VII CORSO del GRUPPO ITALIANO DI EMATOPATOLOGIA

La DIAGNOSTICA EMATOPATOLOGICA nell'ERA della MEDICINA di PRECISIONE

CLL: When Histology changes the Rules

Francesca Capuano

Usl Toscana Centro, presidio Empoli-Prato

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Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

- 64 years old
- Dyslipidemia
- Lymphocytosis
- No organomegaly
- No lymphadenomegaly

Esame emocromocitometrico *Sangue*

Leucociti (WBC)	**21.23**	*	*10^3/µL*	4.00 - 11.00
Eritrociti (GR)	5.47		*10^6/µL*	4.50 - 6.00
Emoglobina (HB)	16.3		*g/dL*	13.0 - 18.0
Ematocrito (HCT)	49		%	41 - 50
MCV	89.2		*fL*	80.0 - 100.0
MCH	29.8		*pg*	26.0 - 33.0
MCHC	33.4		*g/dL*	31.0 - 36.0
RDW	12.5		%	10.0 - 16.0
Piastrine	186		*10^3/µL*	140 - 450
MPV	12.4		*fL*	7.0 - 13.0
Neutrofili	3.46		*10^3/µL*	1.80 - 7.00
Linfociti	**16.96**	*	*10^3/µL*	0.90 - 4.50
Monociti	0.45		*10^3/µL*	0.10 - 1.20
Eosinofili	0.28		*10^3/µL*	0.10 - 0.70
Basofili	0.08		*10^3/µL*	0.00 - 0.20
Neutrofili %	**16.3**	*	%	40.0 - 75.0
Linfociti %	**79.9**	*	%	20.0 - 50.0
Monociti %	2.1		%	2.0 - 13.0
Eosinofili %	1.3		%	0.0 - 7.0
Basofili %	0.4		%	<= 1.5
Commento	Vedi nota Numerosi Linfociti Atipici. Rare Ombre Nucleari. Formula leucocitaria elaborata tramite revisione microscopica dallo specialista di laboratorio.			

IMMUNOFENOTIPO (Citometria a flusso)

Materiale Esaminato: sangue midollare

Cellularità

Linfociti =	56.3 %
	Linfociti T: 10.7%
	Linfociti B: 44.6%
	Cellule NK: 1.0%

Pannello di Ab monoclonali

mAb utilizzati:
Marcatori linfoidi T: CD3, CD4, CD8.
Marcatori linfoidi B: CD19, CD20, CD22, CD23, CD79b, anti-Kappa, anti-Lambda.
Altri: CD5, CD11c, CD25, CD10, CD34, CD43, CD38, CD56, CD200.

Gate citofluorimetrico

Finestra di analisi condotta sulla popolazione di linfociti, che rappresenta il 56.3% della cellularita' totale.

Conclusioni:

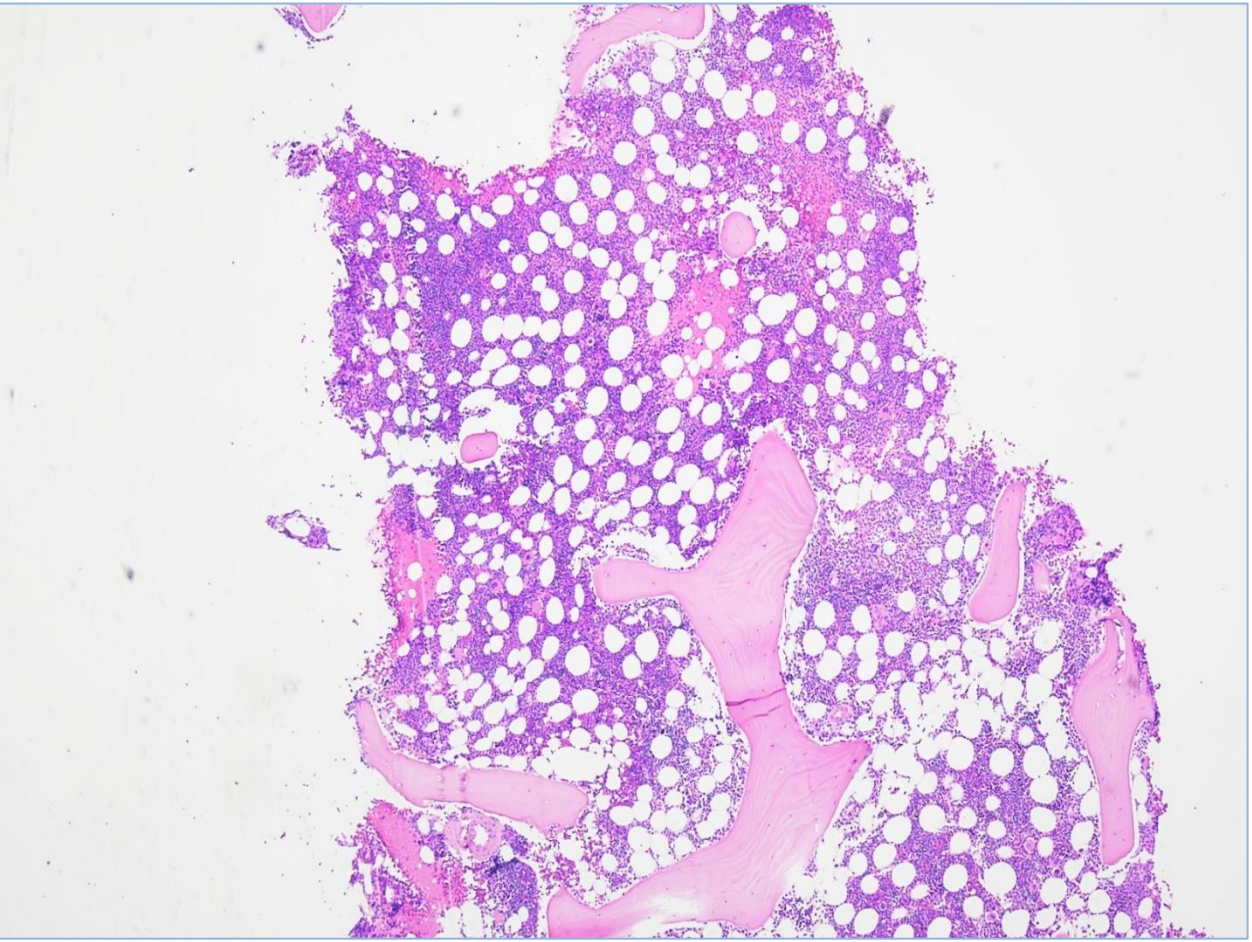
L'analisi eseguita su campione di sangue midollare evidenzia:

1) Normale cellularita' rappresentata prevalentemente dalla serie mieloide alle varie fasi maturative.

