

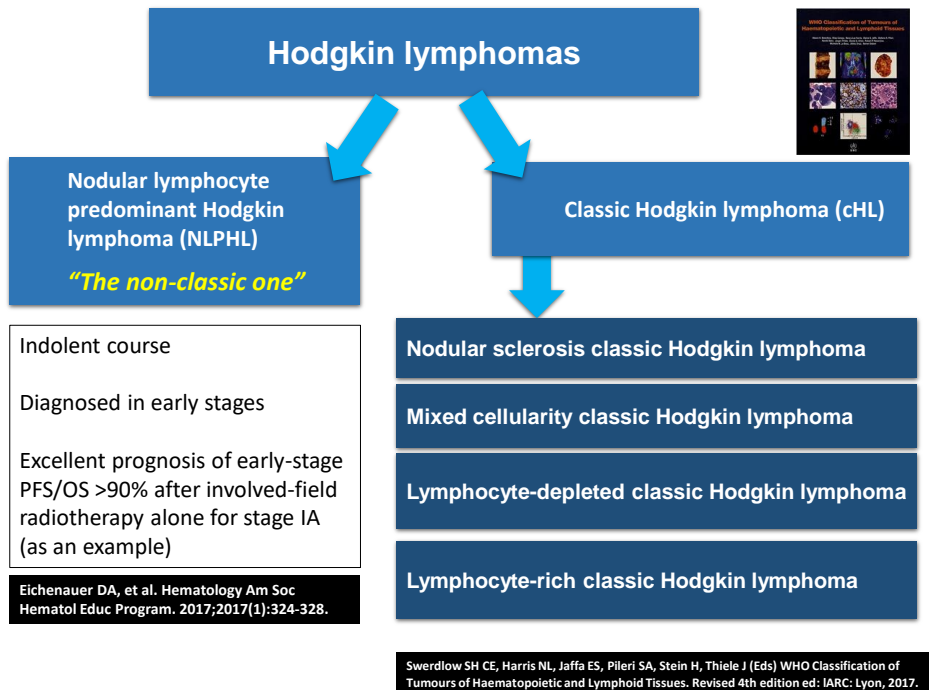
# 2020 Virtual Pathology Course

8/22/2020

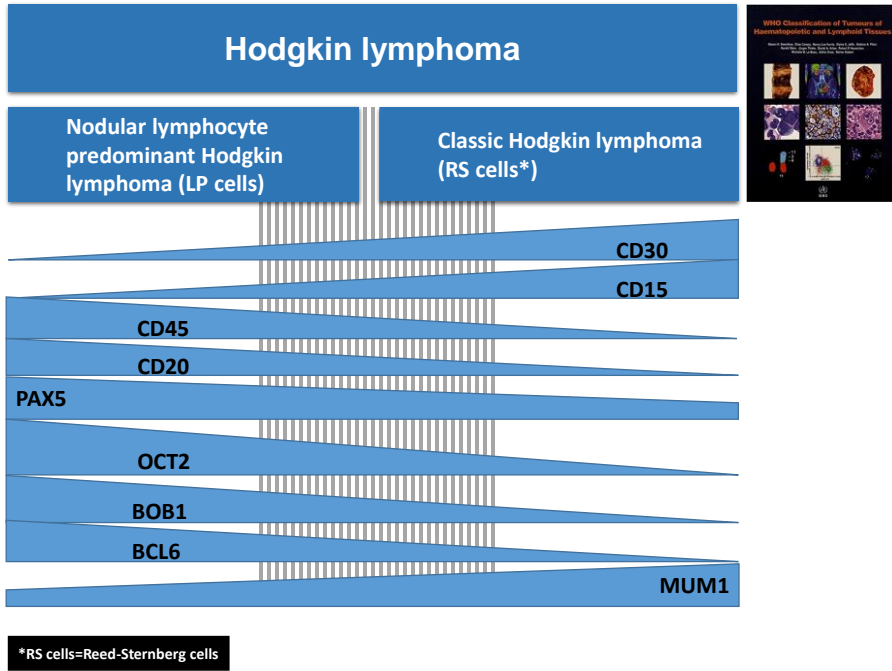
## Diagnostic challenges of Hodgkin lymphoma “the non-classic-Hodgkin lymphoma” in lymph node core needle biopsy

