SESSION I: Histopathology and Biology

Histology

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Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Recordati Rare Disease						X	X
Menarini Stemline						X	X
Kyowa Kyrin							X

FOLLICULAR LYMPHOMA

one of the more common lymphomas

>lymph nodes (LN); extranodal sites not uncommon (duodenal, testis, skin, bone, breats)
>adults; specific pediatric variants do occur (pediatric-type FL, FL of the testis)

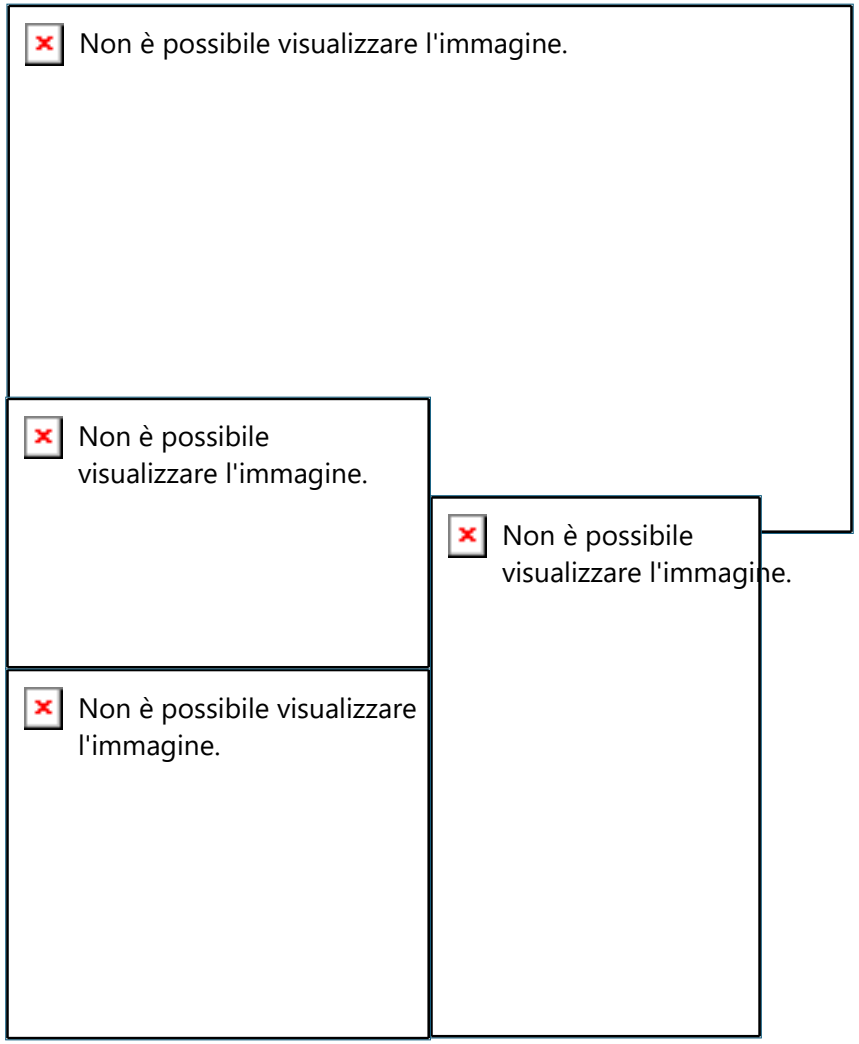
derive from GC-B cells (centrocytes and centroblasts)
centroblasts are variably represented proving different cytologic grades (1, 2, 3a, 3b)

genetics FL:
- epigenetic dysregulation as hallmark feature (*CREBBP, KMT2D, EZH2, ARID1A*, *MEF2B*, and*KMT2C)*
- *TNFRSF14* (1p36 locus) (immune recognition with putative impact on microenvironment)
- *GEP* and heterogenous group of variants sharing *common CNV*
- signaling pathways (BCR, NF-κB in CARD11 and TNFAIP3, JAK/STAT in STAT6, mTOR in RRAGC, ATP6V1B2, ATP6AP1, SESTRIN1)
- most harboring *t(14;18)*

WHO – HAEM5 2022	ICC - 2022
FL classic type	
FL with unusual cytological features FL with a predominantly diffuse growth pattern Follicular large B-cell lymphoma	/ FL with BCL2 R negative CD23 positive FL 3B
In situ follicular B-cell neoplasm Paediatric-type follicular lymphoma Duodenal-type follicular lymphoma Primary cutaneous follicle centre lymphoma	

>follicular growth pattern (at least in parts)
with a back-to-back arrangement
beyond the nodal capsule
perivascular/perineural infiltration
massive necrosis possible due to angioinvasion
often associated with sclerosis