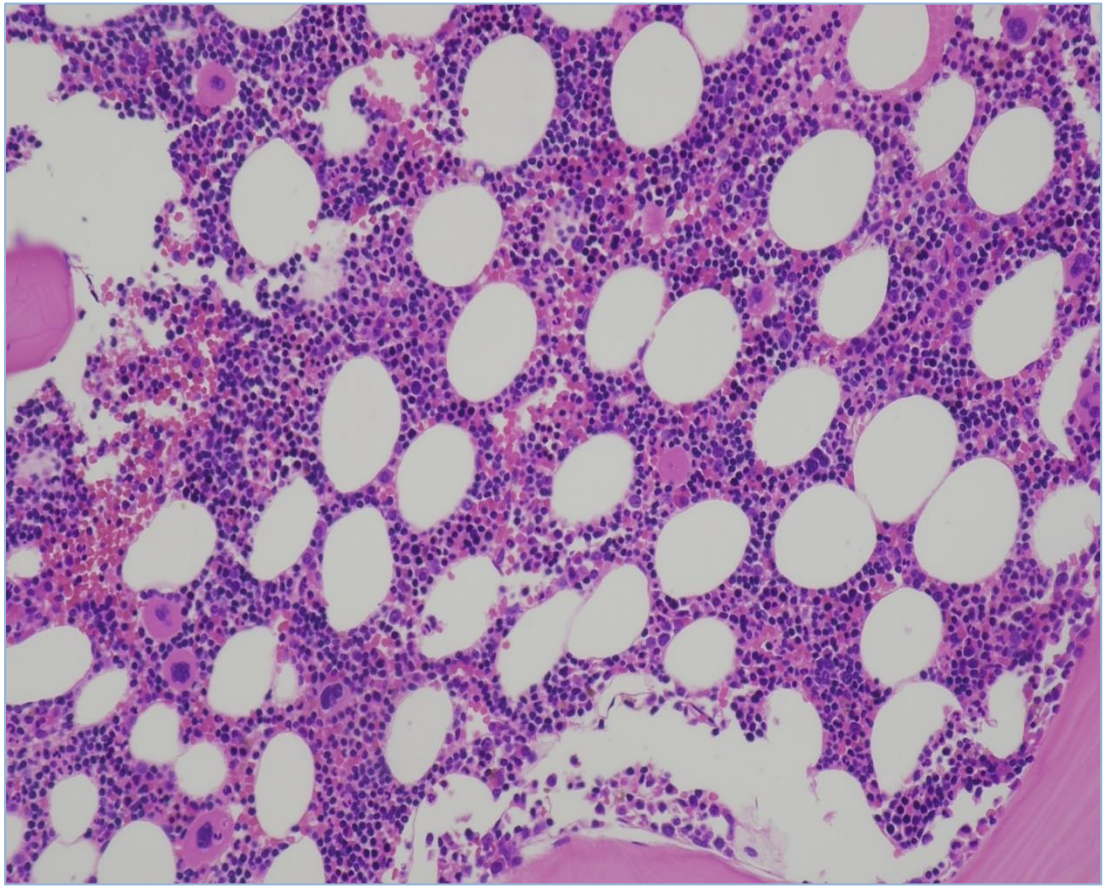
2) Una popolazione di linfociti B maturi (42.0% della cellularita' totale) presenta il seguente profilo immunofenotipico "Atypical CLL like/non CLL like": CD19+, CD20+, CD22-/+, CD5-/+dim, CD23-, CD25-, CD200+, CD79b-/+, CD43-/+dim, CD38-/+, CD10-, CD45+ e catene leggere di superficie clonali Kappa a debole intensita' di espressione.

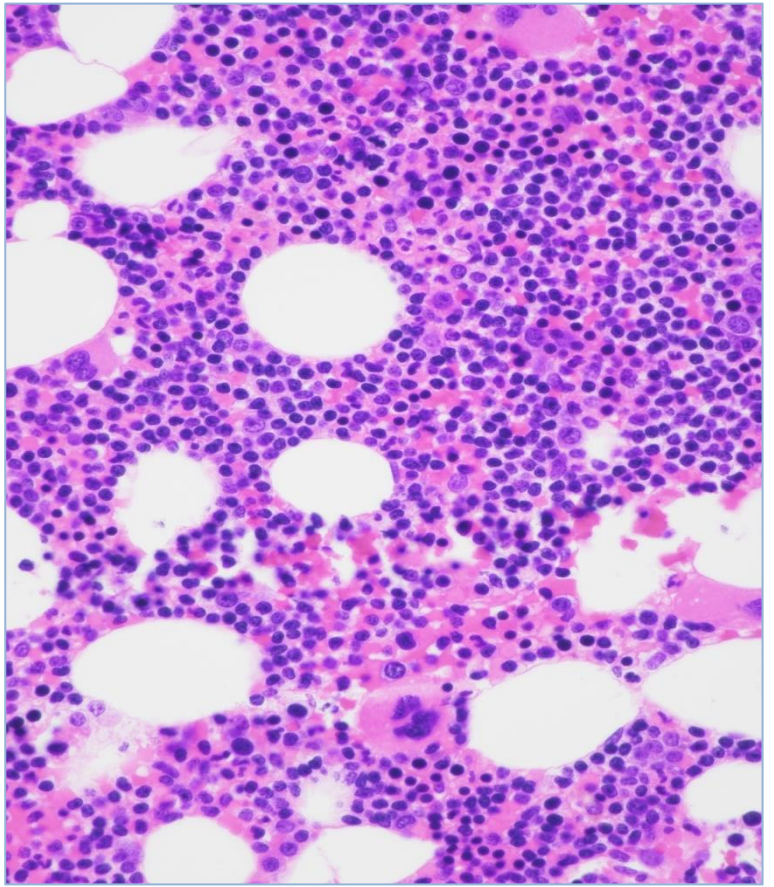
3) Normale distribuzione dei linfociti T.

4) Marcatamente depressi i progenitori emopoietici linfoidi B e mieloidi.