**George Deeb, MD**  
Associate Professor  
Director of Flow Cytometry Laboratory

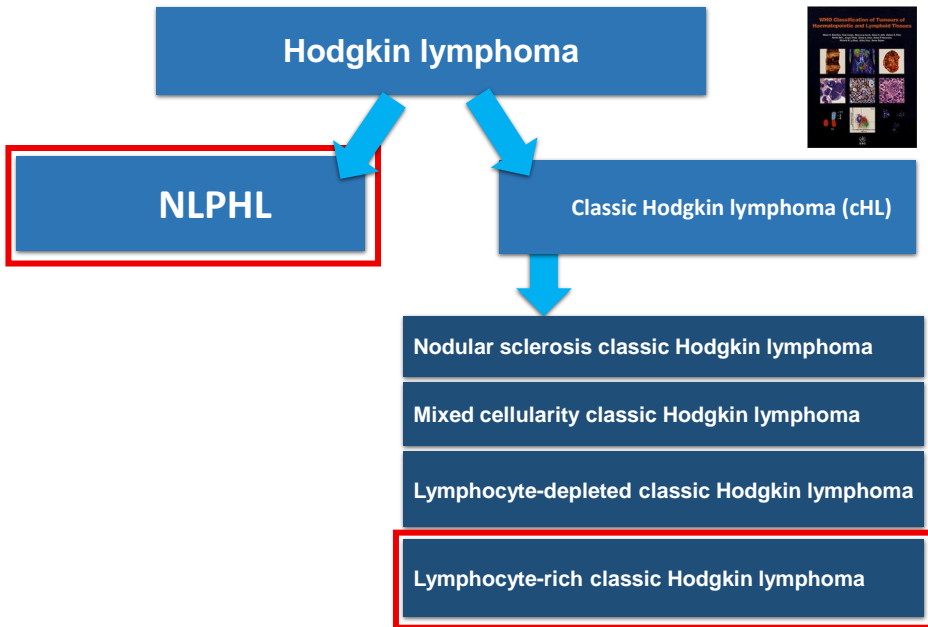
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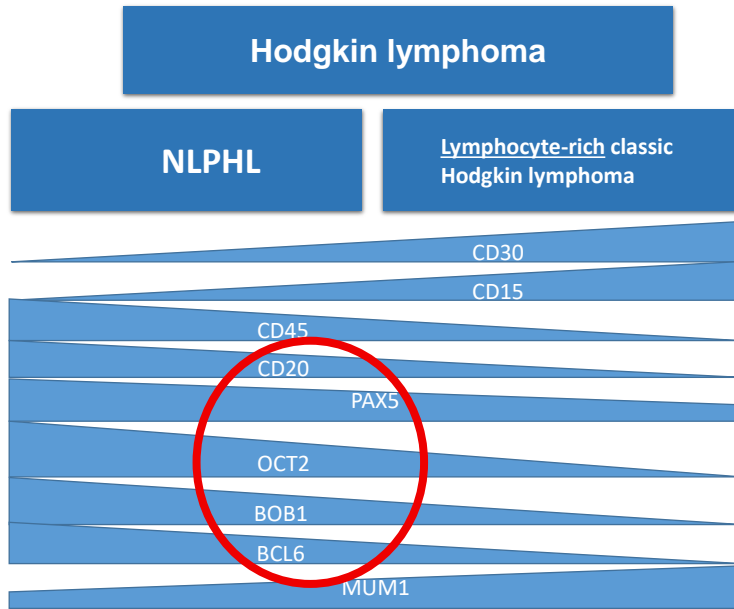


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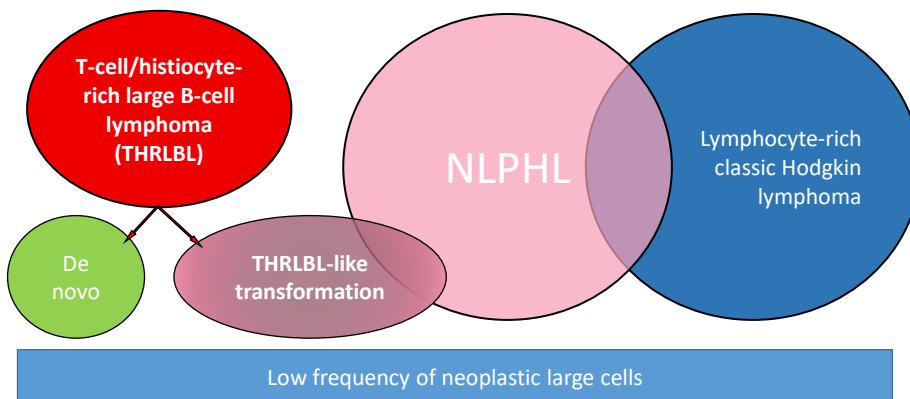
Swerdlow SH CE, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J (Eds) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th edition ed: IARC: Lyon, 2017.

