VII CORSO del GRUPPO ITALIANO DI EMATOPATOLOGIA

La DIAGNOSTICA EMATOPATOLOGICA nell'ERA della MEDICINA di PRECISIONE

To be, or not to be, that is the question…

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La Spezia

Bologna, Aula Prodi | 11-12 maggio 2026

Man 78 yo

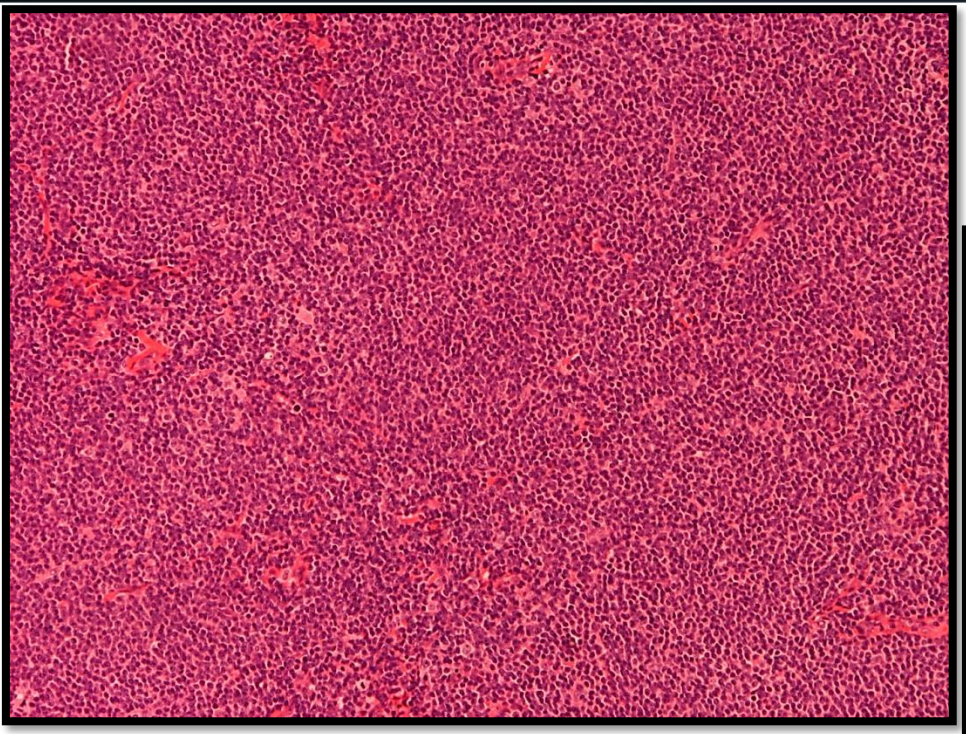
- Dec. 2024: during pre-hospitalization examinations for inguinal hernia surgery, radiological evidence of left pleural effusion
- weight loss of 8-9 kg in the last month
- intense asthenia

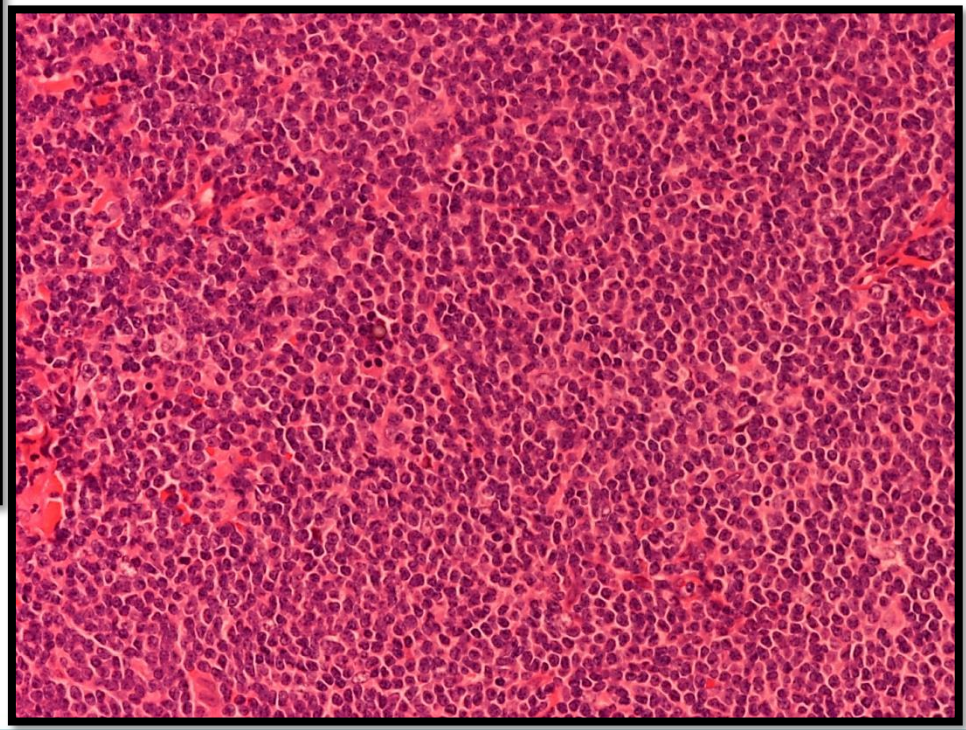
Chest CT

- left pleural effusion
- mediastinal LAPs (subcarenal 45x15 mm)
- bilateral axillary, supra- and subclavicular LAPs (right axillary 46x32 mm)
- multiple LAPs also confluent in small gastric curve (50x27 mm), hepatic hilum and celiac-mesenteric (33x24 mm)

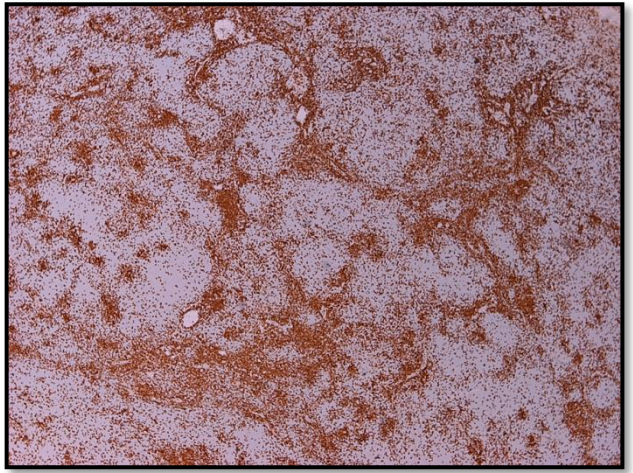
left supraclavicular lymph node excisional biopsy

- multi-lobed LN of 3 cm maximum diameter
- flow cytometry: CD19+, CD20+, CD5+, CD200-, CD10-, CD38+, lambda light chain expression





