

La **DIAGNOSTICA** **EMATOPATOLOGICA** nell'ERA della **MEDICINA** di **PRECISIONE**

Cutaneous blastoid infiltrate: a diagnostic challenge

Cosimo Custoza

Dirigente medico U.O.C Anatomia patologica

Ospedale S. Donato-S.O. Arezzo

Dipartimento oncologico, Azienda UsI Toscana Sudest

Clinical Presentation

Patient: 55-year-old man

Medical History:

- NHL diagnosed 6 years ago

Presenting Symptoms:

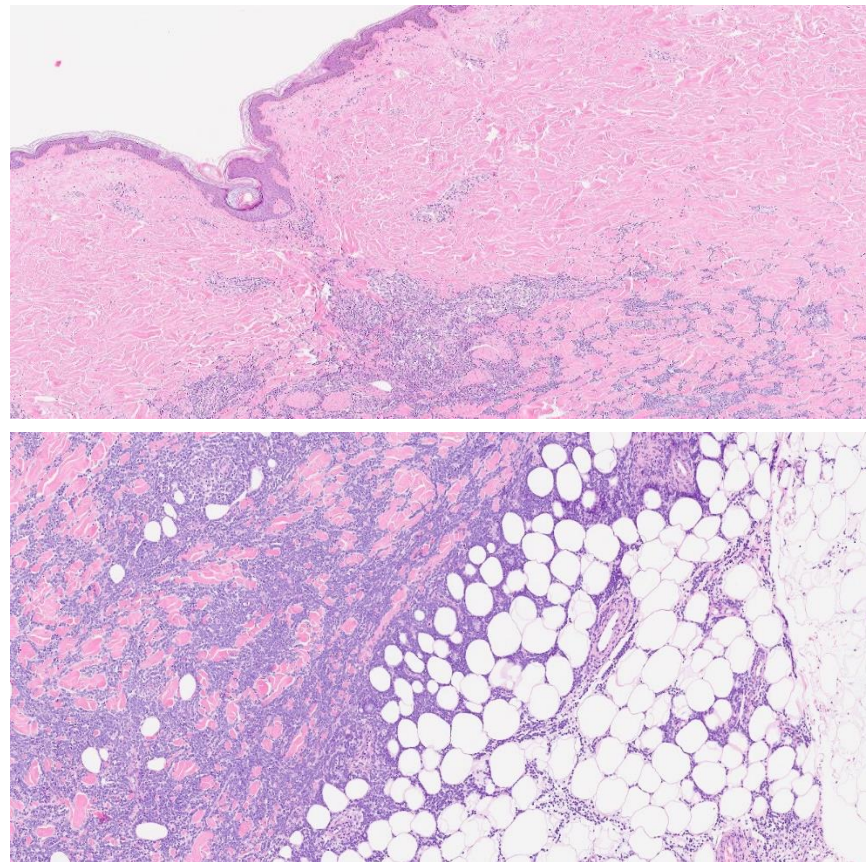
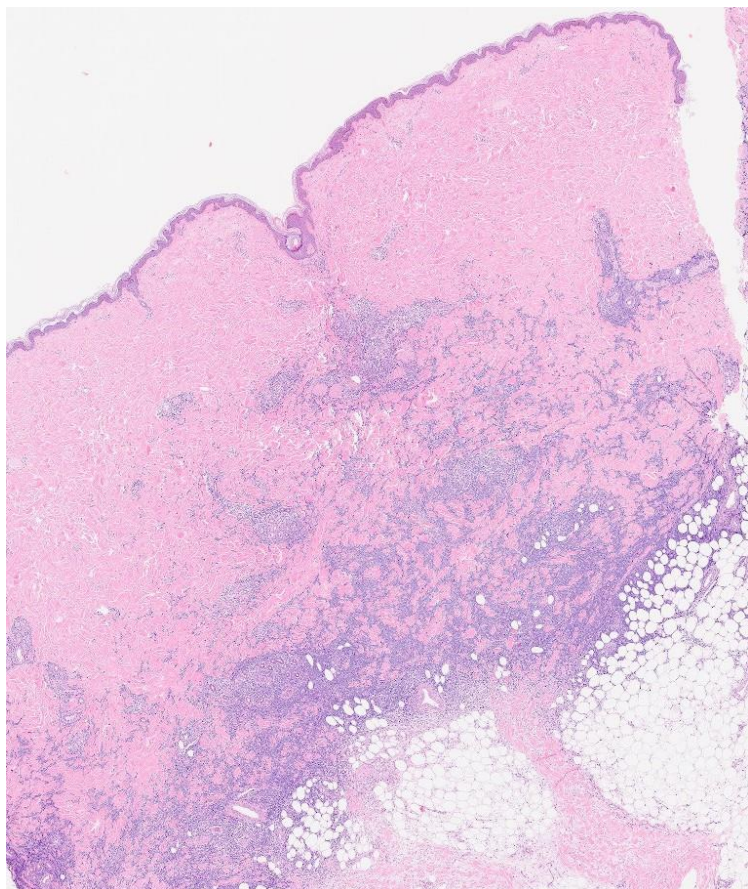
- Abdominal pain
- Nausea
- Vomiting