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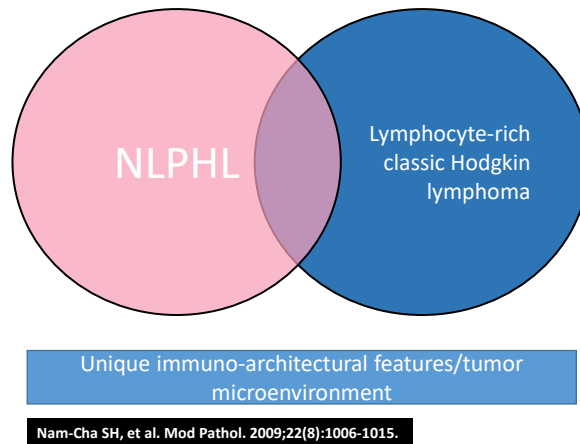


Nam-Cha SH, et al. Mod Pathol. 2009;22(8):1006-1015.

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# NLPHL

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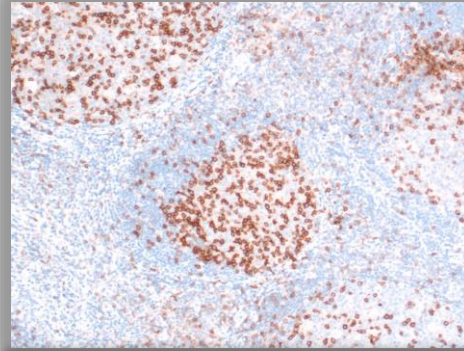
The microenvironment  
 Follicular helper (FH) T-cells  
 Programmed cell death 1 (PD1, CD279)

Nam-Cha SH, Roncador G, Sanchez-Verde L, et al. PD-1, a follicular T-cell marker useful for recognizing nodular lymphocyte-predominant Hodgkin lymphoma. *Am J Surg Pathol.* 2008;32(8):1252-1257.

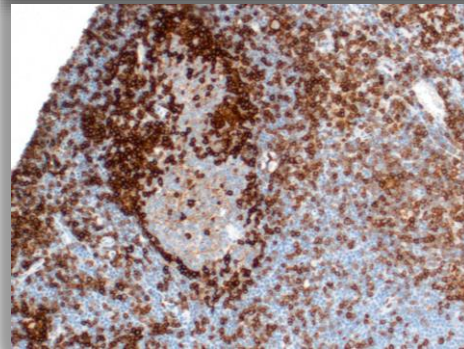
<https://www.ncbi.nlm.nih.gov/gene/5133>

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**PD1 immunostaining pattern in benign tonsil and in NLPHL case with remaining reactive germinal centers**



Tonsil tissue



NLPHL

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## NLPHL

### The immuno-architectural patterns

**Fan Z, Natkunam Y, Bair E, Tibshirani R, Warnke RA. Characterization of variant patterns of nodular lymphocyte predominant hodgkin lymphoma with immunohistologic and clinical correlation. Am J Surg Pathol. 2003;27(10):1346-1356.**

Swerdlow SH CE, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J (Eds) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th edition ed: IARC: Lyon, 2017.

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Pattern A: "Classic" B-cell-rich nodular pattern

Pattern B: Serpiginous nodular pattern

Pattern C: Prominent extra-nodular LP cells pattern

Pattern D: T-cell-rich nodular pattern

Pattern E: Diffuse (no CD21+ FDC) T-cell-rich pattern (THRLBL-like) pattern

Pattern F: (Diffuse), "Moth-Eaten" with B-cell-rich background pattern

Another pattern: Presence of remaining germinal centers

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# NLPHL

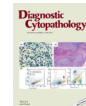
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Flow cytometry immunophenotypic findings

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## Limitations of routine flow cytometry

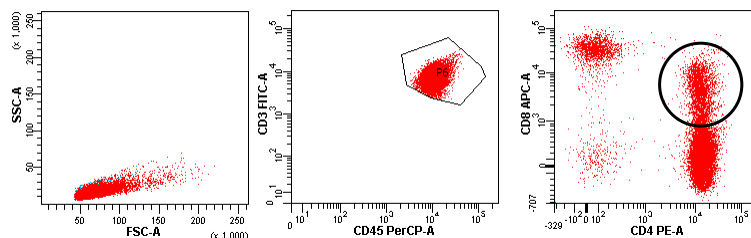
- Routine clinical flow cytometry is limited in diagnosing certain lymphoma entities:
  - Such as large cell lymphomas including diffuse large B-cell lymphoma and Hodgkin lymphoma
  - Due to cell fragility, low frequency of assessable cells of interest, or panel-design
- Hemodilution and sampling variation may affect testing results



Wake LM, VandenBussche CJ, Ali SZ, et al. Flow cytometric analysis of fine needle aspirates is affected by tumor subtype, but not by anatomic location nor technique. *Diagn Cytopathol.* 2020;48(6):538-546.