CD3



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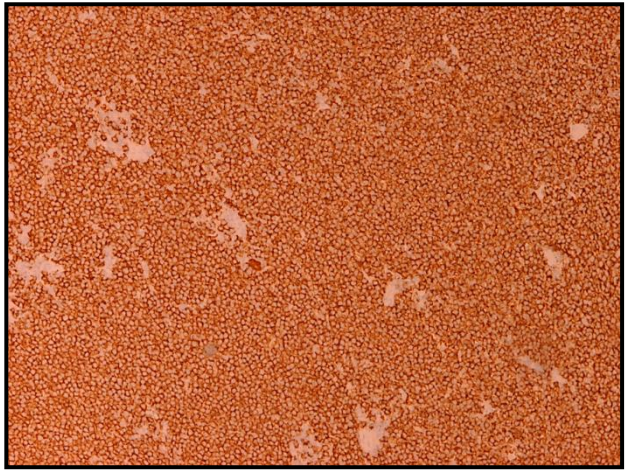

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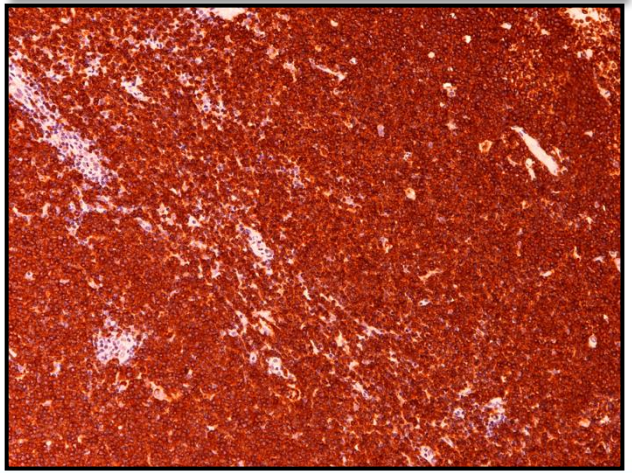
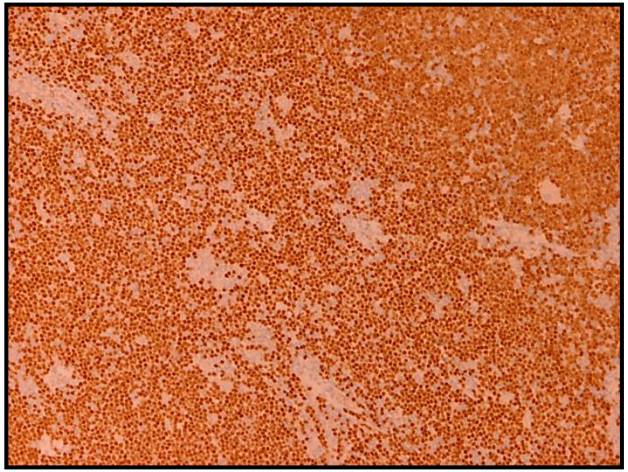


PAX5



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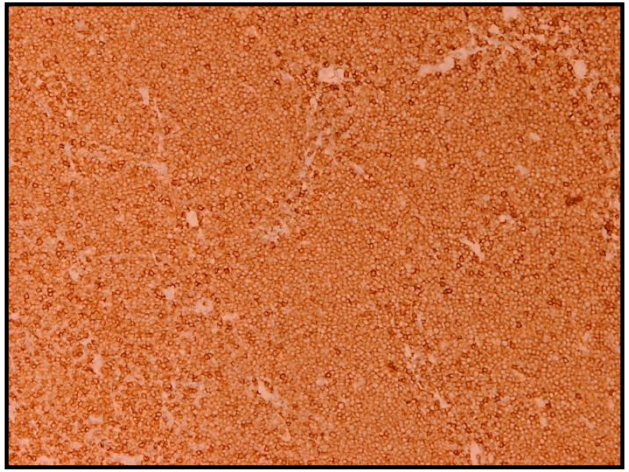

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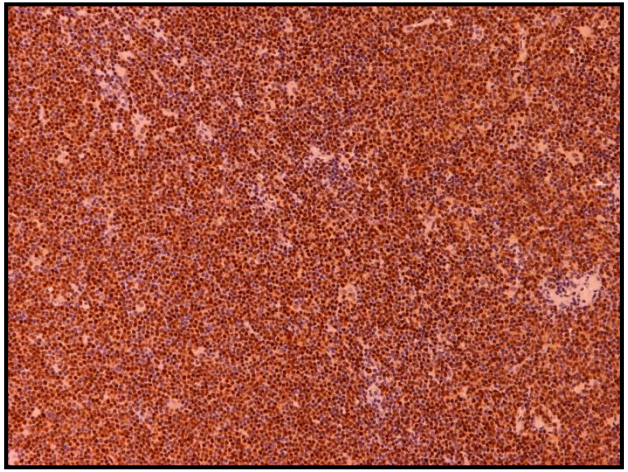