BM: paratrabecular infiltration is typical

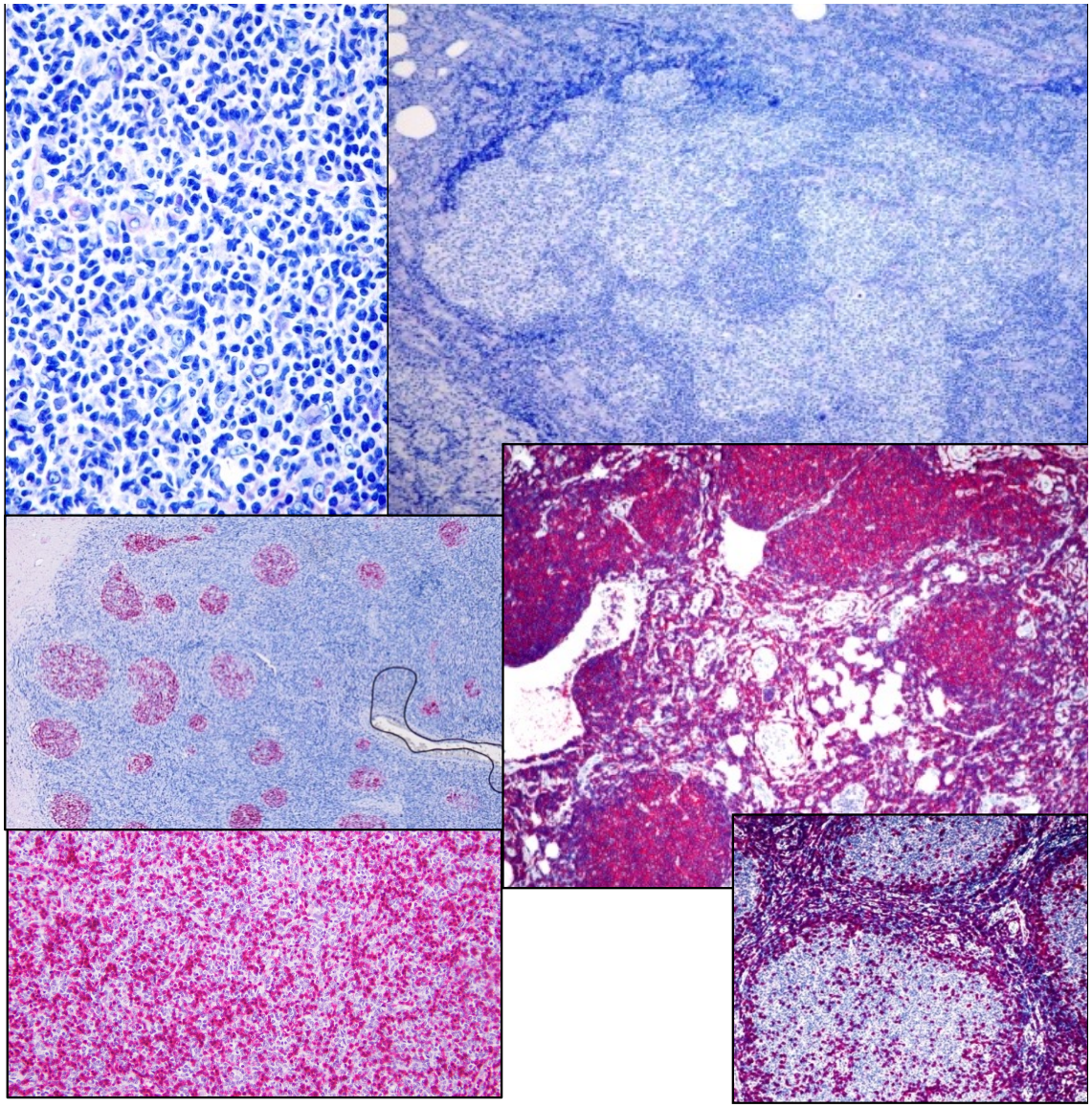


lack polarization of the GCs;
starry-sky pattern usually not seen;
possible sclerotic/depleted GC with CD-like features;