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### NLPHL with dual positive CD4+CD8+ T-cell population



Rahemtullah A, et al. . A double-positive CD4+CD8+ T-cell population is commonly found in nodular lymphocyte predominant Hodgkin lymphoma. *Am J Clin Pathol.* 2006;126(5):805-814

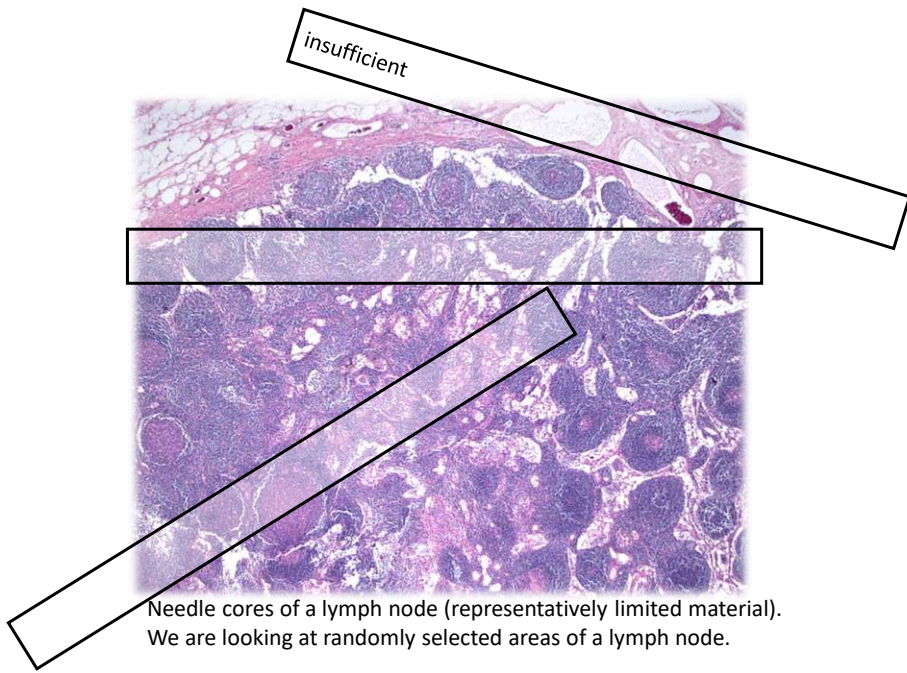


63%	NLPHL
5%	Progressive transformation of germinal centers
2%	in classic Hodgkin lymphoma
3%	in reactive lymphoid hyperplasia

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# Morphologic assessment of NLPHL in core needle biopsy

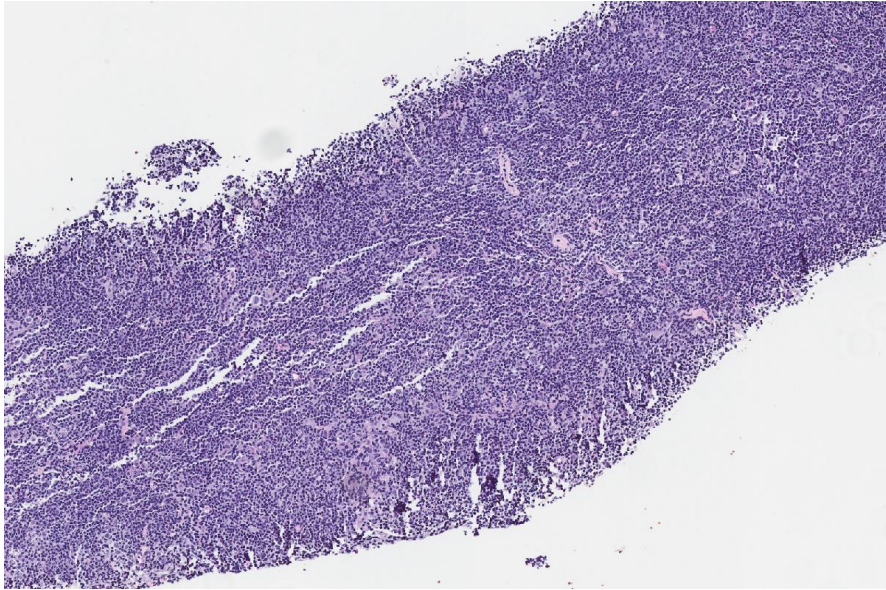
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Sampling a histomorphologically heterogeneous disease: e.g. NLPHL