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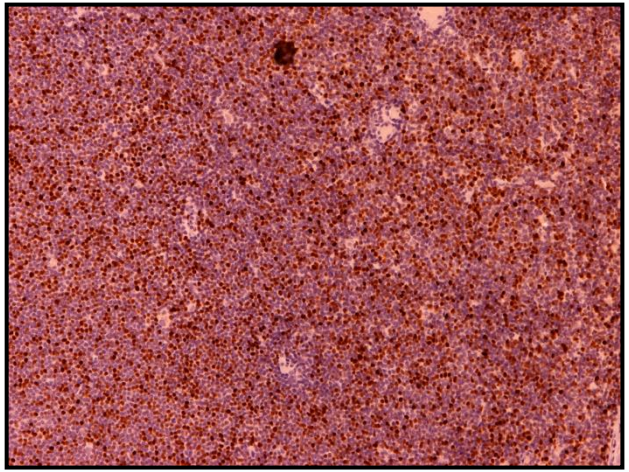
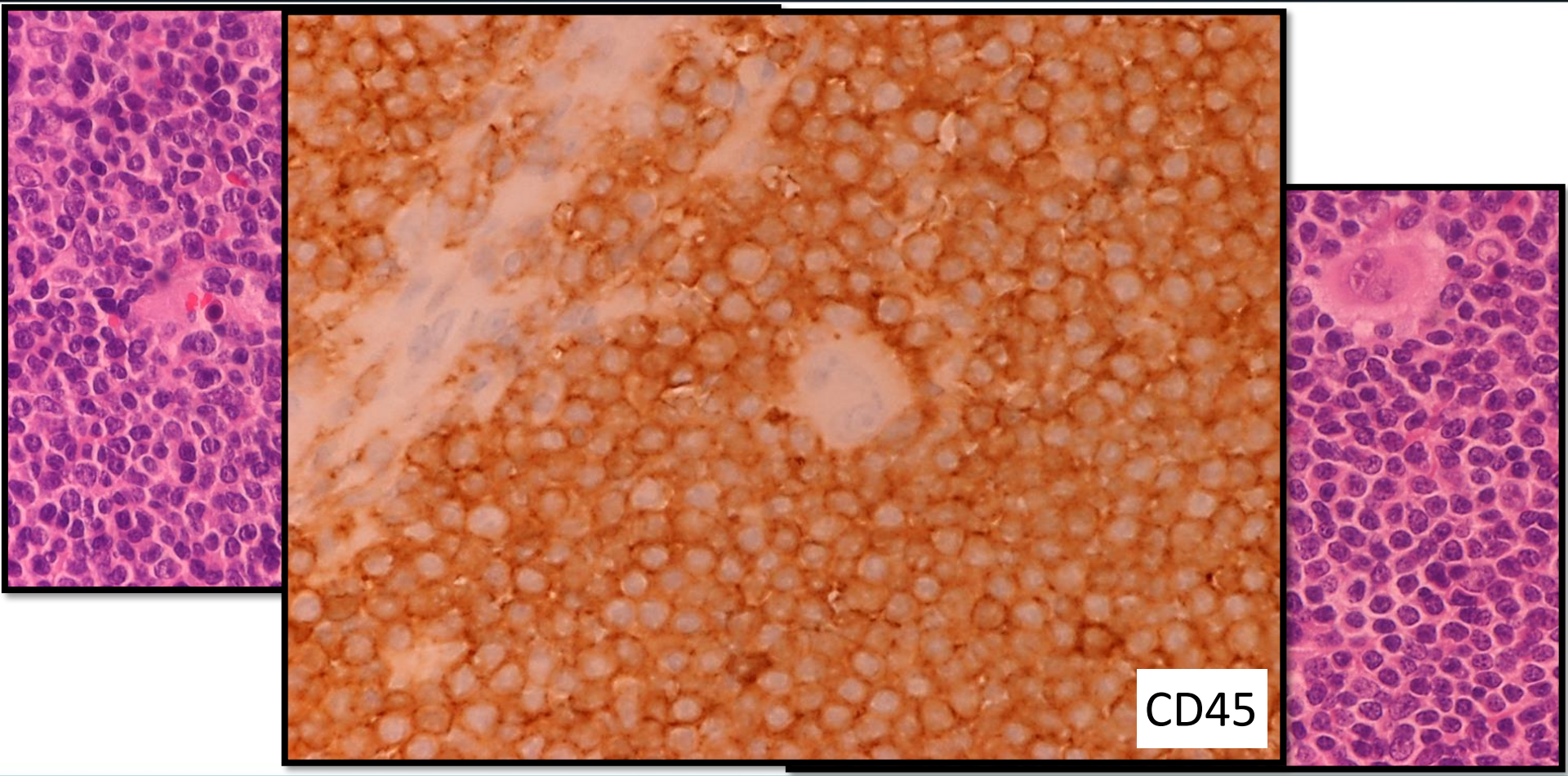
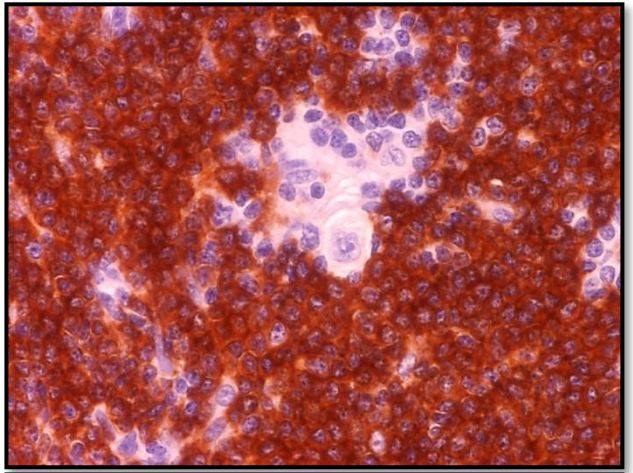


MIB1


CD45



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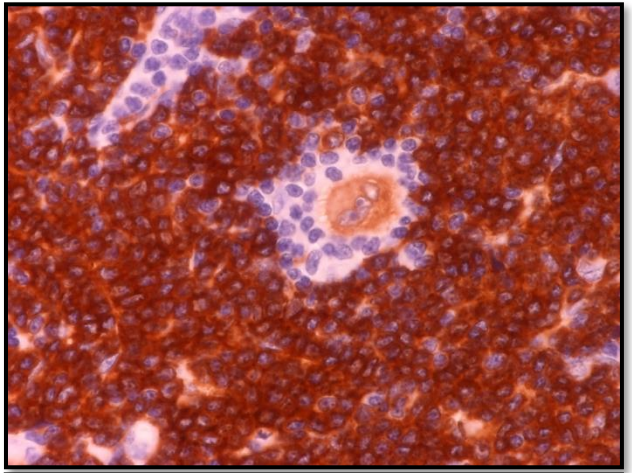

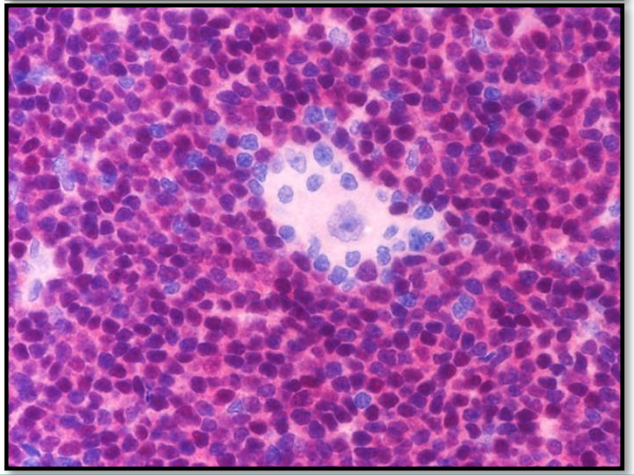

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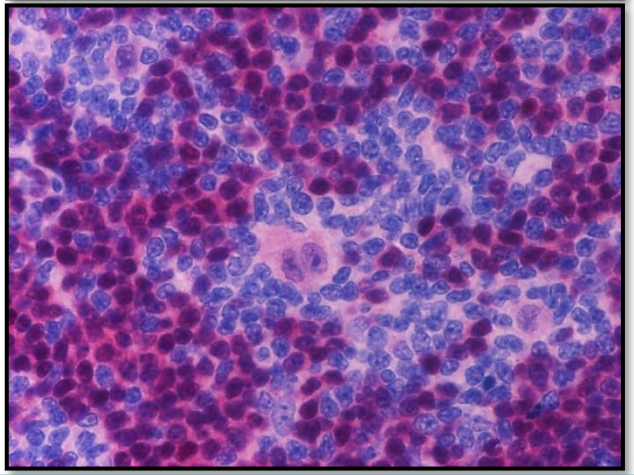
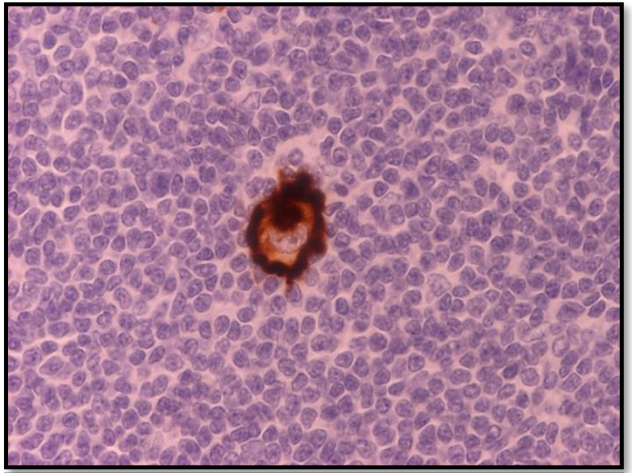
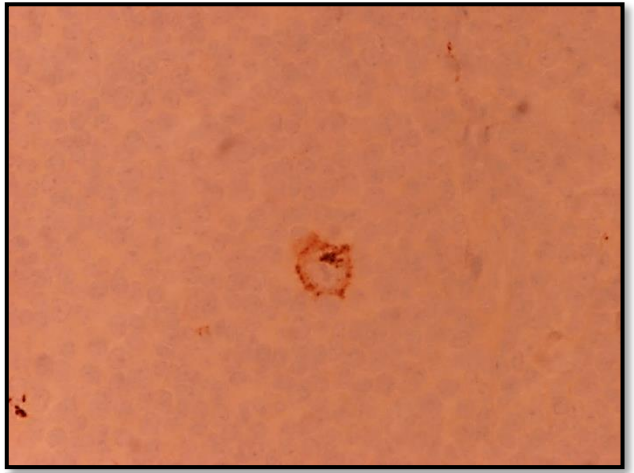