frequent interfollicular spread

T-cells/TFH cells may be abundant

supported by FDC meshworks (CD21, CD23, CD35)*



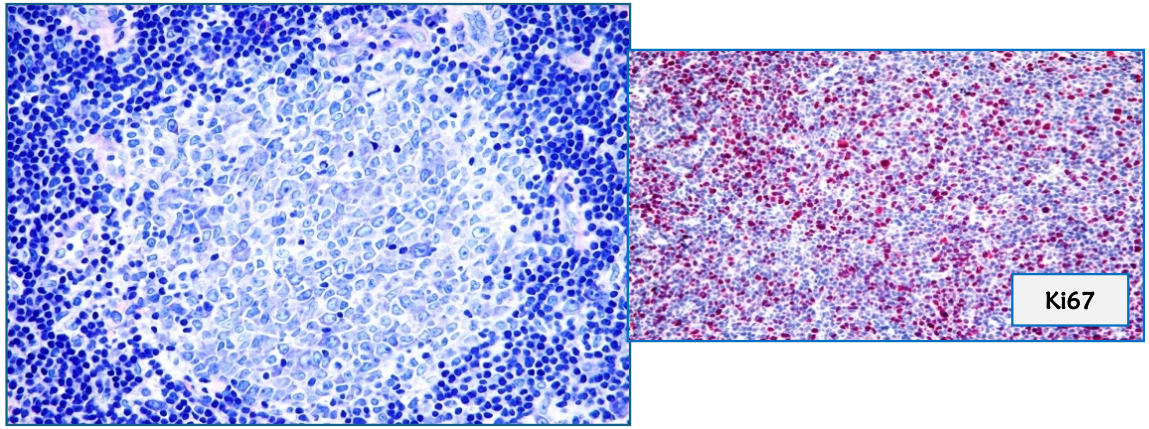
*often irregularly distributed (possible diminished expression of these markers may occur even in obviously follicular areas)

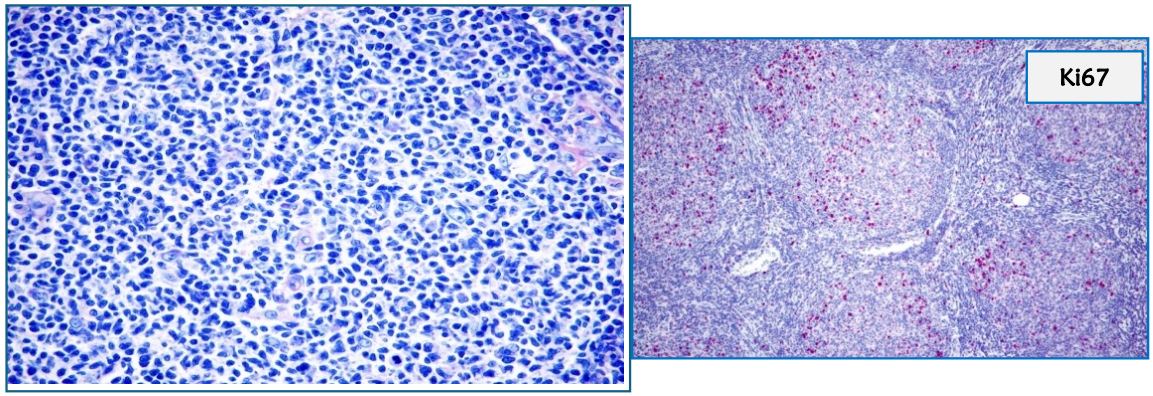
grading FL (centroblasts as the number of cells per high-power-field (HPF) using a 40x objective)
5-15 Cb/HPF: G1-G2
>15Cb/HPF: G3a (not all Cb)

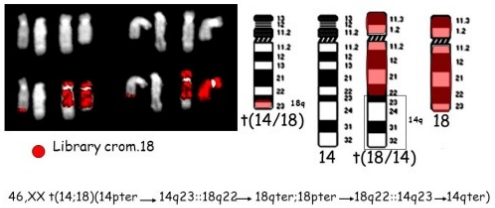
matter of discussion

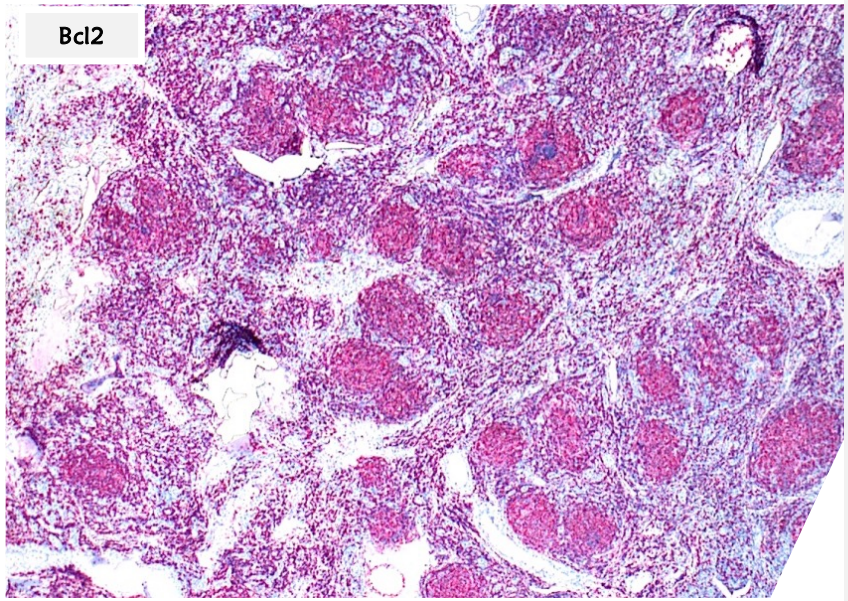
poor reproducibility, definition/recognition of centroblasts, enumeration methods, different microscopes, no significant difference in clinical outcomes between FL grades 1, 2, and 3A