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## Case studies

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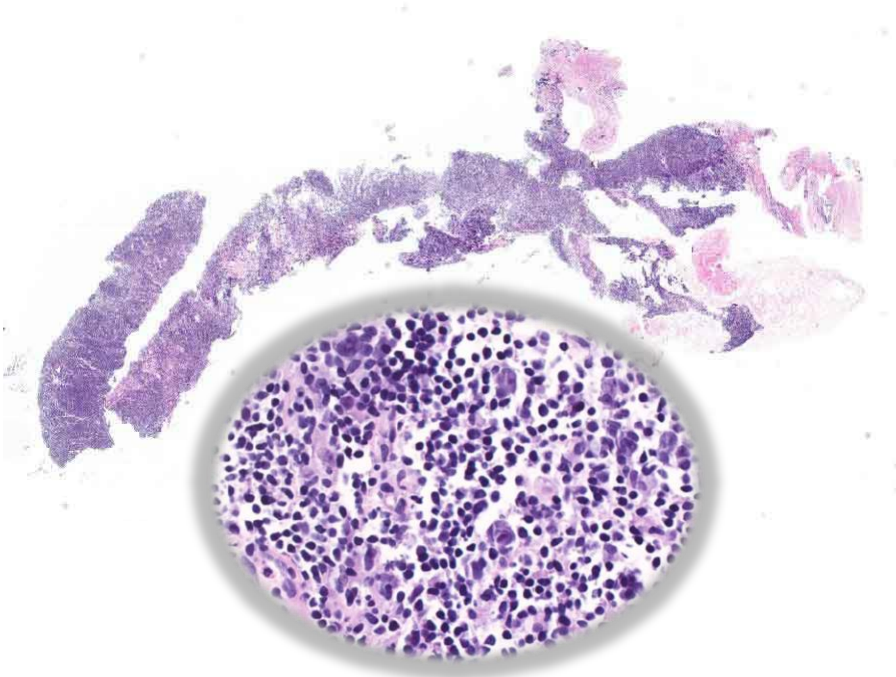
Cases 15 and 16 (digital slide set)

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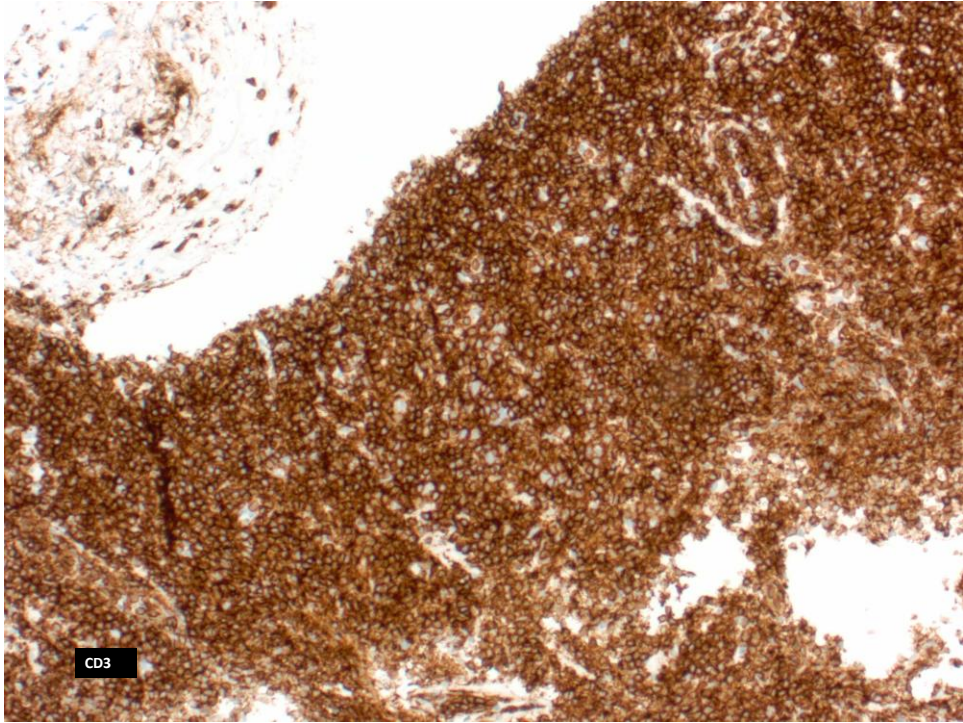
# Case 15