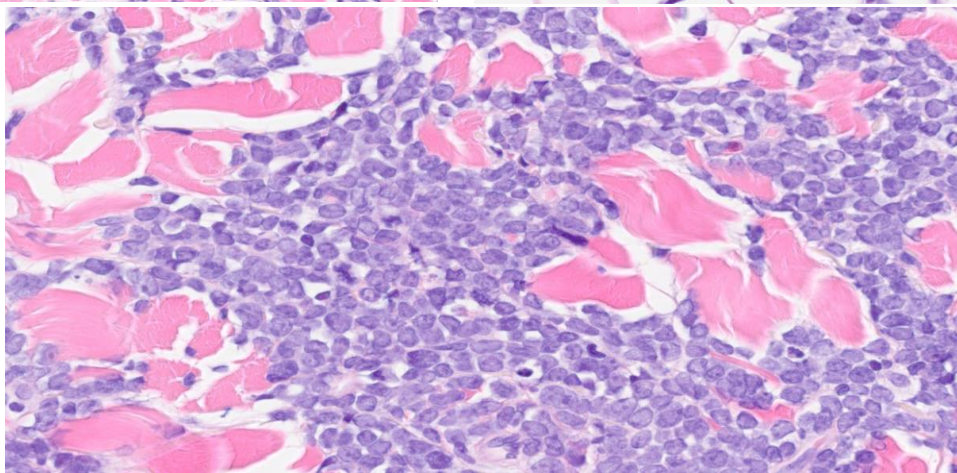
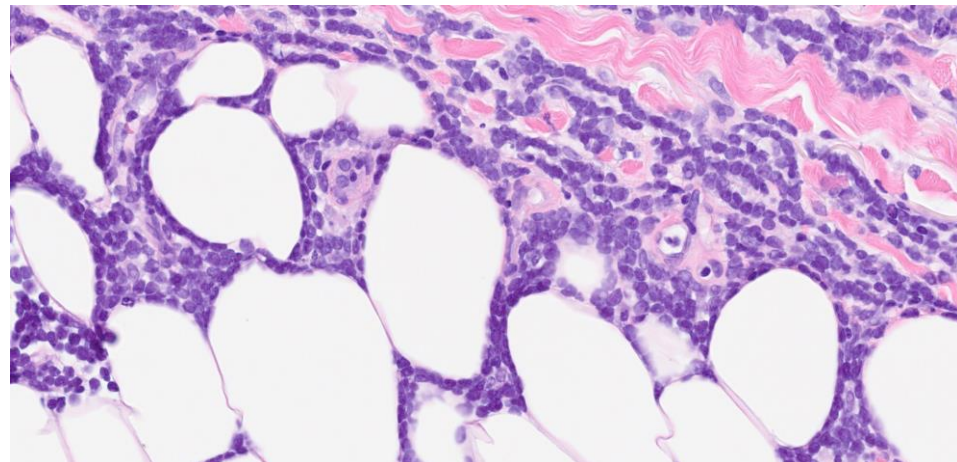
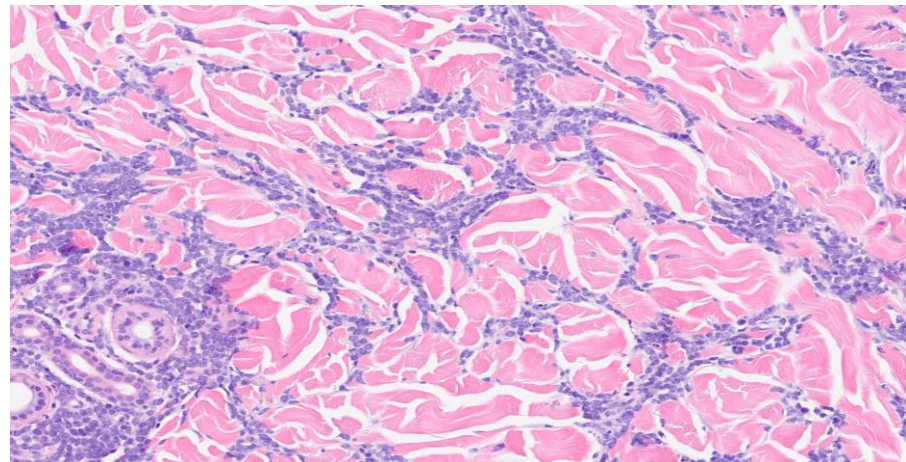
Imaging Findings (CT scan):

- Hepatosplenomegaly
- Multiple lymphadenopathies

Additional Finding:

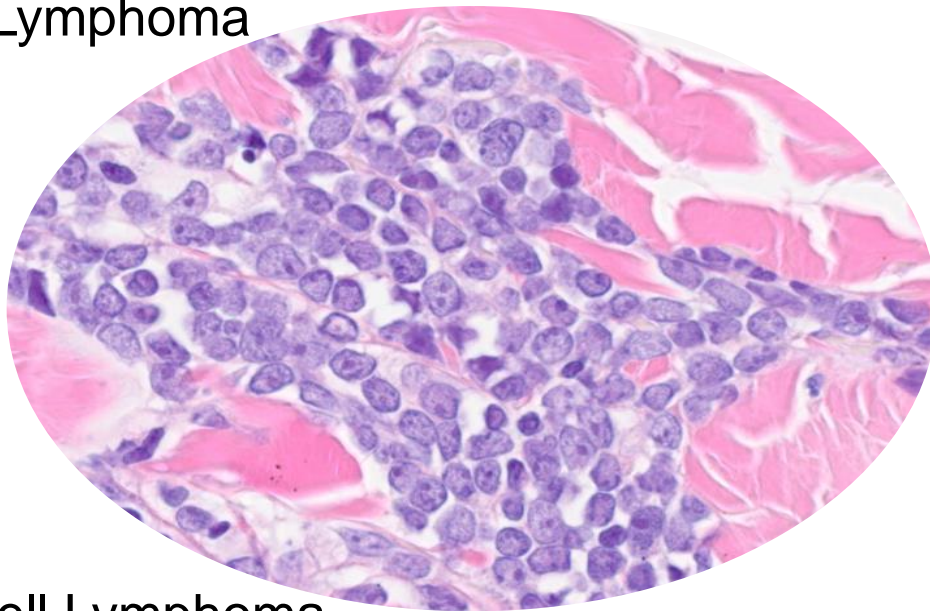
- Laterocervical CNB : *MZL/FL to be confirm on LN excision*
- Paraumbilical subcutaneous lesion → Biopsied