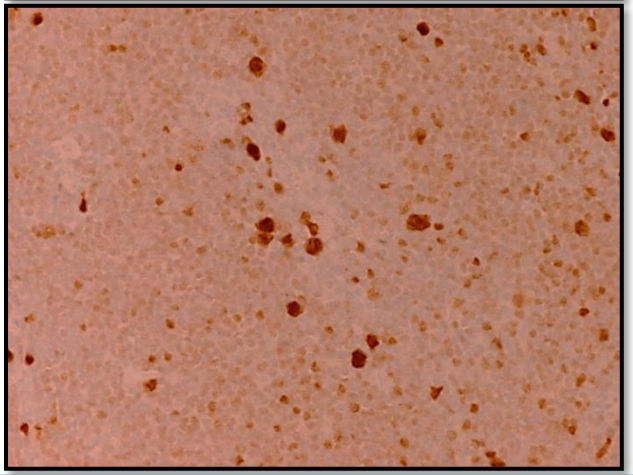
CD30



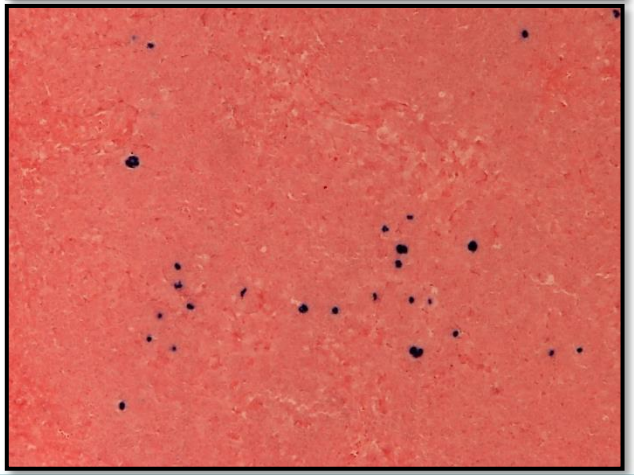
CD15



MUM1



EBER



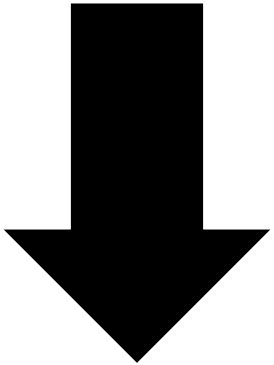
MCL (classic variant) and EBV+ HRS-like cells in Immune Deficiency and Dysregulation (IDD)?

vs

COMPOSITE LYMPHOMA: MCL and CHL?

MCL with t(11;14)

HRS-like cells traslocation not possible to assess



ABSENCE of characteristic cellular microenvironment (small lymphocytes, eosinophils, histiocytes, neutrophils, plasma cells)

MCL (classic variant) and EBV+ HRS-like cells in IDD

PET-CT

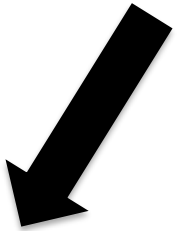
- bilateral laterocervical and axillary LAPs (bulky adenopathy in the right axillary region)
- mediastinal LAPs
- multiple and bulky abdominal LAPs

bone marrow biopsy and aspiration
negative for lymphoma

TREATMENT: six cycles of bendamustine and rituximab (BR)

PET-CT
partial metabolic response (PMR)
(right axillary LAPs)

two further cycles with rituximab



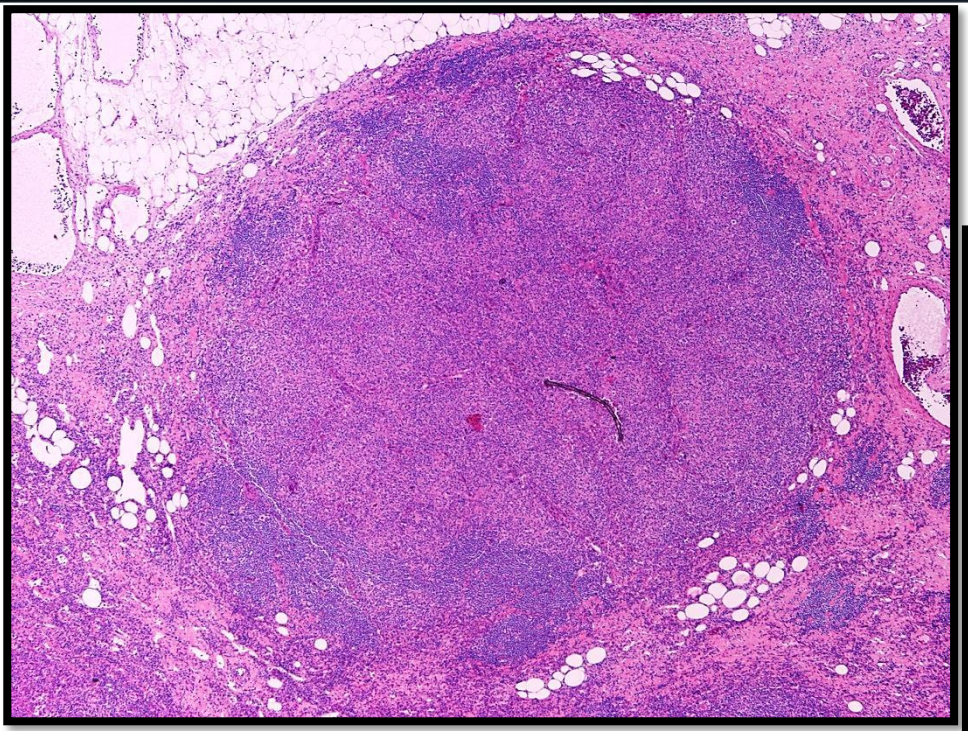
PET-CT
Progressive Metabolic Disease (PMD)