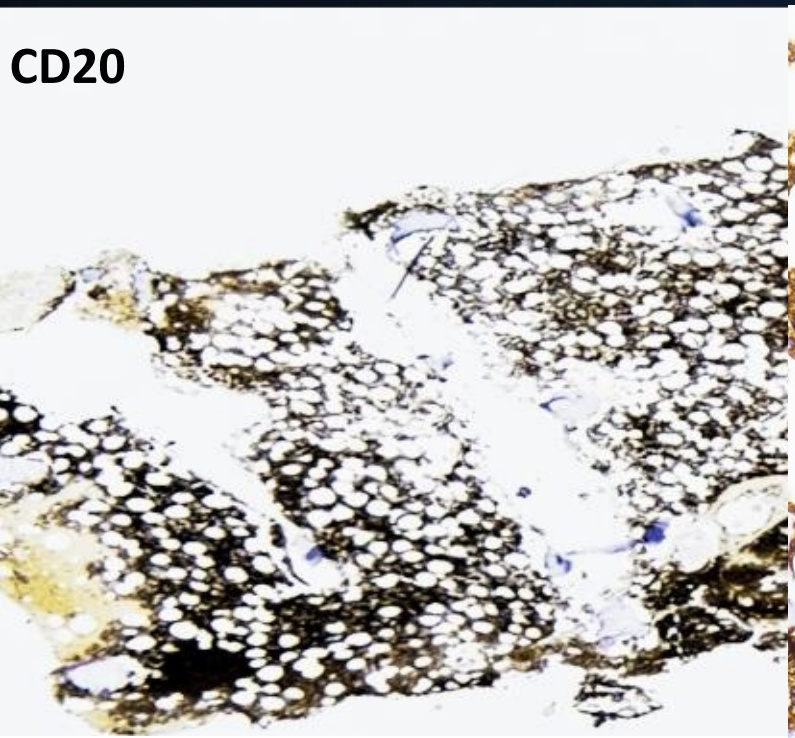


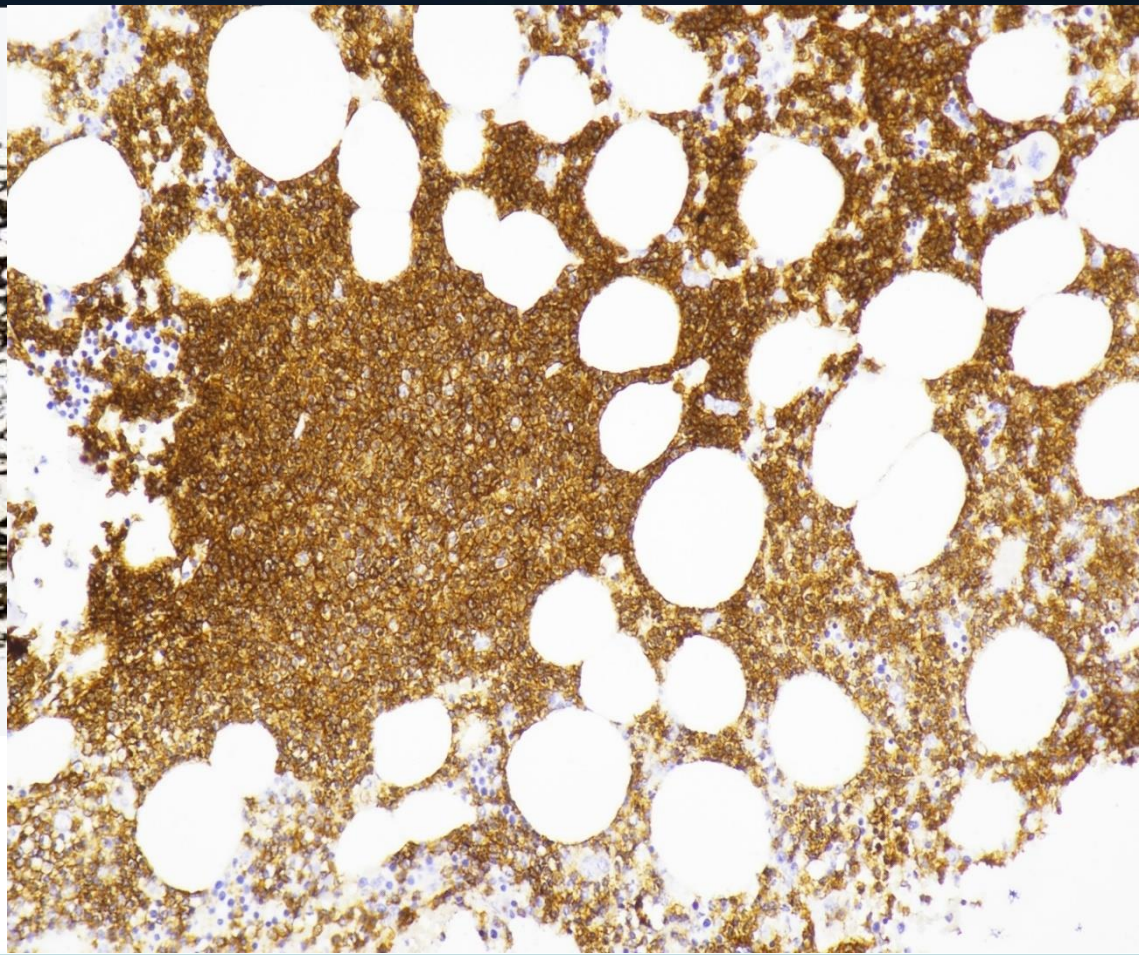
Cellularity 50%



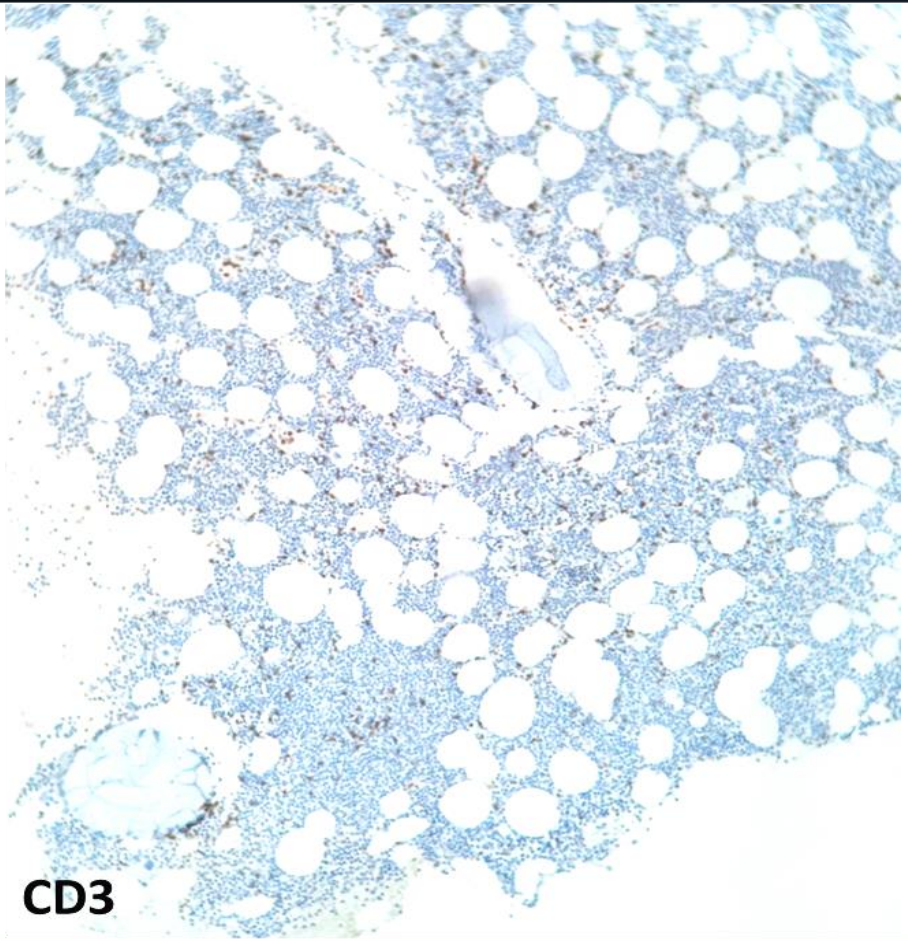


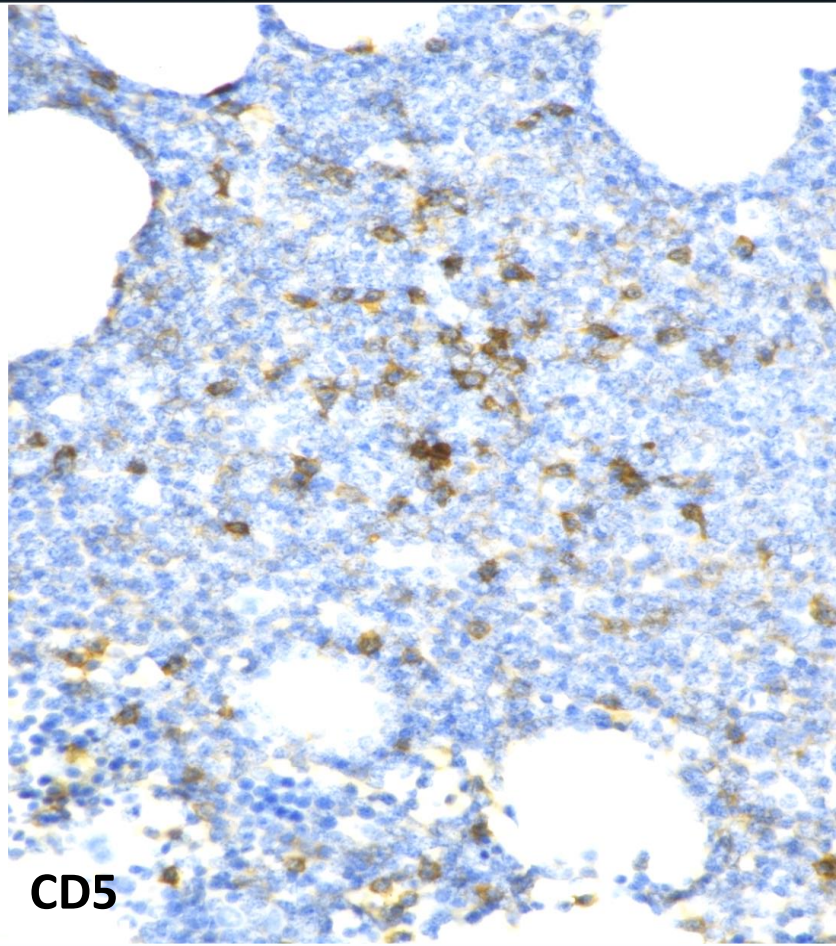
CD20