Blastic Plasmacytoid Dendritic Cell Neoplasm

Lymphoblastic Lymphoma

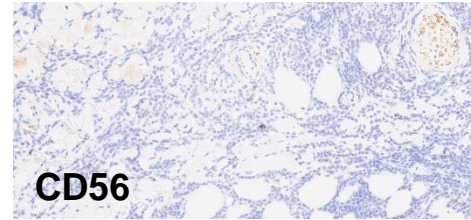
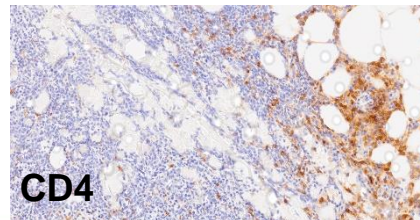
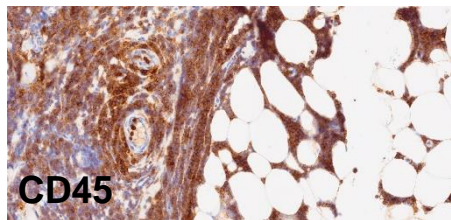
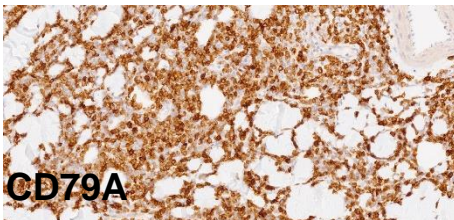
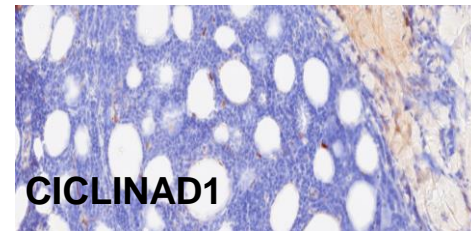
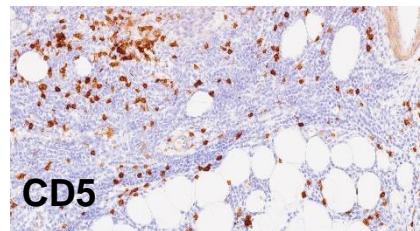
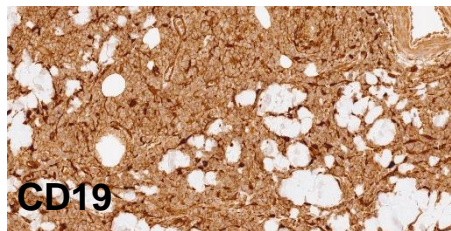
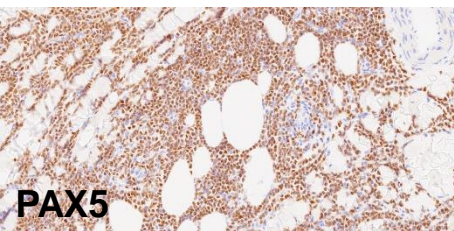
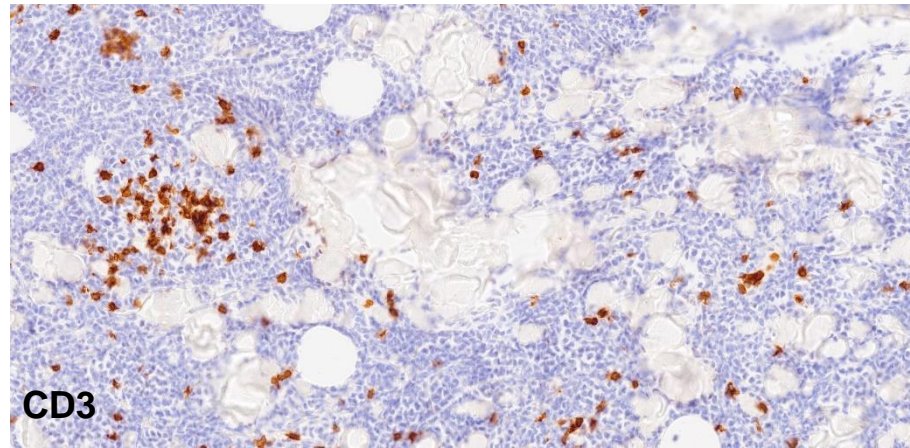
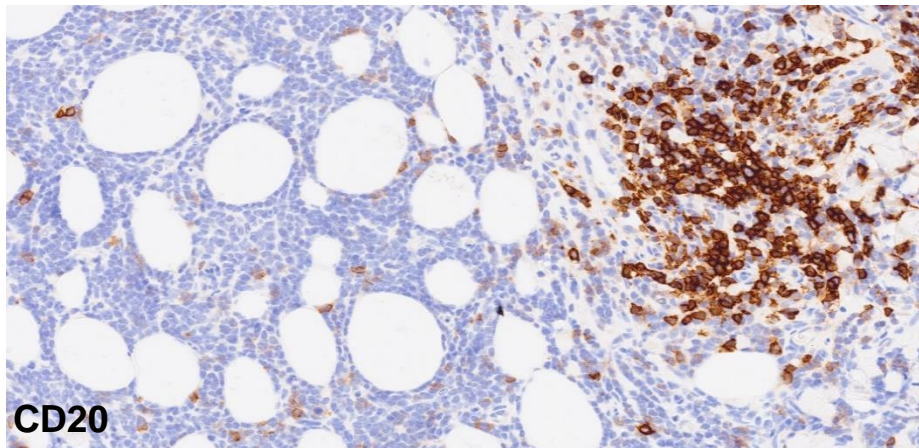


