% are Asymptomatic. - CBC: marked leukocytosis. - Fatigue, weight loss, night sweeting. - Abdominal discomfort → splenomegaly (massive).
Main differential dx	- Chronic myelomonocytic leukemia CMML → monocytosis, BCR-ABL1 –ve. - Leukemoid reaction → leukocytosis due to physiological response to stress or infection.

	CML	Leukimoid
WBC	Very high	High, but <100,000
differential	Myelocytes & segmented neutrophils	Bands neutrophils & neutrophils
Morphology	Hypogranular	Toxic granulation
Splenomegaly	+ve	Mainly **-ve**
NAP score	**Low**	**High**
BCR-ABL	+ve	**-ve**

CML phases	Chronic phase	Accelerated phase	**Blastic phase**
	- Leukicytosis - Blasts ≤10%, basophils ≤20% - Stable course (yrs)	- 10-19% blasts, basophils ≥ 20%. - Unstable course.	- ≥ 20% blasts = acute leukemia - 80% = AML, 20% ALL. - Course: weeks
Myelodysplastic Syndromes MDS			
Features	- Group of myeloid neoplasms. - Peripheral cytopenia (How Hb ± low WBC & low PLT) = pancytopenia MPN عكس - ↑ proliferation – ↑ apoptosis = Ineffective hematopoiesis (hypercellular BM) تموت قبل لا تطلع - Dysplasia (abnormal morphology) - Progression to AML. - Enhanced apoptosis.		
MDS subtypes Many subtypes according to:	1- Blast count	2- Degree of dysplasia	3- Genetics → -5, -7 (deletion in these chrom.)
Chronic Myelomonocytic Leukemia (CMML)			
Features	- Clonal hematopoietic malignancy, characterized by proliferation of both monocytes & neutrophils. - MDS\MPN disease: CMML يجون مع • Features of MDS (dysplasia, enhances apoptosis) • Features of MPN (marked proliferation) - Philadelphia chromosome must be negative! - Blasts must be **< 20%** (less). - It has an aggressive course.		
Lymphoid leukemia			
CLL | Hairt cell leukemia | T-prolymphocytosis leukemia | leukemic phase of lymphoma			
CLL			

Features	- Small, mature lymphocytes in the blood & BM (± spleen and lymph node)
	- Most common adult leukemia. (25% of adult leukemias) → 55-65 yrs. Rare <40yrs. Male more.
	- 40% asymptomatic.
	- Moderate lymphadenopathy & splenomegaly.
	- Lymphocytosis (>5,000)
	- Morphology: small mature appearing lymphocytes →
	  ○ Condensed (**soccer ball**) nuclear chromatin.
	  ○ Numerous (**smudge cells**) CLL إذا مب فيه لازم أصبر وأستنى لما تصير سنستف عشان أقول إنها
	- Predisposition to infection.
	- Autoimmune phenomena → autoimmune hemolytic anemia.
	- Transformation to DLBCL (Richter's syndrome)		

Markers	- CD5, CD23, CD20, CD19, IgM & IgD → Mature naïve B-cell		

Lymphoma

Mature cells	Lymphoid leukemia	Discussed above.	
	Lymphoma	**Non-Hodgkin lymphoma**	B cell: - Burkitt's lymphoma - DLBL - Follicular lymphoma. - Multiple myeloma
			T cell: - Adult T leukemia lymphoma. - Sezary syndrome. - Large anaplastic T lymphoma.
		Hodgkin lymphoma	- presence of few large binucleated cells (**Reed-Sternberg**) surrounded by reactive cells (lympo, plasma, eosinophils) - Involving cervical lymph nodes in young adults. - **CD30** & **CD15.**

Burkitt's lymphoma

High grade | Fastest growing tumor in human (24hs) & highly aggressive | **t (8;14)** **c-MYC at 8 with Ig at 14)** c-myc: (nuclear transcription factor) (proto-oncogen)

Types of Burkitt's lymphoma

1- Endemic	2- Sporadic	3- Immunodeficiency-associated
w\ chronic malariam EBV → Africa. Affects the jaw & facial bone & breast.	Throughout the world, affects GIT	HIV & immunosuppressive drugs

Morphology	- BMA: Homogenous medium size, deeply basophilic, vacuolated cytoplasm. - Biopsy: **Diffused infiltration** w\ **Starry sky** (macrophage engulfing the apoptotic cells)

Follicular lymphoma

Proliferation of **germinal center B cells centrocyte** | over expression of **Bcl2** by **t (14;18)** | most common type of indolent lymphoma → but it is incurable ☹

Presenting problem	✓ **Lymphadenopathy** (100%) ✓ **Splenomegaly** (80%) ✓ BM involvement (40%) ✓ Blood involvement (40%)	Diagnosis	- Positive for **CD10**, **CD20** & **Bcl2**. - Negative for CD5.

Multiple myeloma

Triad of abnormalities: 1- Accumulation of plasma cells in BM. 2- Lytic bone lesions أكثر شيء في الجمجمة.
3- Production of a monoclonal immunoglobulin (Ig)

Markers of Lymphoproliferative disorders

	CD34 & TDT	s-Ig	CD19	CD20	CD5	CD10
ALL	+	-	+	+	-	-
CLL	-	+	+	+	+	-
Mantle lymphoma t(11;14) cyklin D	-	+	+	+	+	-
Burkitt's lymphoma t(8;14) c-myc	-	+			-	+
DLBCL t(3;14) Bcl-6						
Follicular lymphoma t(14;18) Bcl-2						
Multiple myeloma (CD38 ,CD138, IgG, IgA, IgE)	-	+	-	+	-	-

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