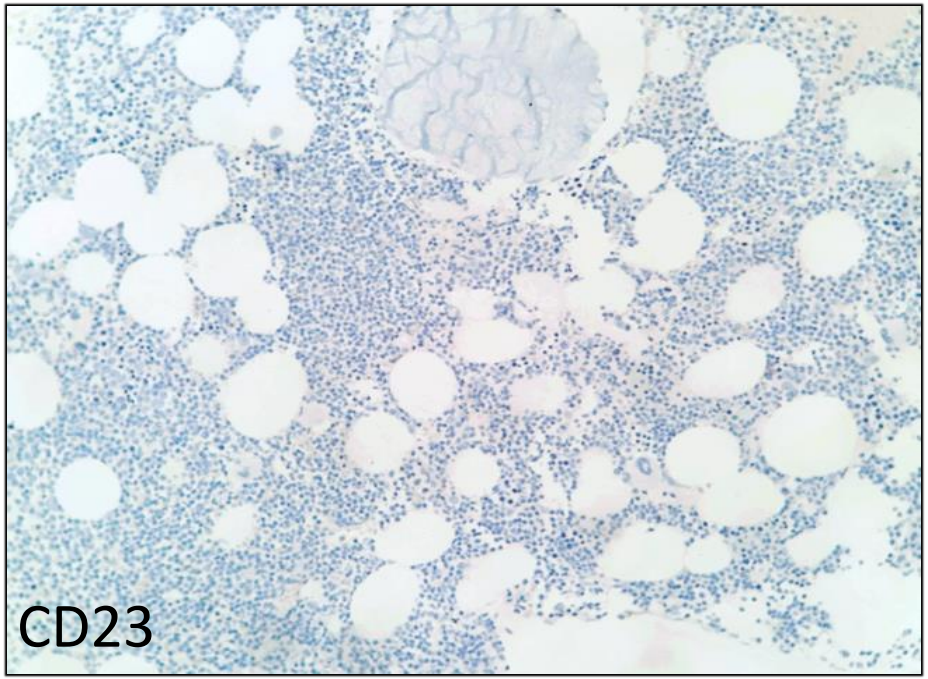




Medullary infiltration:
nodular and interstitial
70%


CD3


CD5



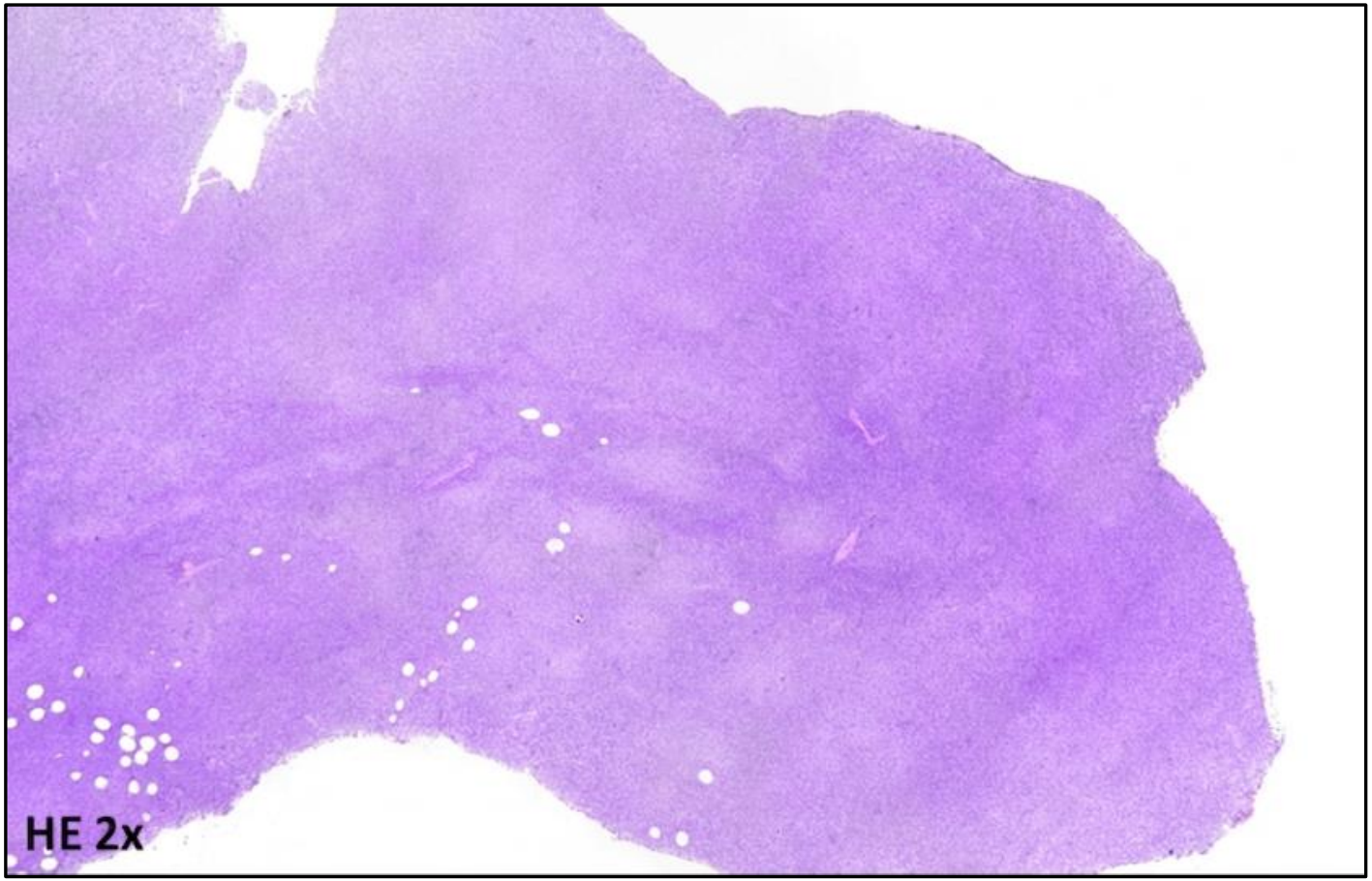
- Ciclina D1-
- SOX11-
- Bcl6-
- Ki67 5%
- Reticulin stain: 1+