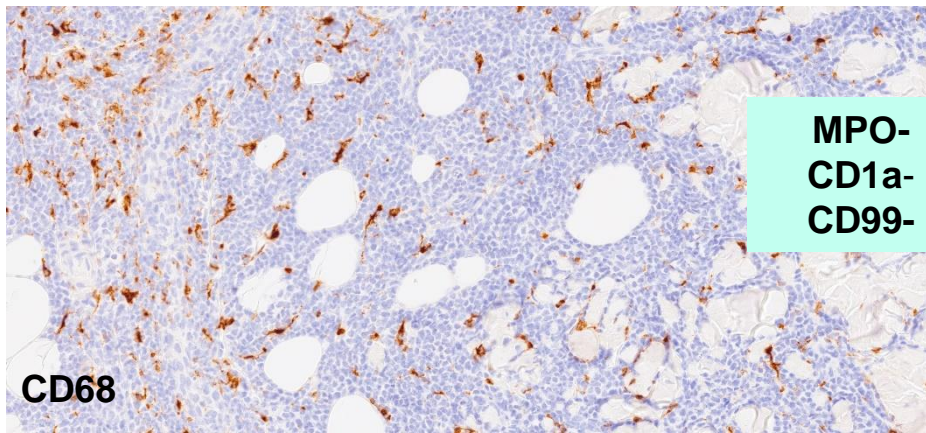
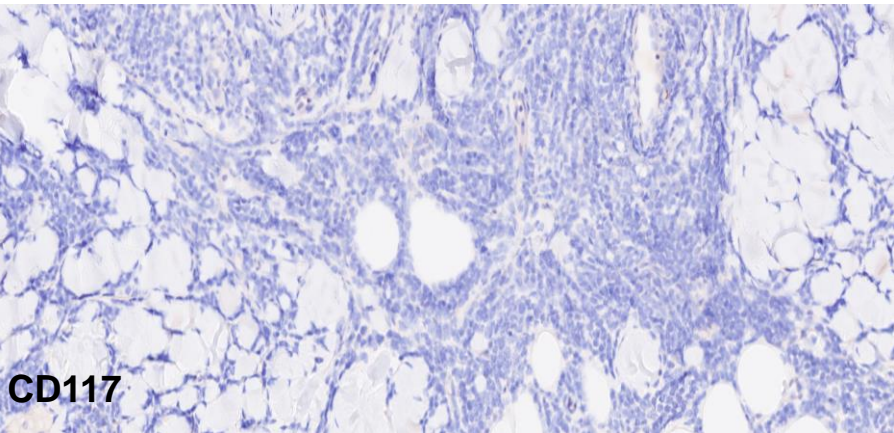
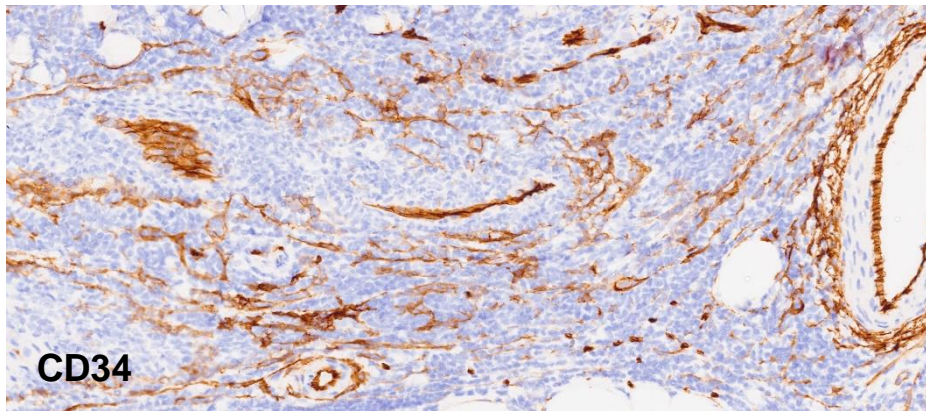
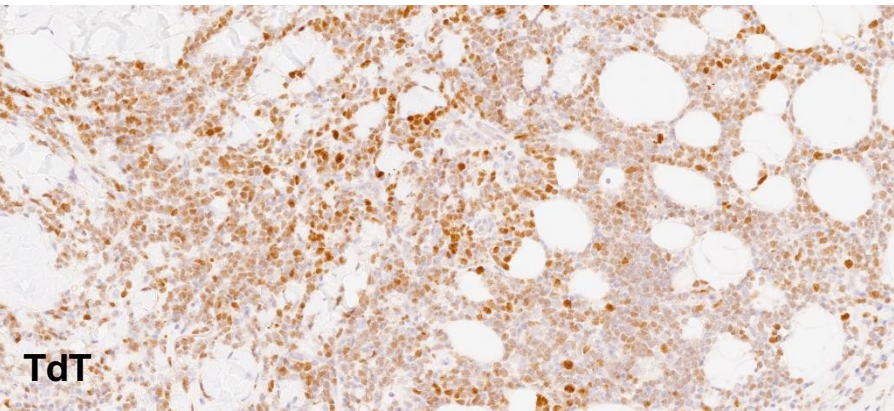
Acute Myeloid Leukemia