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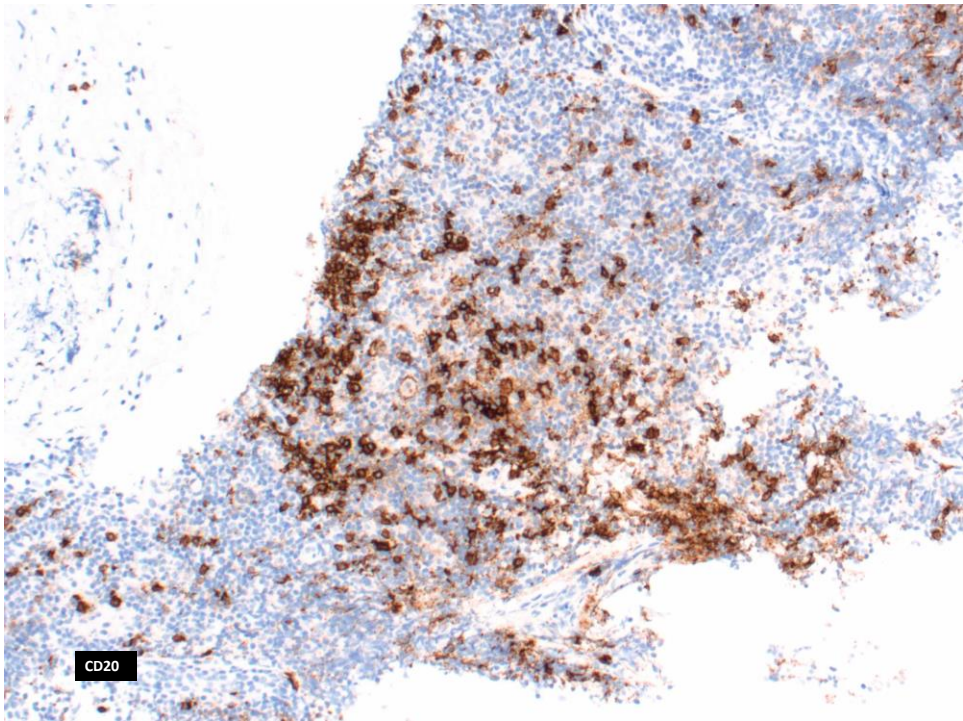
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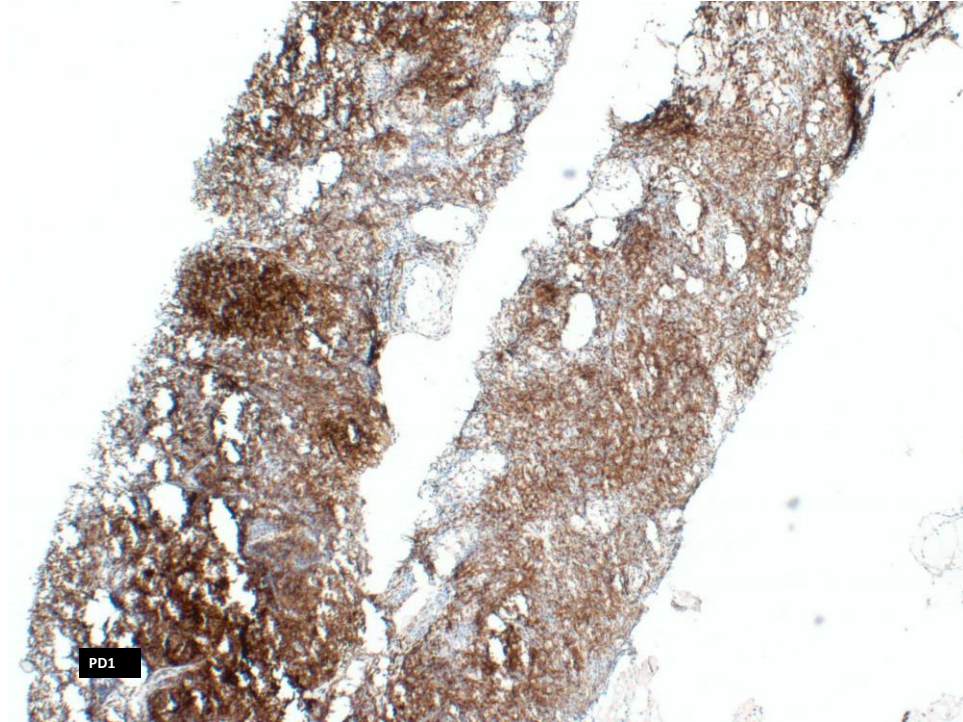
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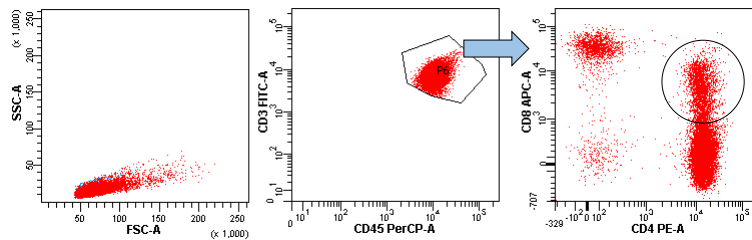
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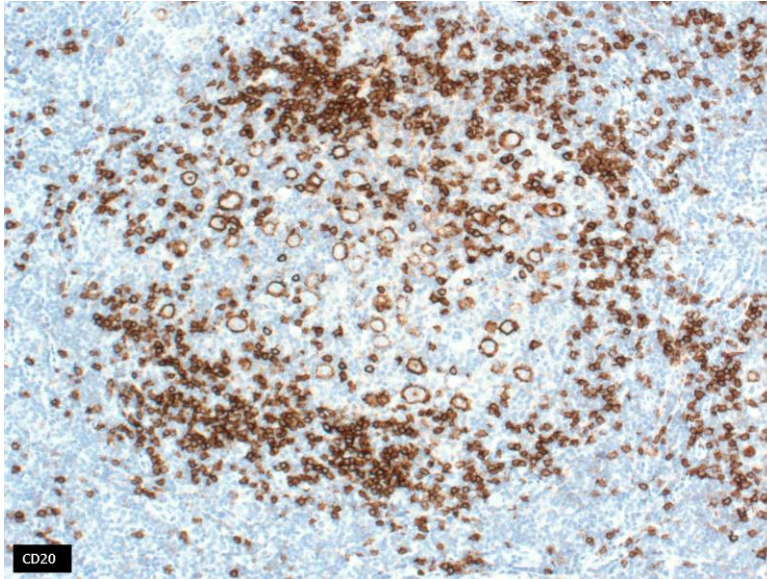
## Flow cytometry analysis on biopsy sample