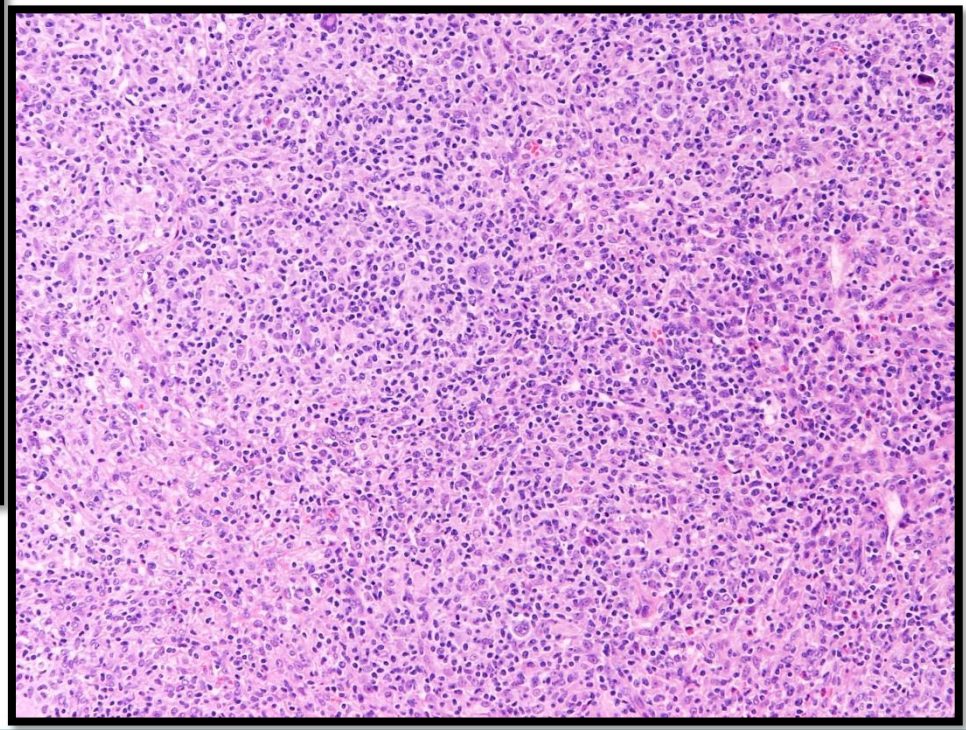
right axillary LAP

multiple abdominal LAPs

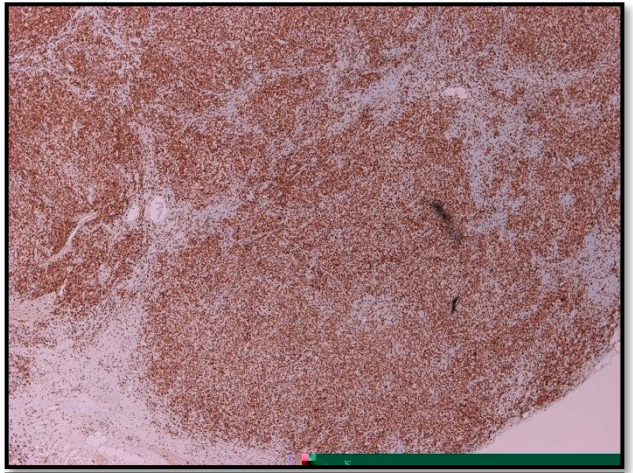
right axillary lymph node excisional biopsy

- multi-lobed LN of 4 cm maximum diameter
- flow cytometry: CD19+, CD20+, CD5+, CD200-, CD10-, CD38-, lambda light chain expression