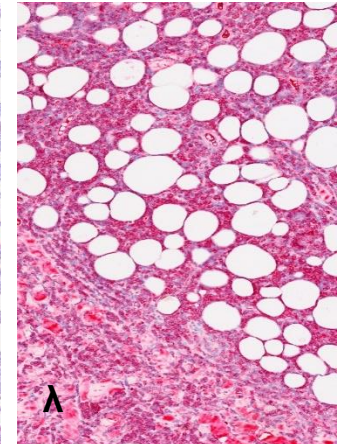
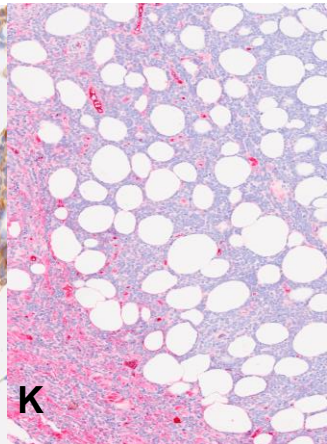
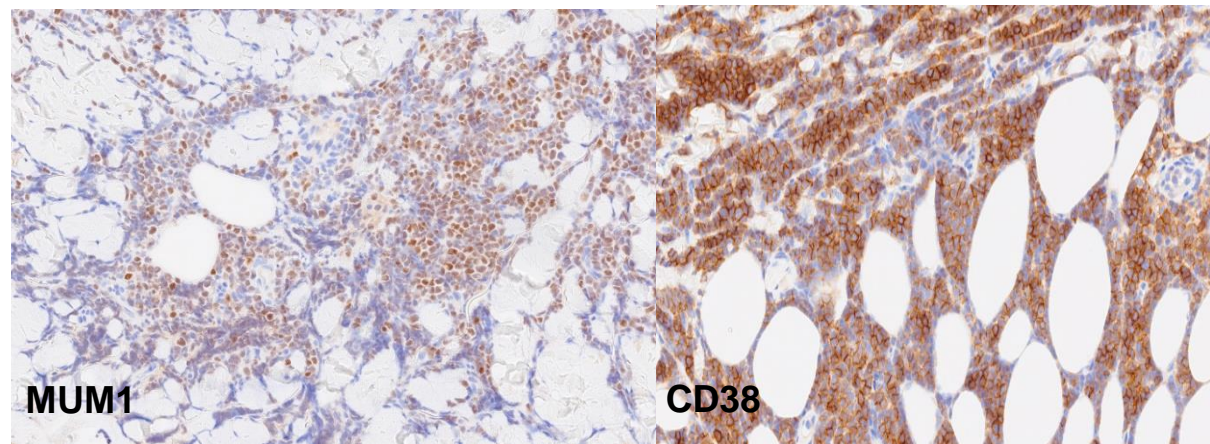
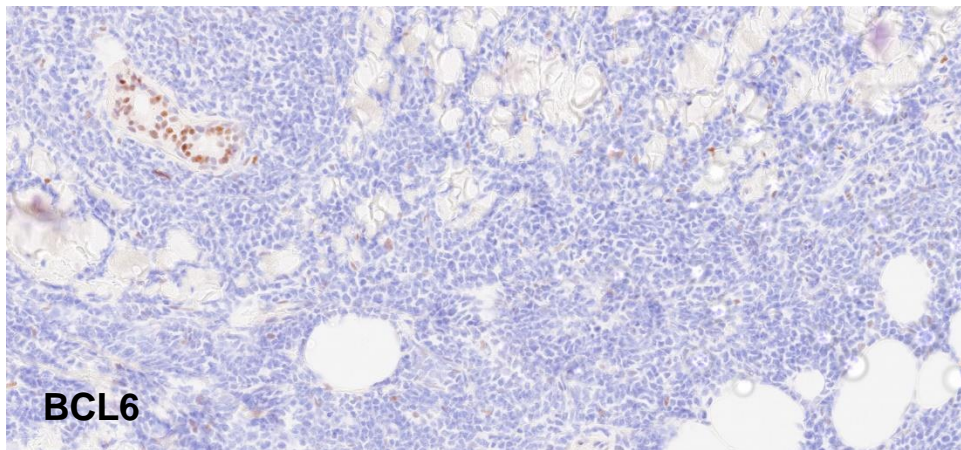
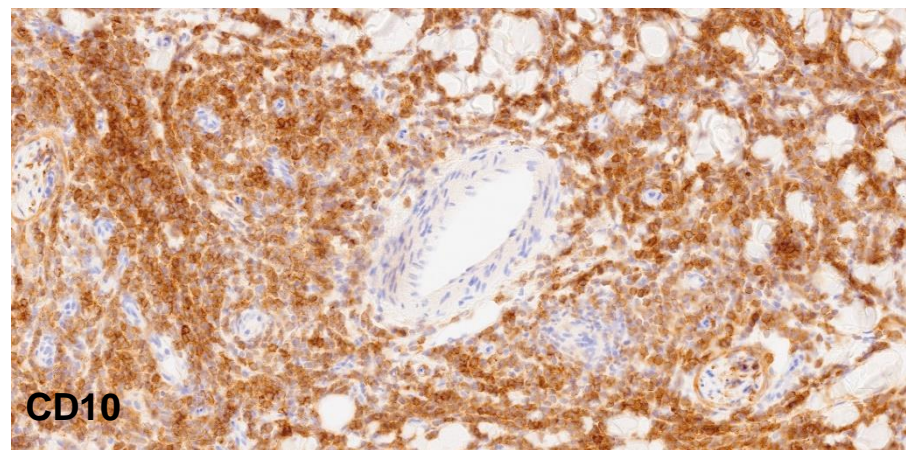
High-grade B cell Lymphoma