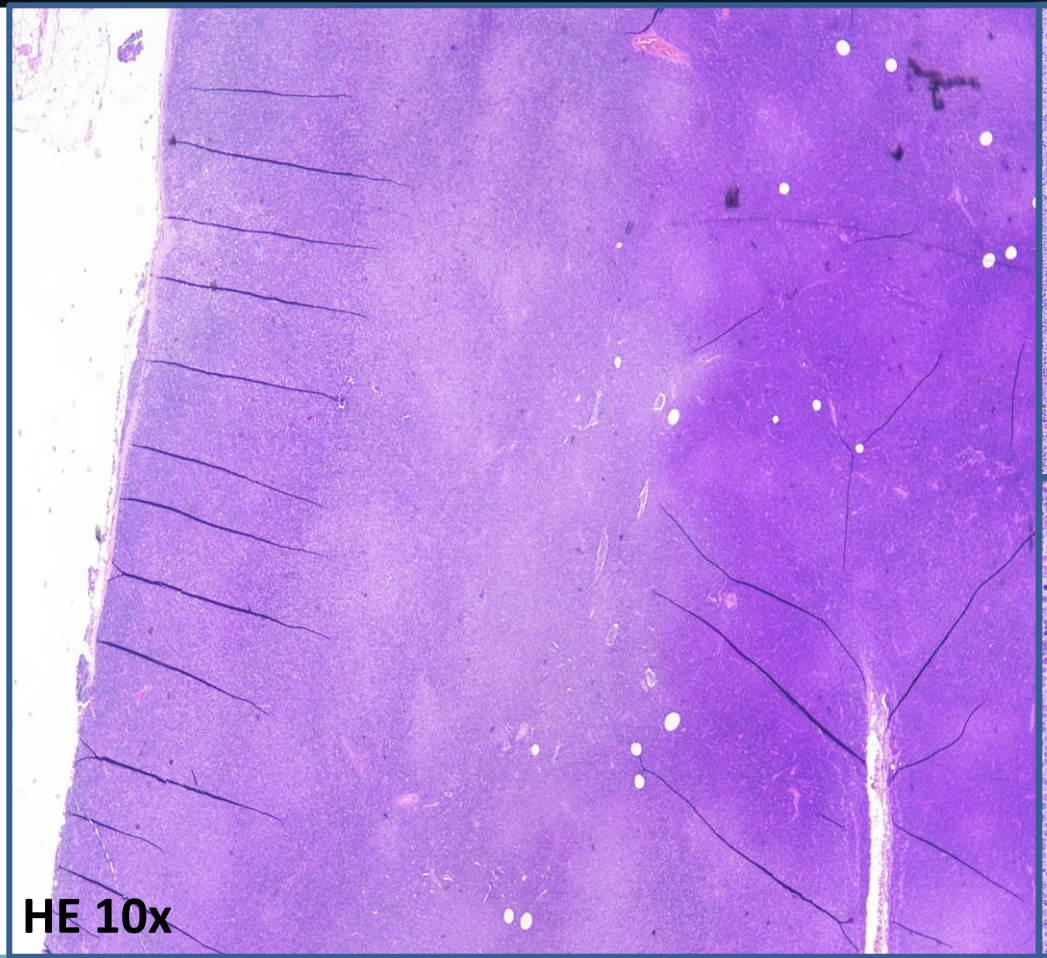
Bone marrow localization of chronic lymphocytic leukemia with atypical immunophenotypic profile

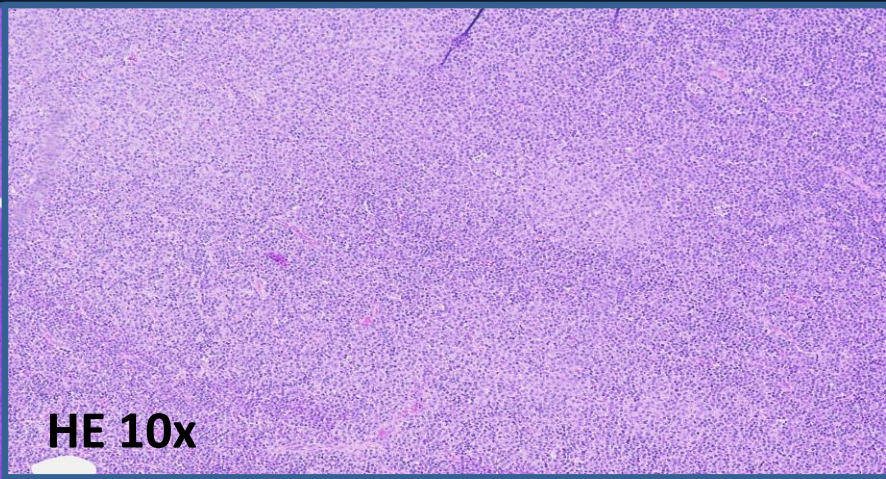
Staging CT demonstrates multiple supra- and sub-diaphragmatic lymphadenopathies, with the largest measuring approximately 2 cm in the axillary region

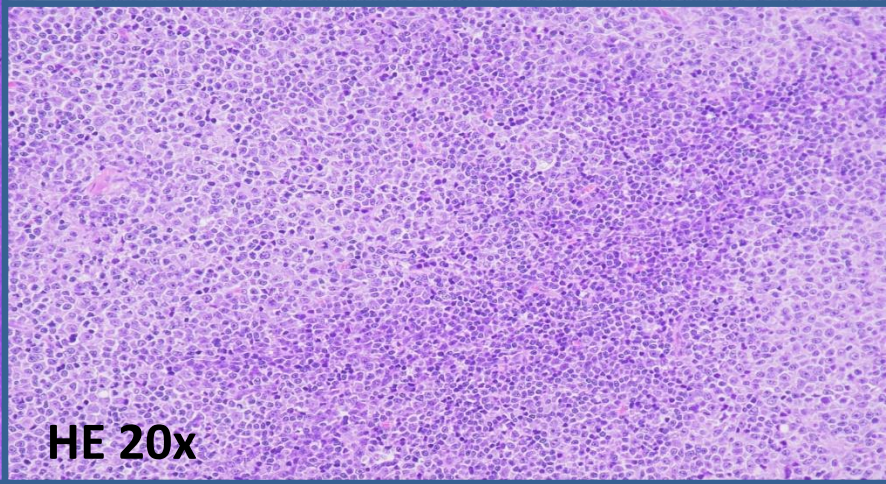
PET imaging confirmed multiple hypermetabolic lymph nodes with a maximum SUV of 8.