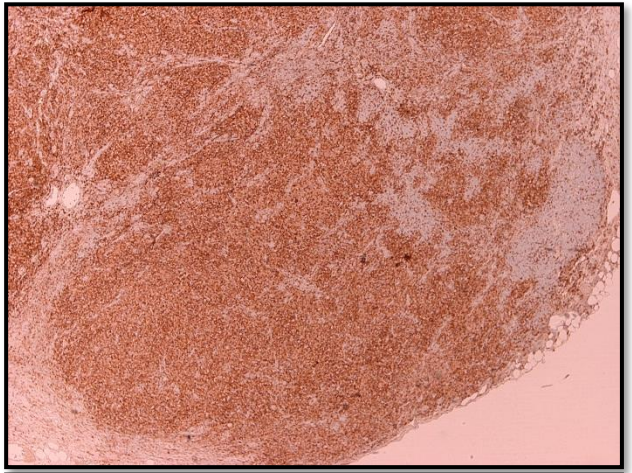




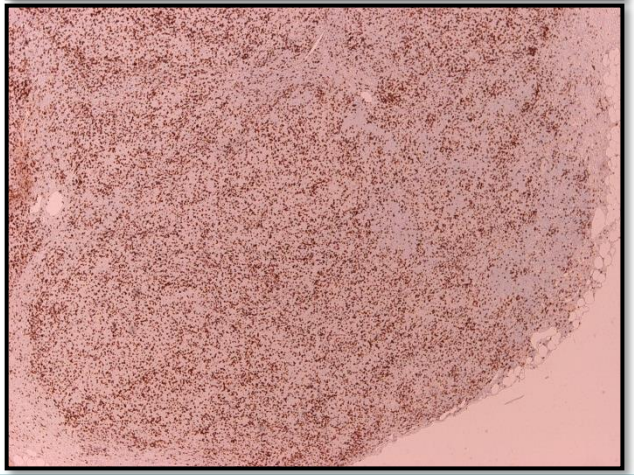
CD3



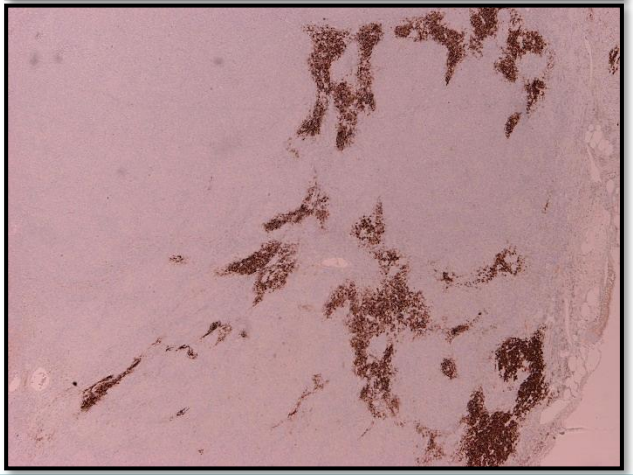
CD4



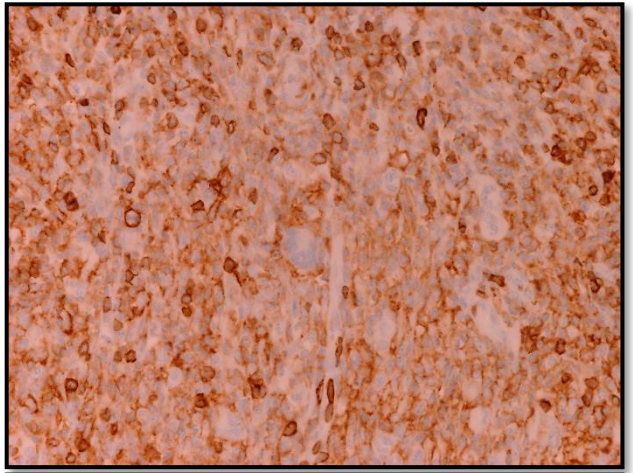
CD8



CD20



CD45



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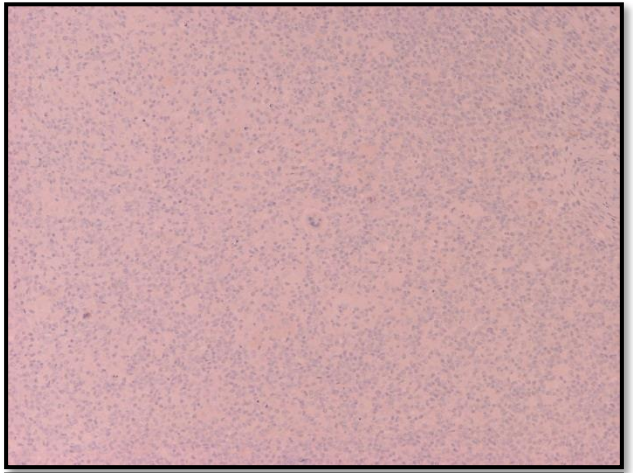
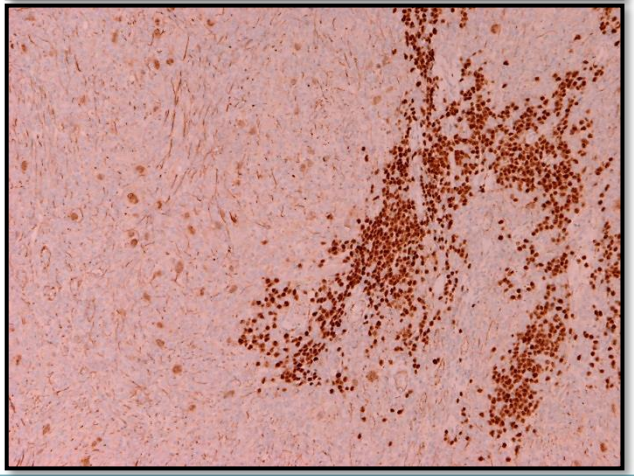
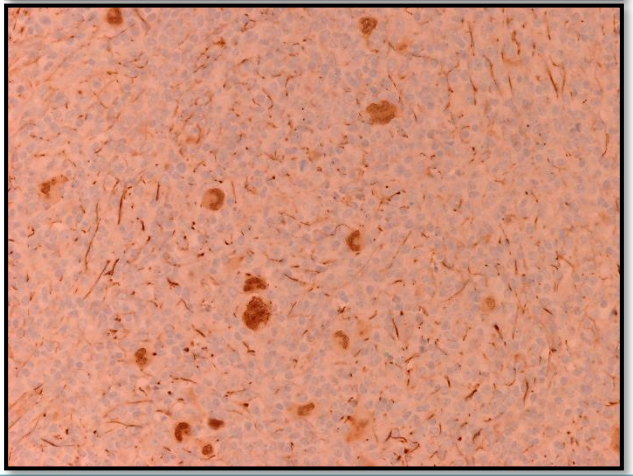