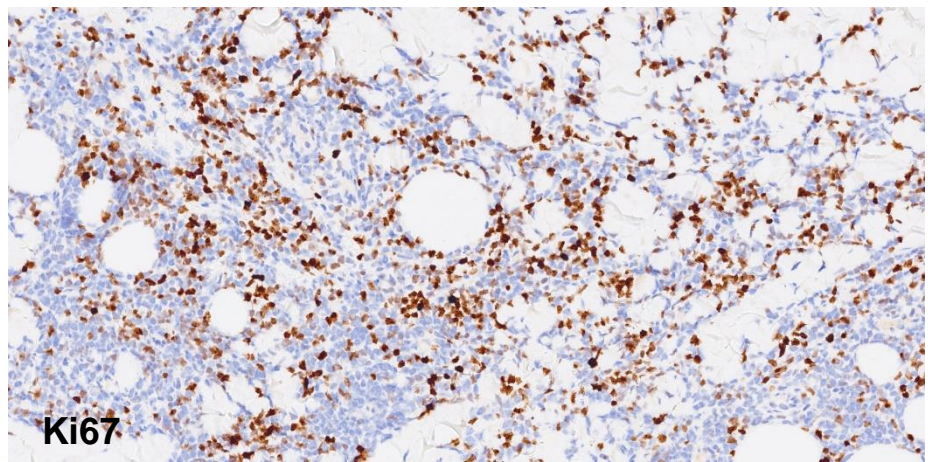
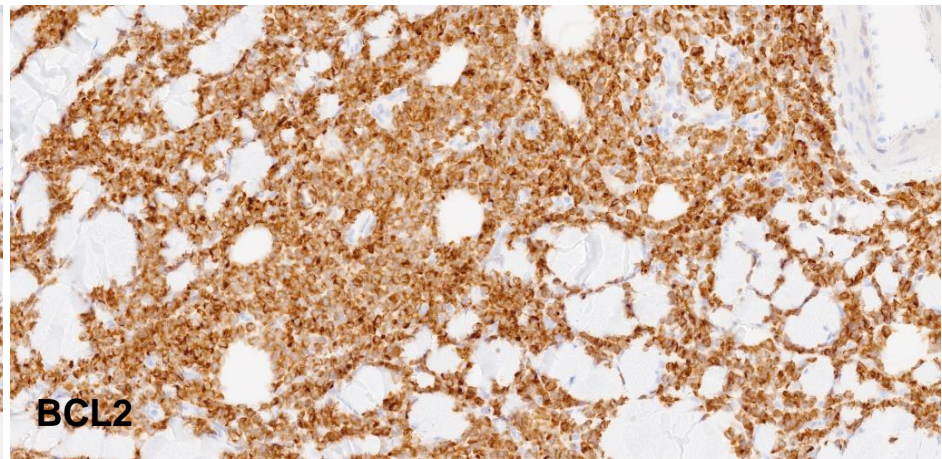
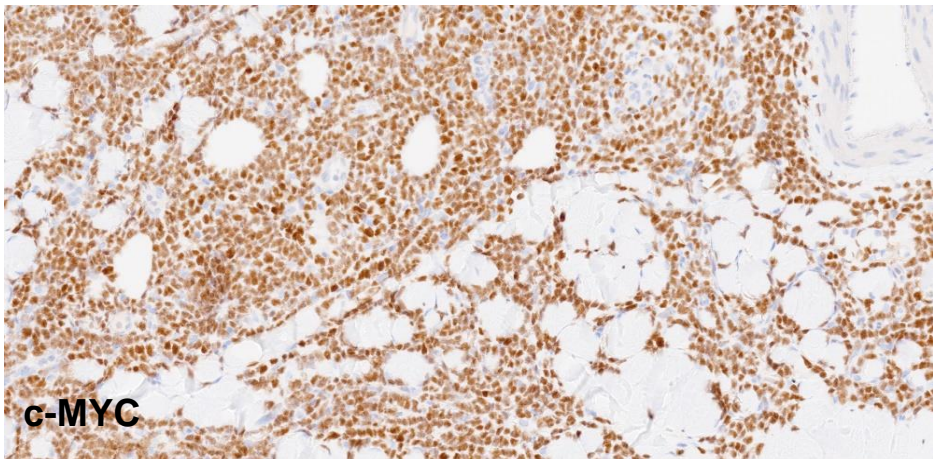
Blastoid Mantle Cell Lymphoma

IMMUNOHISTOCHEMISTRY









B Lymphoblastic lymphoma

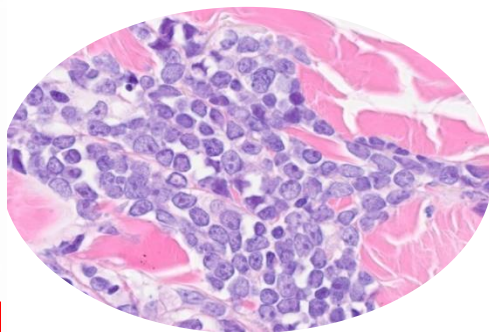
Immunophenotypic features supporting the differential diagnosis

Marker	Present case	Differential diagnostic implication
PAX5, CD19, CD79a	positive	non-discriminant
CD10	positive	non-discriminant
BCL2	positive	non-discriminant
MYC	positive	non-discriminant
TdT	positive	favors B-lymphoblastic lymphoma
CD20	negative	favors B-lymphoblastic lymphoma
BCL6	negative	favors B-lymphoblastic lymphoma
CD34	negative	favors high-grade B-cell lymphoma
CD38	positive	favors high-grade B-cell lymphoma
MUM1	positive	favors high-grade B-cell lymphoma
Light chains	restricted	favors high-grade B-cell lymphoma

High-grade B-cell lymphoma

Blastic plasmacytoid dendritic cell neoplasm

CD4 / CD56/ CD123



Acute myeloid leukemia

CD117 / CD34 / CD68/ MPO



Blastoid mantle cell lymphoma

CD5/ Cyclin D1



FISH analysis

Performed at Pathology Lab AOU Senese

IgH::BCL2: positive

BCL6 BA: negative

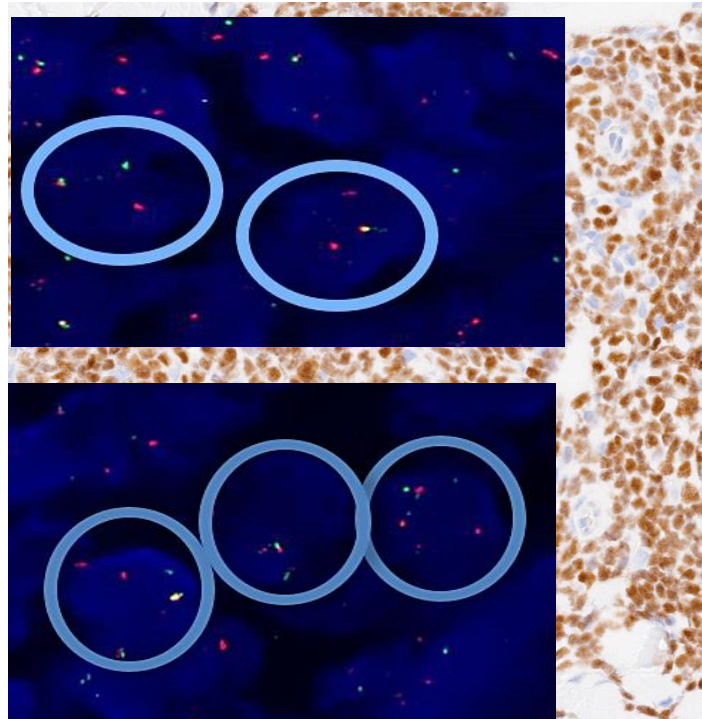
MYC BA: negative

IgH::MYC: negative

IgK::MYC*: negative

IgL::MYC*: positive

* Courtesy of Prof.Siebert



Double Hit

NGS results

Performed at Pathology Lab AOU Senese

Targeted NGS mutation profiling

Gene	cDNA	Protein	NM	VAF (%)	Pathogenic score
CDKN2A	c.330G>A	p.Trp110*	NM_000077.5	39	P
CREBBP	c.1270C>T	p.Arg424*	NM_004380.3	33.7	P
TET2	c.162G>A	p.Trp54*	NM_001127208.2	32.6	P

CREBBP mutations are recurrent epigenetic alterations in germinal center-derived lymphomas, particularly follicular lymphoma. No recurrent alterations typical of precursor B-cell neoplasms were identified.