- B-cells polytypic
- T-cells with no abnormal loss of tested pan-T-cell markers. A double-positive CD4+CD8+ T-cell population is noted (black circle)



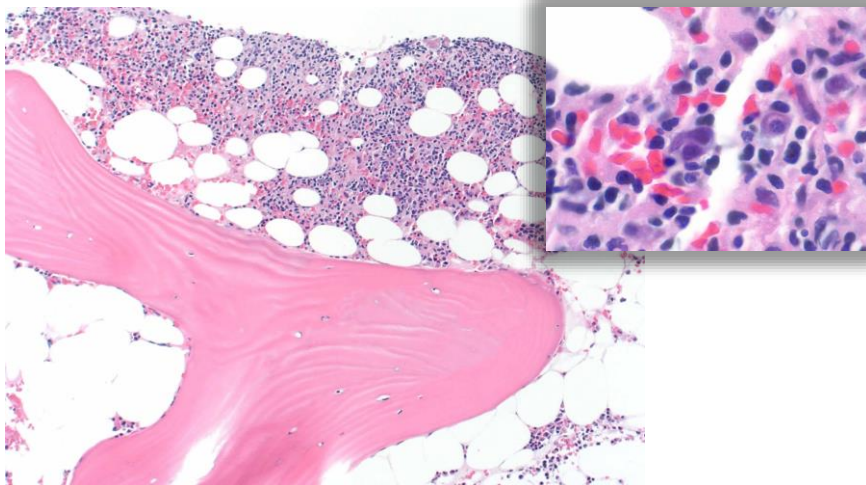
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- Excision was performed confirming NLPHL
- Mixed Patterns A and D