AXILLARY LN
cm 1,9x1,2x0,9

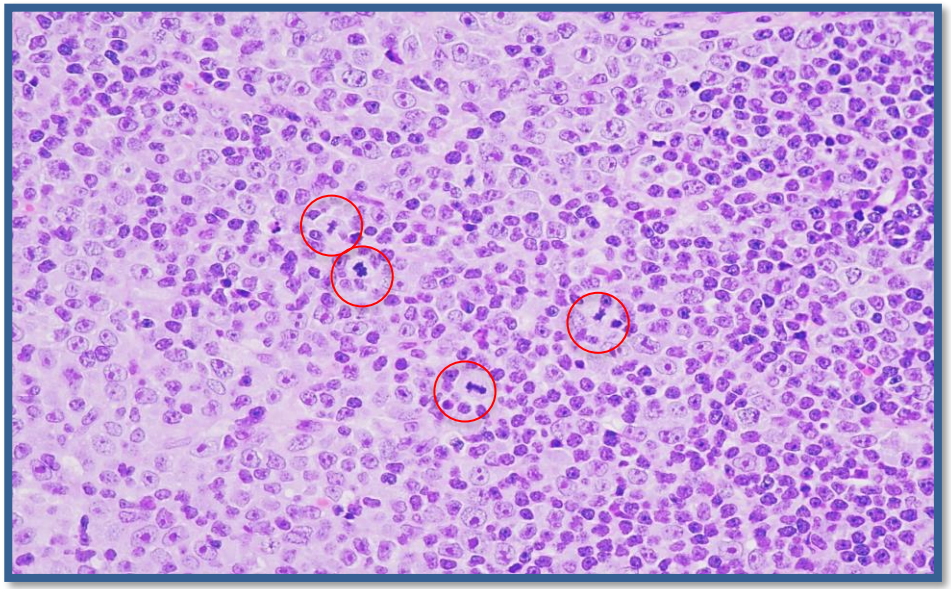


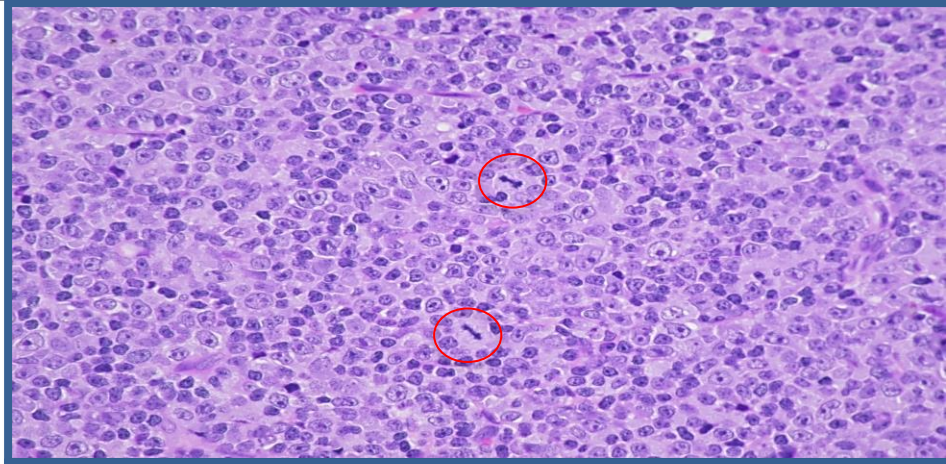

HE 10x

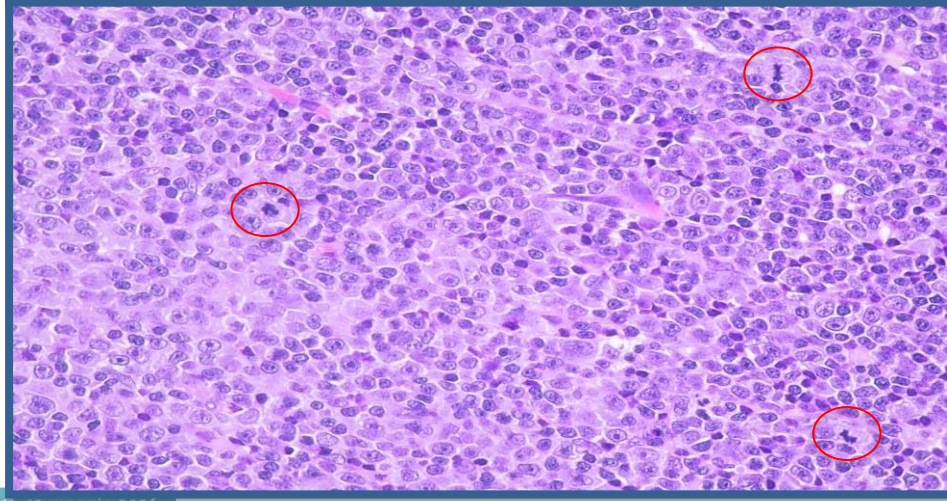

HE 10x

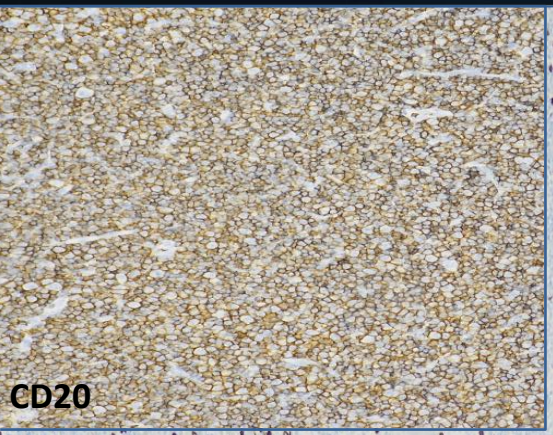

HE 20x

3-4 mitoses per PC

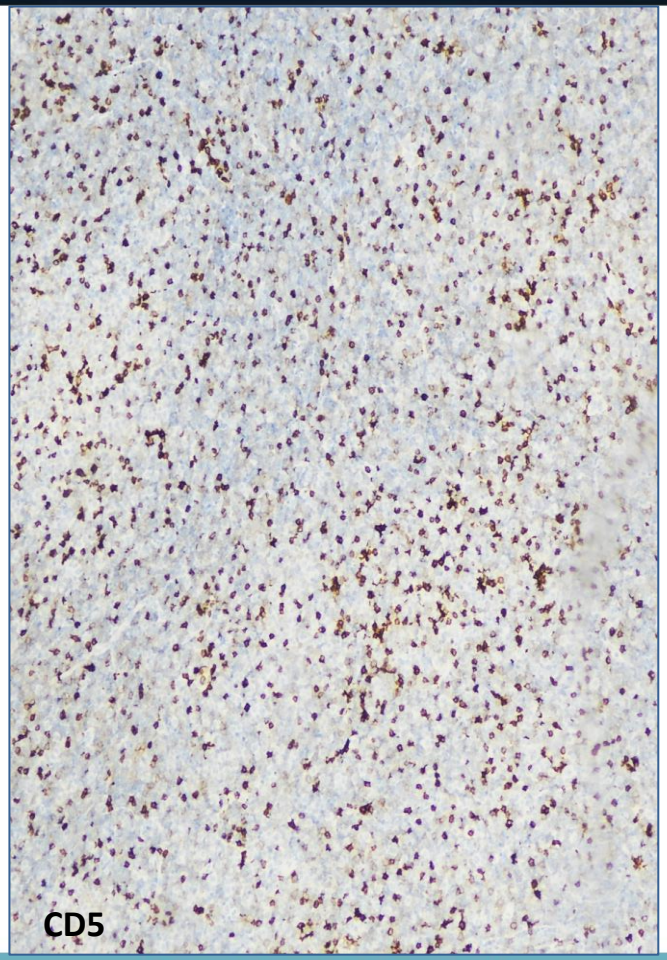


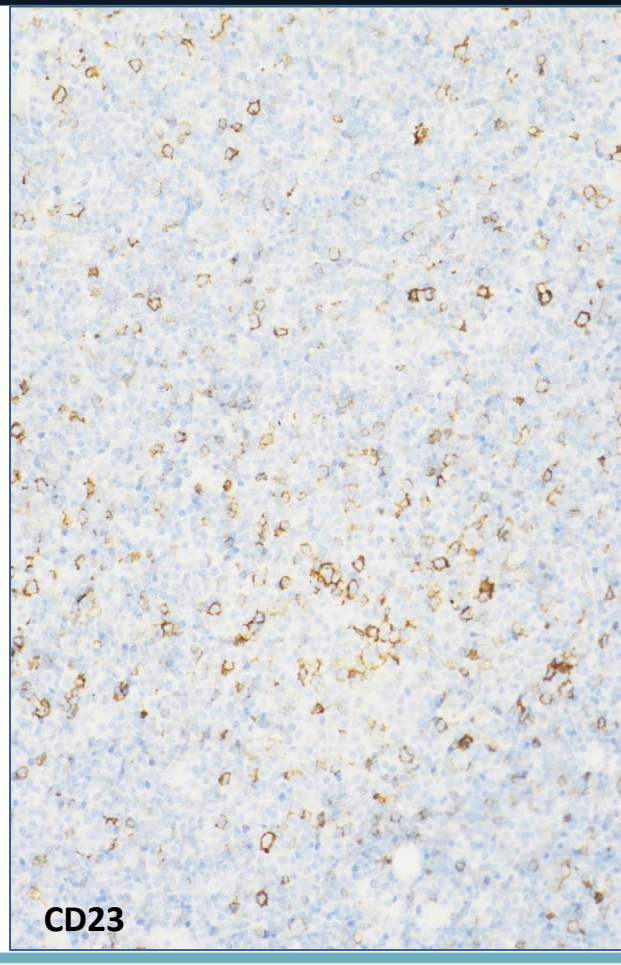


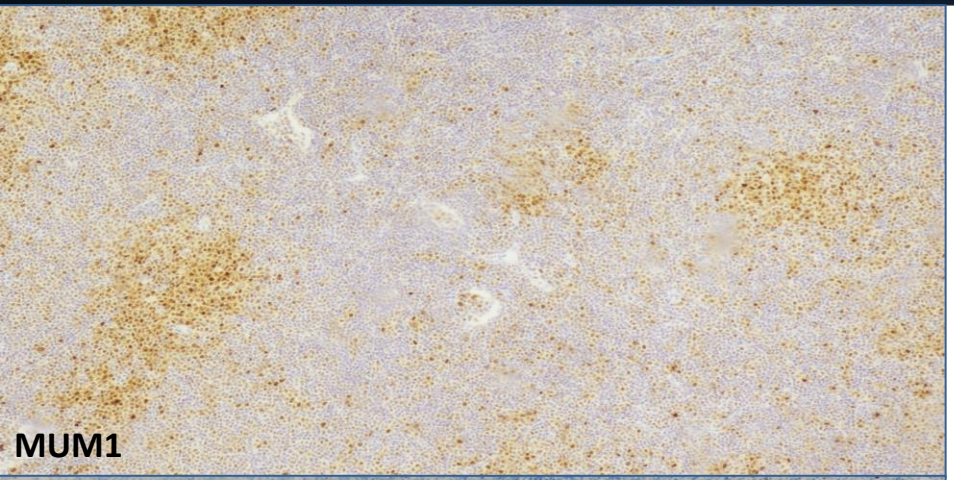


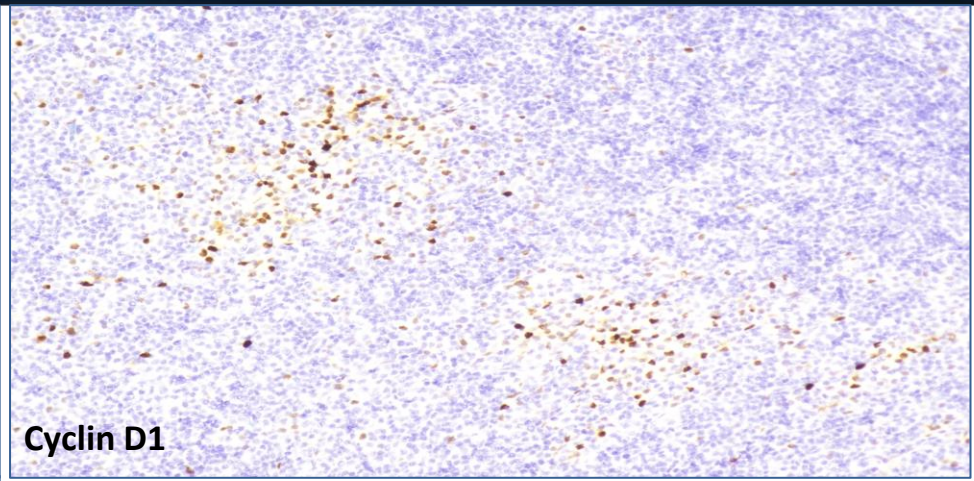