CD79a

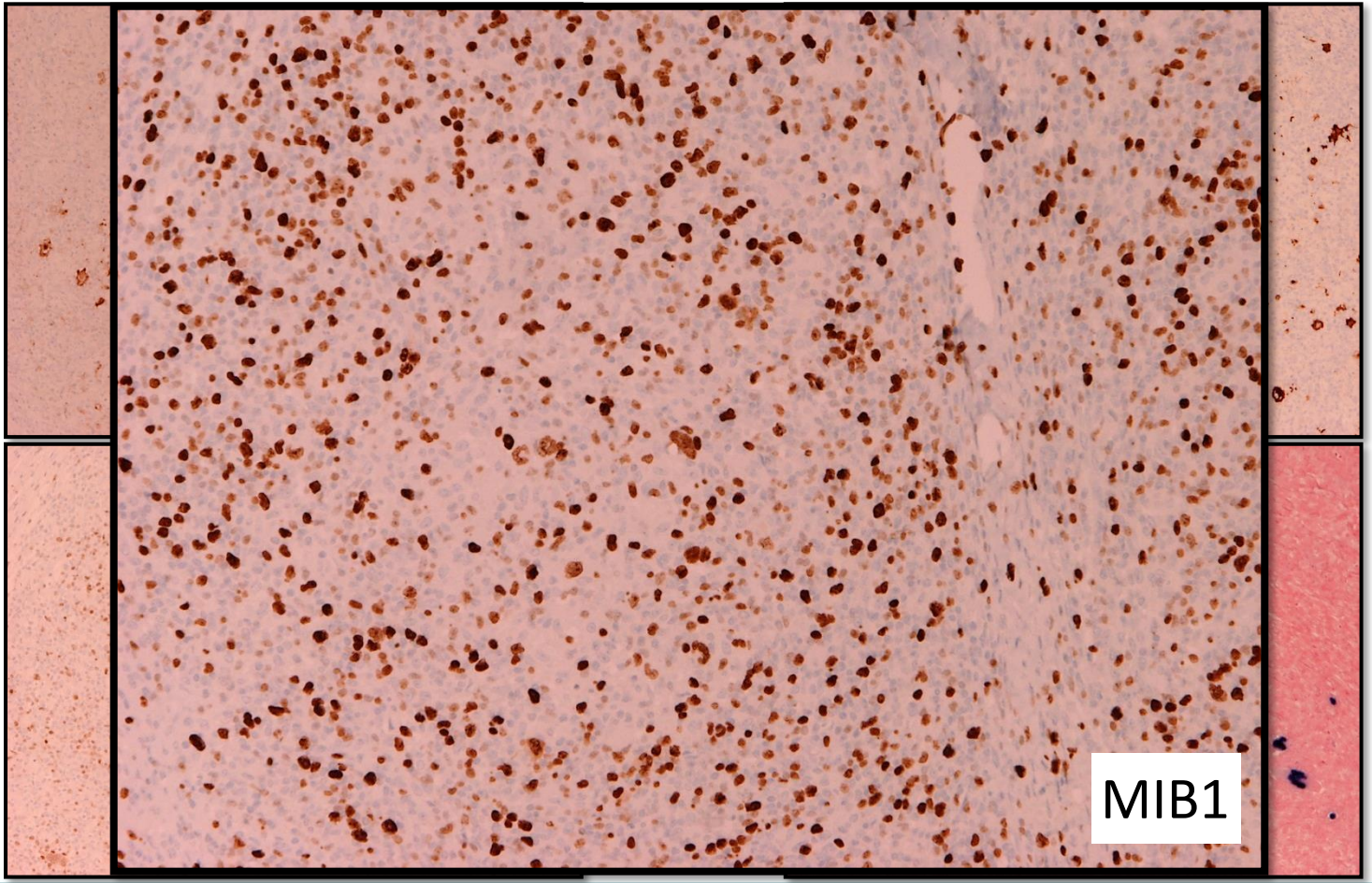


PAX5



CD30

CD15

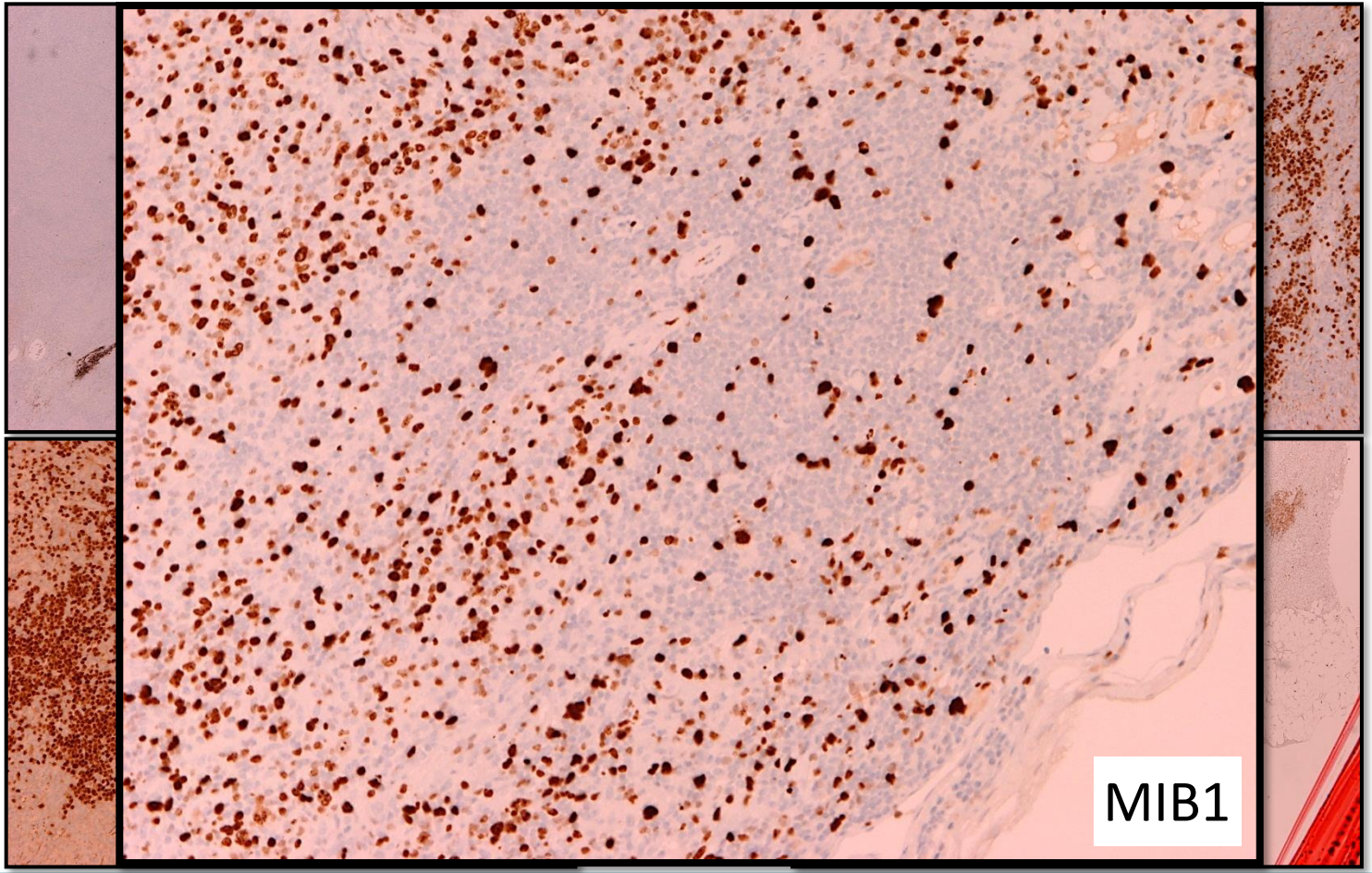


MUM1

EBER

CD20

CD79a



PAX5

BCL1

COMPOSITE LYMPHOMA

CHL absence of t(11;14)

CHL, nodular sclerosis

+

MCL

MCL with t(11;14)

FIRST-LINE TREATMENT FOR ADVANCED-STAGE cHL

B-AVD

(**B**rentuximab - **A**driamycin, **V**inblastine, **D**acarbazine)

COMPOSITE LYMPHOMA

- first described by Philip Custer in 1954 as *two or more distinct lymphomas that occur in the same patient*
- definition refined by Kim et al. in 1977 as *simultaneous occurrence of more than one type of lymphoma in the same organ or tissue*
- definition commonly accepted today is the one given by Küppers et al. in 2014: ***concurrent or sequential occurrence of two or more distinct types of lymphoma in the same anatomical location or tissue***

COMPOSITE LYMPHOMA

- rare
- combination of MCL and cHL is extremely rare: only few cases reported in the literature

Review > Pathol Oncol Res. 2023 Mar 17:29:1611051. doi: 10.3389/pore.2023.1611051. eCollection 2023.

Case report: Composite mantle cell lymphoma and classical Hodgkin lymphoma

Hongyu Wang [1], Liqun Yang [2], Qiuyao Li [1], Haiyun Song [1], Hong Ji [1]

Case Reports > Cureus. 2023 Sep 21;15(9):e45727. doi: 10.7759/cureus.45727. eCollection 2023 Sep.

Composite Classical Hodgkin Lymphoma and Mantle Cell Lymphoma: A Case Report

Rajdeep Kaur [1], Bingjun Zhang [2], Kuixing Zhang [3], Mohamed Eldaly [1], Jincy Clement [1]

COMPOSITE LYMPHOMA

- origin is still unclear
- chance occurrence or common origin?
- if two distinct lymphomas derive from a common precursor, it is likely that the latter carried shared genetic lesions but also carry distinct genetic lesions explaining the distinct histopathology of the lymphomas

Case Reports > N Engl J Med. 1999 Apr 22;340(16):1239-47.
doi: 10.1056/NEJM199904223401604.

Identification of common germinal-center B-cell precursors in two patients with both Hodgkin's disease and non-Hodgkin's lymphoma

A Bräuninger [1], M L Hansmann, J G Strickler, R Dummer, G Burg, K Rajewsky, R Küppers

Case Reports > J Clin Oncol. 1999 Dec;17(12):3804-9. doi: 10.1200/JCO.1999.17.12.3804.

Classical Hodgkin's disease and follicular lymphoma originating from the same germinal center B cell

T Marafioti [1], M Hummel, I Anagnostopoulos, H D Foss, D Huhn, H Stein

Case Reports > Int J Cancer. 2014 Feb 15;134(4):832-43. doi: 10.1002/ijc.28422.
Epub 2013 Aug 29.