WHO-HAEM5: grading optional
ICC: required









GENETIC INITIATING EVENT (85-90% cases)
t(14;18)(q32;q21); *IGH* (rarely involve *IGL)* and *BCL2* genes: constitutive expression of Bcl2 protein

15% negative (>mutations in *BCL2* gene "pseudo-Bcl2 negative FL"; more rarely true lack of *BCL2-R)*

arises from a VDJ recombination error in a BM pre-B-cell

but pre-B or naive B-cells with t(14;18) not documented differentiated t(14;18)+ memory-like B-cell clones detected in PB at very low levels (~1-100 cells per million B cells) in >70% healthy adults; tissue equivalent is ISFN*

routine molecular testing is currently not required, but can be useful in selected cases for differential diagnosis

*number rises with age, smoking, exposure to pesticide; >individuals never develop FL though it increases the risk of accumulation of genomic instability; carry some mutations found in established FL (*CREBBP)*

B-markers CD19, CD20, CD22, CD79a, PAX-5

>IgM isotype ± IgD; IgG > IgA

GC-associated markers
CD10*, BCL6*,
GCET1, HGAL (GCET2), LMO2,
AID*
MEF2B, Stathmin)
with variable sensitivity/specificity

MUM1 negative

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BCL-6

Non è possibile visualizzare l'immagine.

CD10

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CD10

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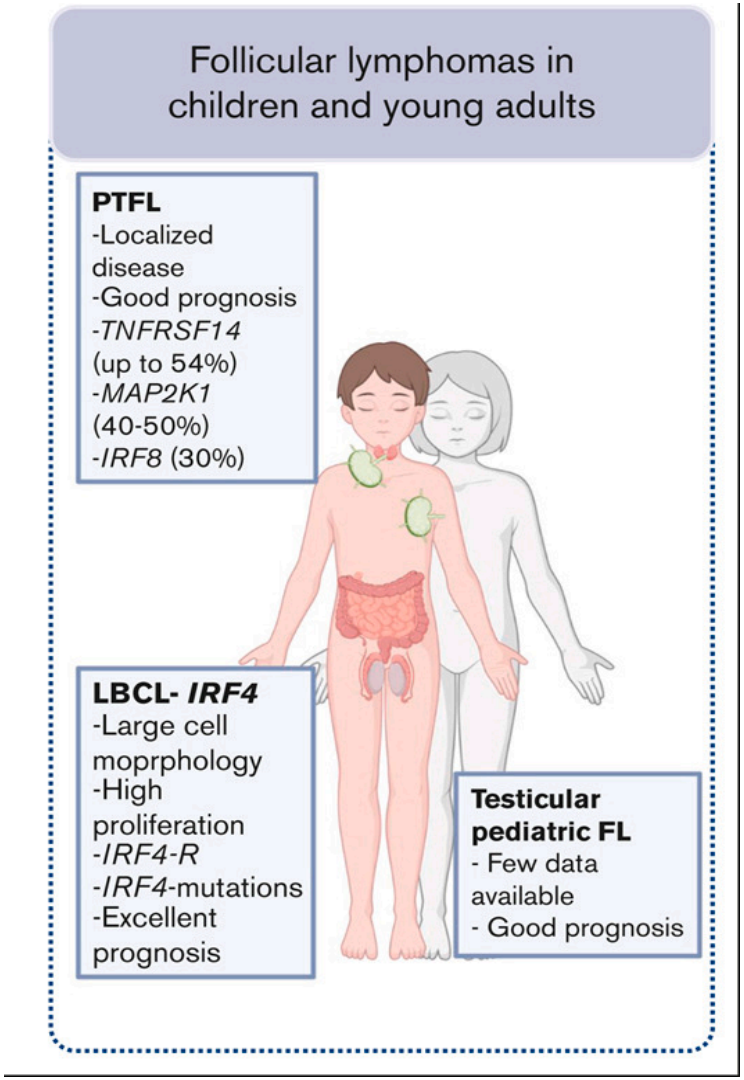
CD10

*CD10 and BCL6 may be absent in FL cells located in areas of MZ differentiation, peripheral blood or BM; activation induced cytidine deaminase mediates process of somatic hypermutation (SHM) and class switch recombination, leading to genomic instability and accumulation of genetic alterations



Salaverria et al.Blood Adv, 2023