CD20

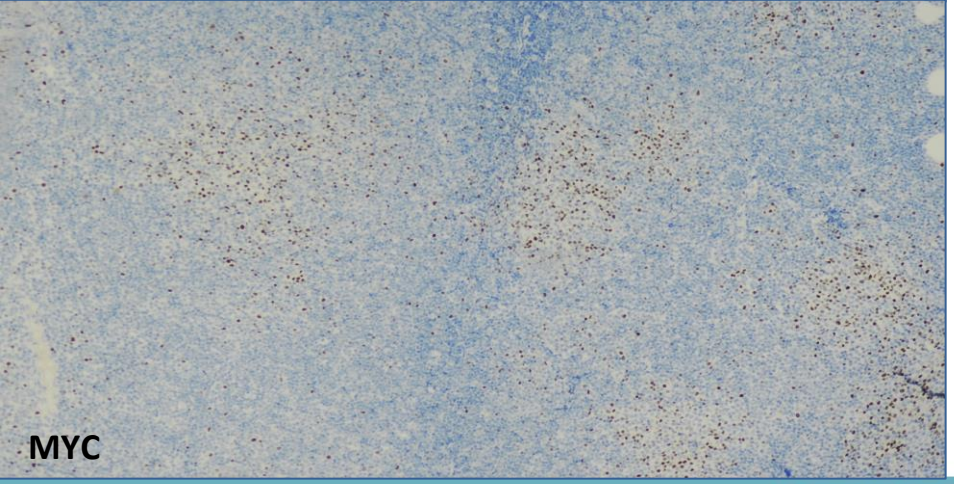
CD3


CD5


CD23







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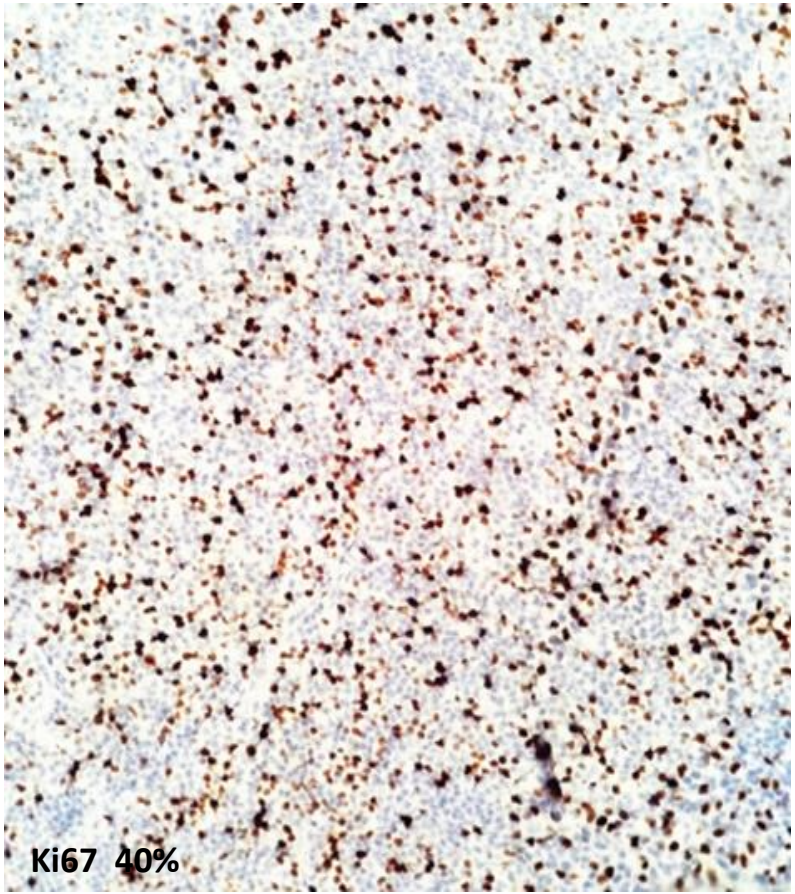
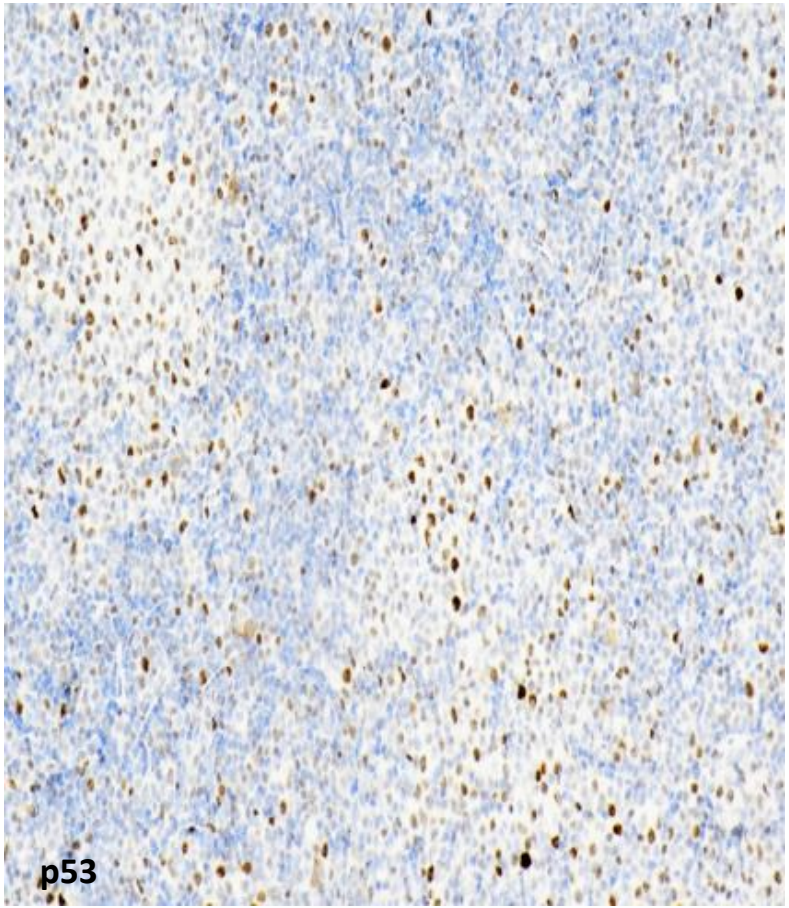
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma With Cyclin D1 Positive Proliferation Centers Do Not Have *CCND1* Translocations or Gains and Lack SOX11 Expression