► *Histopathology*. 2024 Nov 15;86(1):94–105. doi: [10.1111/his.15350](https://doi.org/10.1111/his.15350)

Evolving molecular classification of aggressive B-cell lymphoma

[Stefan K Aljig](#)¹, [Björn Chapuy](#)^{2,3}, [Daisuke Ennishi](#)³, [Kieron Dunleavy](#)⁴, [Daniel J Hodson](#)⁵

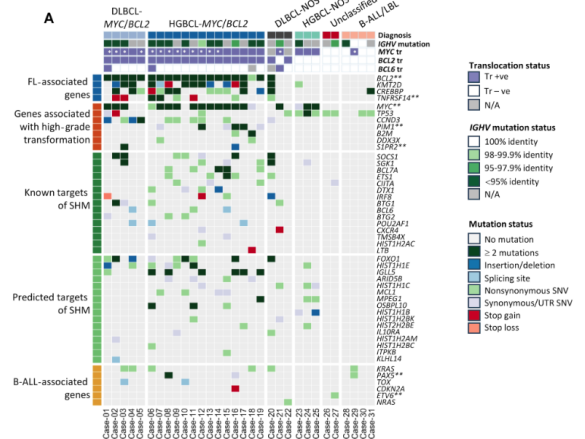
DLBclass	LymphGen	HMRN	Landmark Alterations	COO Enrichment
C1	BN2	NOTCH2	<i>BCL6</i> SV, <i>NOTCH2</i> , <i>SPEN</i> , <i>CD70</i> , <i>BCL10</i> , <i>TNFAIP3</i>	ABC, unclass
C2	A53	-	Biallelic <i>TP53</i> inactivation, aneuploidy	ABC, GCB
C3	EZB EZB-MYC+	BCL2 BCL2-MYC	<i>BCL2</i> SV, <i>EZH2</i> , <i>CREBBP</i> , <i>KMT2D</i> , <i>TNFSF14</i>	GCB
C4	ST2	TET2/SGK1 SOCS1/SGK1	<i>SGK1</i> , <i>TET2</i> , <i>KLHL6</i> , <i>BRAF</i> <i>SGK1</i> , <i>TET2</i> , <i>SOCS1</i> , <i>CD83</i> , <i>NFKBIA</i> , <i>NFKBIE</i> , <i>STAT3</i>	GCB
C5	MCD	MYD88	<i>MYD88</i> ^{L265P} , <i>CD79B</i> , <i>PIM1</i> , <i>TBL1XR1</i> , <i>ETV6</i>	ABC
-	N1	NOTCH1	<i>NOTCH1</i> , <i>ID3</i>	ABC

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([wileyonlinelibrary.com](https://www.wileyonlinelibrary.com)) DOI: 10.1002/path.6476

ORIGINAL ARTICLE

Mutation profiling in differential diagnosis between Td⁺-positive high-grade/large B-cell lymphoma and B-lymphoblastic leukaemia/lymphoma

Maria-Myrtsini Tzioti¹, Francesco Cucco^{1,2}, Livia Rásó-Barnett¹, Zi Chen¹, Andrew Wotherspoon¹, Katrin S Kurz³, Ewelina Madaj⁴, Jasmine Makker⁵, Anna E Strazda¹, Fang Guo^{1,6}, Caoimhe Egan¹, Elizabeth Soilleux⁷, Liz Hook⁸, László Krenacs⁹, Julia T Coey⁹, Camille Laurent¹⁰, Luc Xerri¹¹, Lenaig Mescarni¹², Lukian Plank¹³, Lise Mette Rahbek Gjerdrum¹², Nicolas Lopez-Hijos¹⁴, Timothy Greiner¹⁵, Joseph Khoury¹⁶, Wolfram Klapper¹⁷, Ilse Oschlies¹⁸, Andreas Rosenwald¹⁹, German Ott²⁰ and Ming-Qing Du²¹ ✉

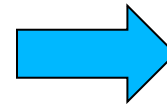


Based on:

- Previous History
- 55 years old patient
- CD34 negative
- Restricted light chain, MUM1+, CD38+
- C-MYC and BCL2 translocation
- CREBBP mutation



**High-grade B-cell lymphoma
with MYC and BCL2 rearrangements (double-hit)
and TdT expression (WHO 5TH Edition)**



BOM : negative
Therapy: POLA-R-CHP 3 cycle

Revaluation in progress

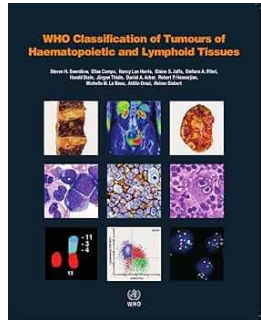
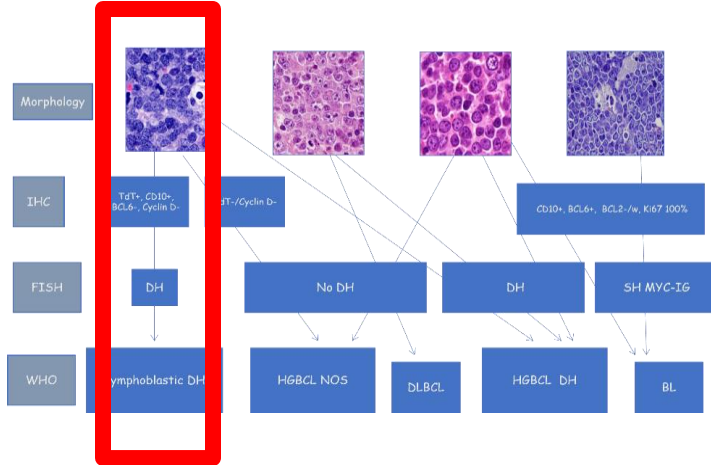
***De Novo MYC and BCL2 Double-hit B-Cell Precursor
Acute Lymphoblastic Leukemia (BCP-ALL) in
Pediatric and Young Adult Patients Associated With
Poor Prognosis***