Subclonal evolution of a classical Hodgkin lymphoma from a germinal center B-cell-derived mantle cell lymphoma

Stefanie Schneider [1], Barbara Crescenzi, Markus Schneider, Stefano Ascani, Sylvia Hartmann, Martin-Leo Hansmann, Brunangelo Falini, Cristina Mecucci, Enrico Tiacci, Ralf Küppers

Review > Cancers (Basel). 2022 Nov 19;14(22):5695. doi: 10.3390/cancers14225695.

Plasticity in Classical Hodgkin Composite Lymphomas: A Systematic Review

Alexis Trecourt [1 2], Marie Donzel [1 3 4], Juliette Fontaine [1], Hervé Ghesquières [3 4 5], Laurent Jallade [3 4 6], Gabriel Antherieu [5], Camille Laurent [7], Claire Mauduit [1 3 8], Alexsandra Traverse-Glehen [1 3 4]

Case Reports > Mol Med. 2001 May;7(5):285-92.

Common germinal-center B-cell origin of the malignant cells in two composite lymphomas, involving classical Hodgkin's disease and either follicular lymphoma or B-CLL

R Küppers [1], A B Sousa, A S Baur, J G Strickler, K Rajewsky, M L Hansmann

COMPOSITE LYMPHOMA

> Leukemia. 2025 Aug;39(8):1960-1971. doi: 10.1038/s41375-025-02549-y. Epub 2025 May 22.

Common origin and somatic mutation patterns of composite lymphomas and leukemias

Victoria Berg [# 1], Anna Lollies [# 1 2], Markus Schneider [1 3], Patricia Johansson [1 4], Marc A Weniger [1], Emma Albertini [5], Fabio Facchetti [5], Stefano Ascani [6], Abubakar Moawia [7], Susanne Bens [7], Anja Fischer [7], Reiner Siebert [7], Wolfram Klapper [8], Luisa Lorenzi [5], Enrico Tiacci [9], Sylvia Hartmann [10], Bettina Budeus [1], Martin-Leo Hansmann [11], Ralf Küppers [12 13]

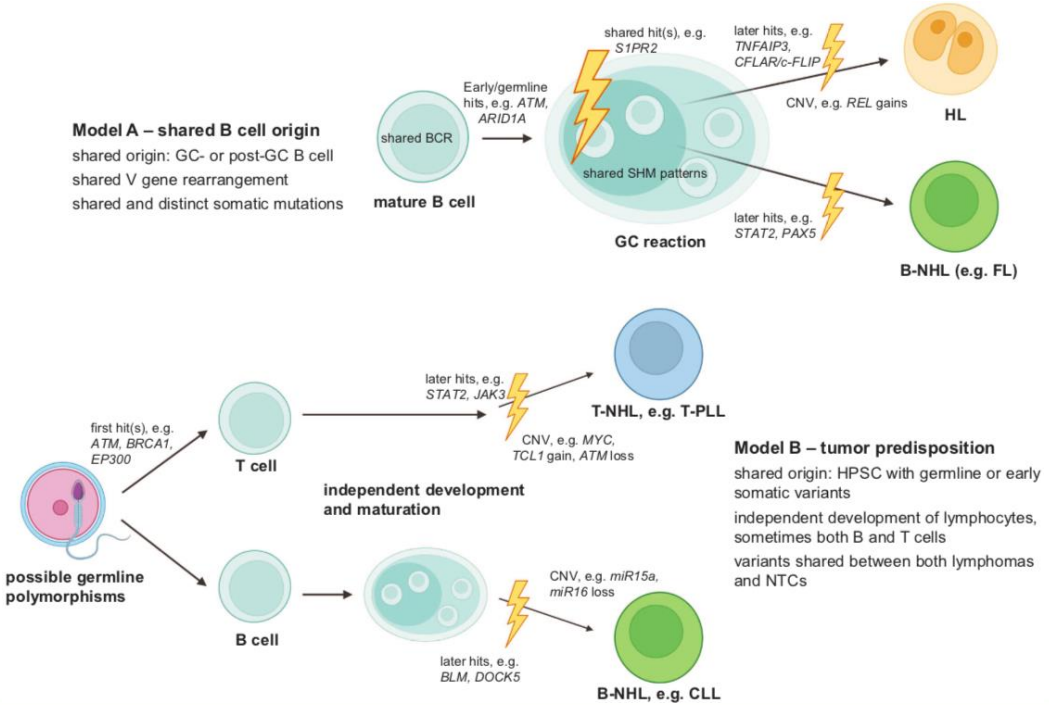
Composite lymphomas consisting of a cHL and another B-cell lymphoma are frequently clonally related and derive from GC-experienced B cells

- shared somatic mutations drive tumorigenesis
- distinct somatic mutations determine the lymphoma type

Case	Lymphoma/leukemia	Age at diagnosis (years)	Gender	Concurrent or sequential	Tissue	Markers of tumor cells
1	HL and CLL	70	Male	Concurrent[a]	Lymph node (HL and CLL)	HRS cells: CD30$^+$, CD20$^-$, CD3$^-$, PAX5$^+$, EBV$^+$
						CLL cells: CD20$^+$, CD5$^+$, CD23$^+$, CD30$^-$
2	HL and SMZL	67 (SMZL),	Male	Sequential	Lymph node (HL), spleen (SMZL)	HRS cells: CD30$^+$, CD15$^-$, PAX5$^+$, CD20$^-$, EBV$^-$
		70 (HL)				SMZL cells: CD20$^+$, CD5$^-$, CD23$^-$, CCND1$^-$
3	HL and MCL	85	Female	Concurrent	Lymph node (HL and MCL)	HRS cells: CD30$^+$, CD19$^-$, CD20$^-$, PAX5^{weak}, CD5$^-$, CD45$^-$, CCND1$^-$, EBV$^-$, *CCND1::IGH* translocation
						MCL cells: CD45$^+$, CD19$^+$, CD20$^+$, CD5$^+$, CCND1$^+$, SOX11$^-$, CD30$^-$, *CCND1::IGH* translocation
4	HL and FL	61 (FL),	Female	Sequential	Lymph node (HL and FL)	HRS cells: CD30$^+$, CD15$^{+/-}$, CD20$^-$, EBV$^-$
		64 (HL)				FL cells: CD20$^+$, BCL6$^+$, CCND1$^-$, BCL2$^{+/-}$, CD10$^{+/-}$
5	CLL and T-PLL	77	Female	Concurrent[b]	PBL	CLL cells: CD19$^+$, CD5$^+$, CD23$^+$, Igκ$^+$
						T-PLL cells: CD3$^+$, CD4$^+$, CD5$^+$, CD8$^-$
6	PCL and ALCL	73	Female	Concurrent[c]	PBL	PCL cells: CD38$^+$, CD138$^+$, cyIgλ$^+$
						ALCL cells: CD3$^+$, CD4$^+$, CD30$^+$, CD52$^+$, ALK$^-$

[a]First CLL diagnosis 2 years earlier.
[b]First, the CLL was diagnosed, and four months later both leukemias concurrently.
[c]PCL first diagnosed two years earlier.

COMPOSITE LYMPHOMA



Grazie dell'attenzione