Joel F. Gradowski, MD[1], **Rachel L. Sargent, MD**[1], **Fiona E. Craig, MD**[1], **Kathleen Cieply, MSL**[2], **Kim Fuhrer, HT**[2], **Carol Sherer, MS**[2], and **Steven H. Swerdlow, MD**[1]

[1]Division of Hematopathology, Department of Pathology, University of Pittsburgh School of Medicine, Pittsburgh, PA

[2]Department of Pathology Development Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, PA


Ki67 40%


p53

Diagnosis

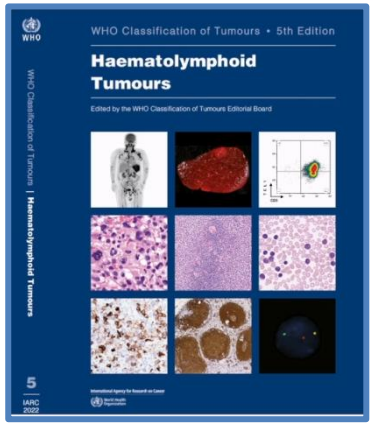
Histologically Aggressive Chronic Lymphocytic Leukemia/
Small Lymphocytic Lymphoma
sec. WHO 2022

Molecular evaluation

Karyotype on peripheral blood: trisomy chromosome 12 and chromosome 18

Molecular analysis of TP53: no evidence of a TP53 coding region

Unmutated IGHV status



WHO 2022 CLASSIFICATION

ACCELERATED CLL/SLL 5% of cases

Histologically aggressive CLL/SLL (5%)

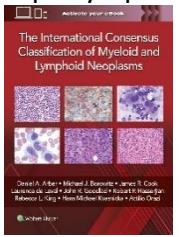
The size of PCs and the numbers of prolymphocytes or paraimmunoblasts vary between cases.

Very large, prominent/confluent PCs
traditionally spanning the diameter of a visual field using a 20× objective lens and a 10× ocular lens
High proliferation indexes
- 2.4 mitoses per PCs **OR**
- >40% Ki-67+ cells in PCs

whereby traditionally PC size is not defined

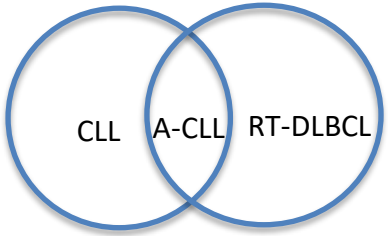
Prolymphocytic progression

Total proportion of prolymphocytes (medium-sized cells with basophilic cytoplasm and a prominent nucleolus)
> 15% in PB
> 55% in PB ⇨ ICC: B-cell prolymphocytic leukemia



Diagnostic pitfalls

- Total lymph node excision
- Histologic gray zone



- Differential diagnosis with progression in DLBCL

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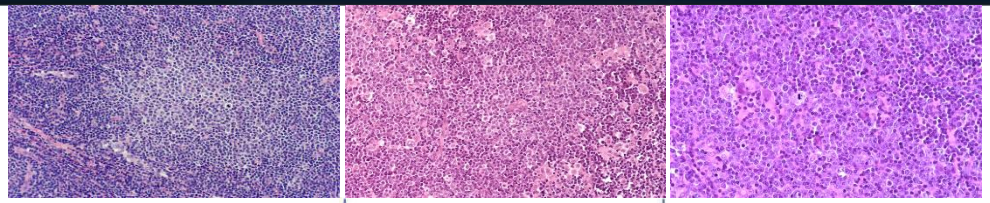
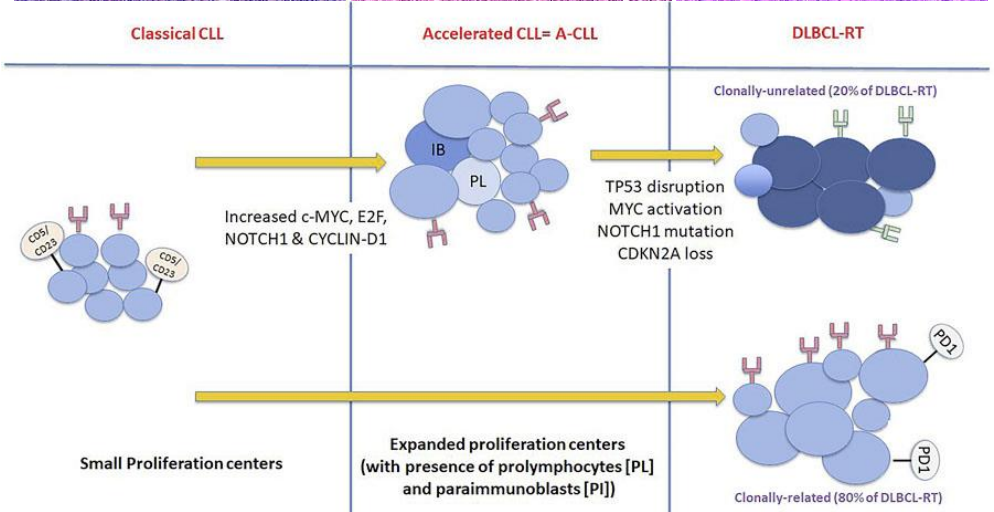
REVIEW ARTICLES | SEPTEMBER 04 2023

Accelerated Chronic Lymphocytic Leukemia and Richter Transformation in the Era of Novel Agents

Subject Area: Hematology, Oncology
Special Collection: Karger e-Journal Backfile Collection 2024

Ilana Levy Yurkovski; Tamar Tadmor





	Ki67 0-10%	30% < Ki67 < 70%	Ki67 > 70%
ARCHITECTURAL PATTERN	Expanded or confluent CPs but nodular architecture still recognizable	Diffuse sheets of large cells forming part of a proliferation center
SIZE OF CPs	Expanded/fused CPs >20x (>0.95 mm)	CP no longer identifiable as such; diffuse laminae growth
PREDOMINANT CYTOLOGY	Increased prolymphocytes and paraimmunoblasts still mixed with small lymphocytes	Large confluent B cells (immunblasts/centroblasts) with prominent nucleoli
Mitosis	>2,4mitosis/CP	Numerous diffuse mitoses, not confined to the CPs

Non-GC B immunophenotype
CD10-BCL6- MUM1+
CD5 + occasionally
CD23 - typically
EBV -

THANK YOU FOR YOUR ATTENTION

My thanks go to:

Prof. Stefano Lazzi
Dott. Carlo Ammatuna