Wei Liu,¹⁻² Shimin Hu,¹ Marina Konopleva,³ Joseph D. Khoury,¹
Neda Kalhor,⁴ Guilin Tang,¹ Carlos E Bueso-Ramos,¹ Jeffrey
L. Jorgensen,¹ Pei Lin,¹ L. Jeffrey Medeiros,¹ and Xinyan Lu¹

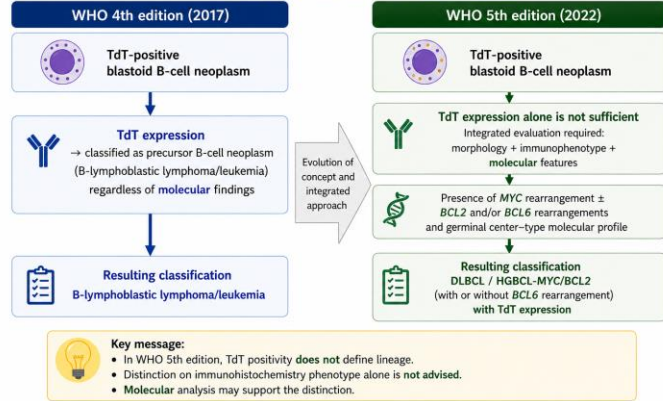
“Very rare B-lymphoblastic leukaemias/lymphomas (B-ALL/LBLs) have MYC and BCL2 dual translocations and are seen particularly in the **paediatric / young adult setting**”

Evolution of WHO classification

Diagnostic Algorithm for Aggressive B cell lymphomas



Evolution of classification of TdT-positive blastoid B-cell neoplasms from WHO 4th to WHO 5th edition



Contents lists available at ScienceDirect
Human Pathology: Case Reports
 Journal homepage: www.elsevier.com/locate/hpcr

Case Report
Blastic transformation of mantle cell lymphoma with B-lymphoblastic features
 David Cantu^a, Yuridia Alvarado^a, Joyce Murata-Collins^a, Dennis D. Weisenburger^{a,b}

^a Department of Pathology, City of Hope National Medical Center, 1500 East Duane Road, Duane, CA 92010, USA
^b Department of Pathology, Eastern Hospital, Calle Ecuador 2331, Instituto de Medicina, 84030 Montevideo, MV, Uruguay

Manuscript Archive (2021) 479:133–145
<https://doi.org/10.1007/s00428-021-03023-8>

ORIGINAL ARTICLE

Mantle cell lymphomas with concomitant MYC and CCND1 breakpoints are recurrently TdT positive and frequently show high-grade pathological and genetic features

Sietse M. Aukema^{1,2}, Giorgio A. Croci^{3,4}, Susanne Berns⁵, Kathrin Oehli-Huber⁶, Rabea Wagener^{6,8}, German Ott⁶, Andreas Rosenwald⁷, Philip M. Klün⁸, Eva van den Berg⁹, Anneke G. Bosga-Bouwer¹⁰, Mels Hoogenboom¹¹, Eva Hoste^{11,12}, Iris Bittmann¹³, Inga Nagel^{13,14}, Eva M. Murga Penas¹⁵, Markus Kreuz¹⁶, Julia Bauslinger¹⁷, Wilfried Balder¹⁸, Ilke Ouchlous¹, Martin J. S. Dyer¹⁹, Sandrine Jayne²⁰, Reiner Siebert⁶, Wolffram Klapper²

Diffuse large B-cell lymphoma / high-grade B-cell lymphoma with MYC and BCL2 rearrangements

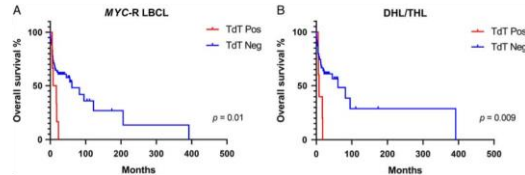
Subtype(s)

DLBCL/HGBCL-MYC/BCL2 without BCL6 rearrangement;

DLBCL/HGBCL-MYC/BCL2 with BCL6 rearrangement;

DLBCL/HGBCL-MYC/BCL2 (with or without BCL6 rearrangement) with TdT expression

- TdT expression in 2% of DLBCL/HGBL-MYC/BCL2 R
- Male, 55-77y, *Extranodal*, IPI ≥ 3 , Stage III -IV
- **Blastoid morphology** \gg DLBCL
- **TdT expression partial distribution** $>10\%-70\%$
- Phenotype: varying levels of (im)maturity
- Mutational profile : **BCL2/EZB/C3** $>$ NOTCH2/BN2/C1
- Somatic hypermutation supports these to be mature lymphomas
- In all cases, the prognosis was very poor after emergence of the TdT+ neoplasm
- Rare de novo; mostly had prior FL or HGBCL TdT-



TdT as an additional risk factor



TAKE-HOME MESSAGES

- DLBCL/HGBL-MYC/BCL2 R with TdT expression should be differentiated from B-ALL
- Correct classification directly impacts prognosis and treatment strategy
- TdT alone should not be considered evidence of immaturity
- Integrated clinical, immunophenotypic, cytogenetic and NGS molecular data are essential in challenging blastoid B-cell neoplasms
- Strong c-MYC expression should prompt investigation for MYC rearrangements, including non-IGH partners