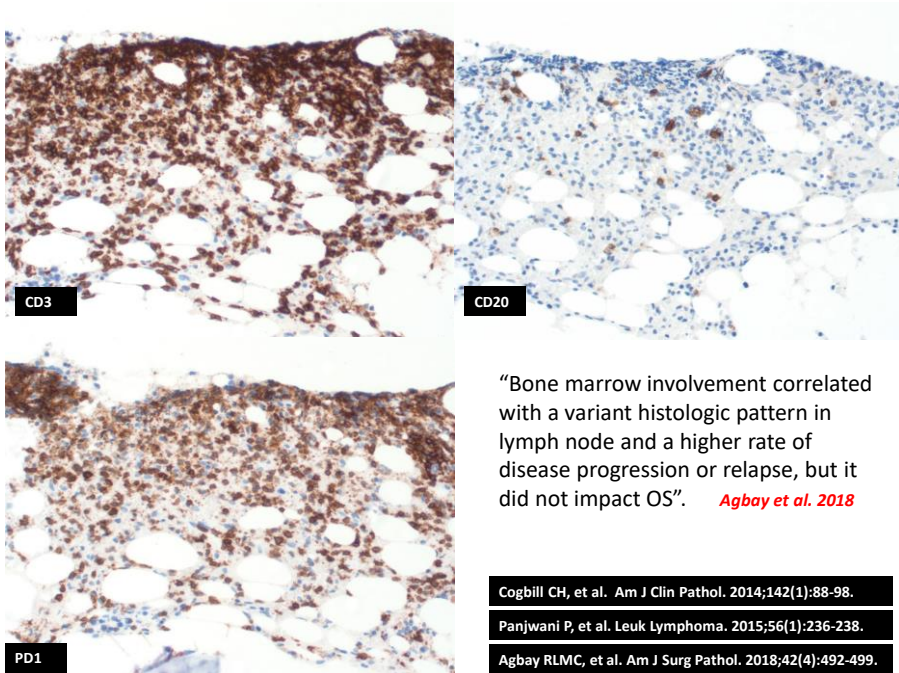


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## Staging bone marrow



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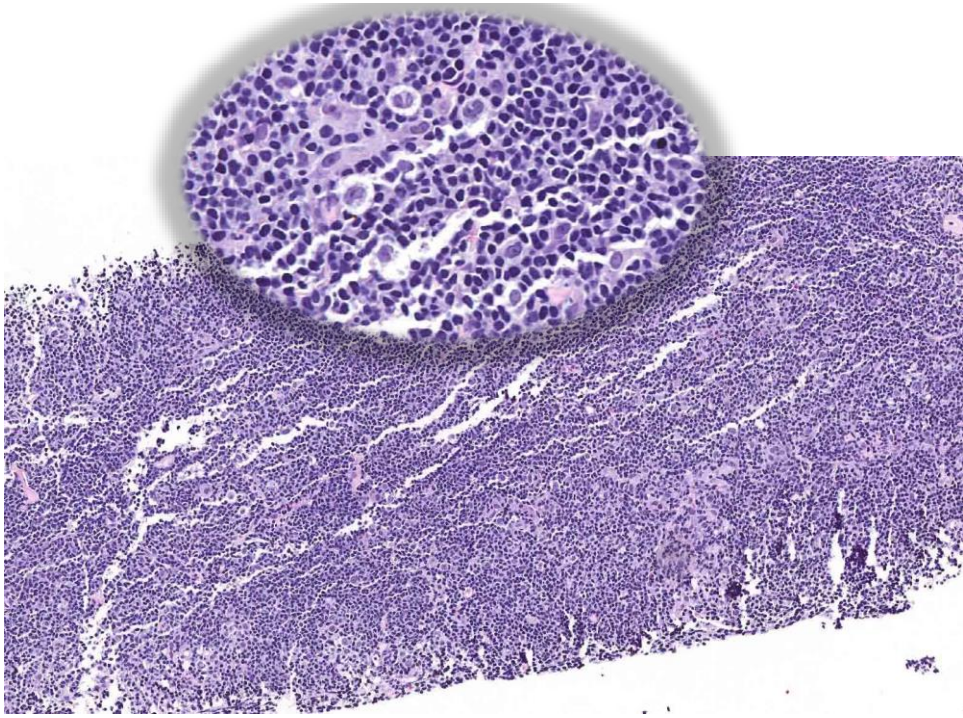


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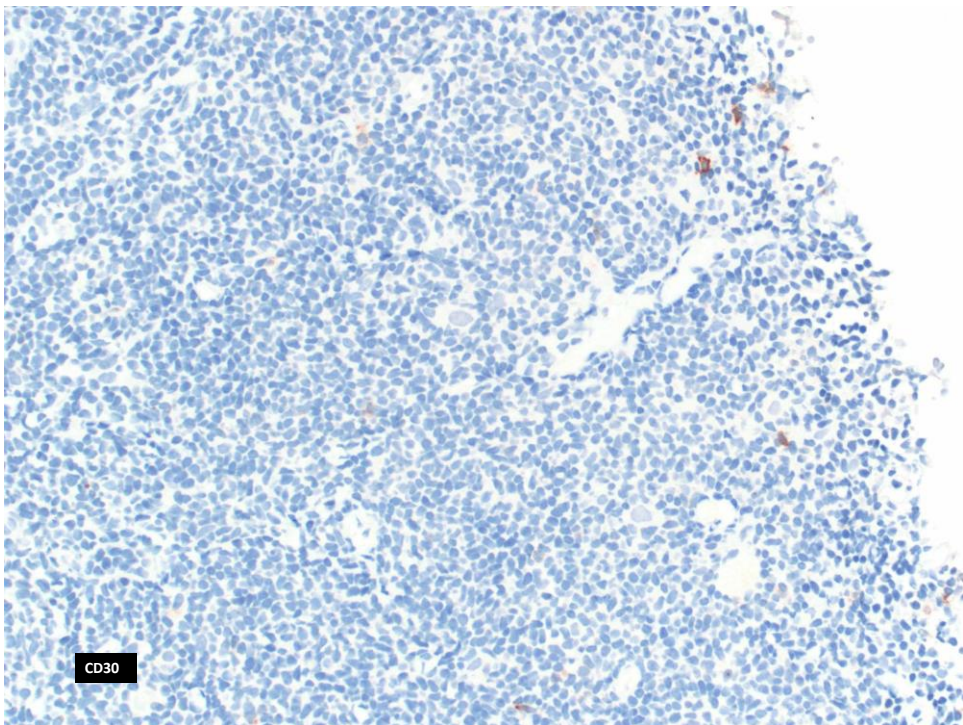
## Case study

Case 16

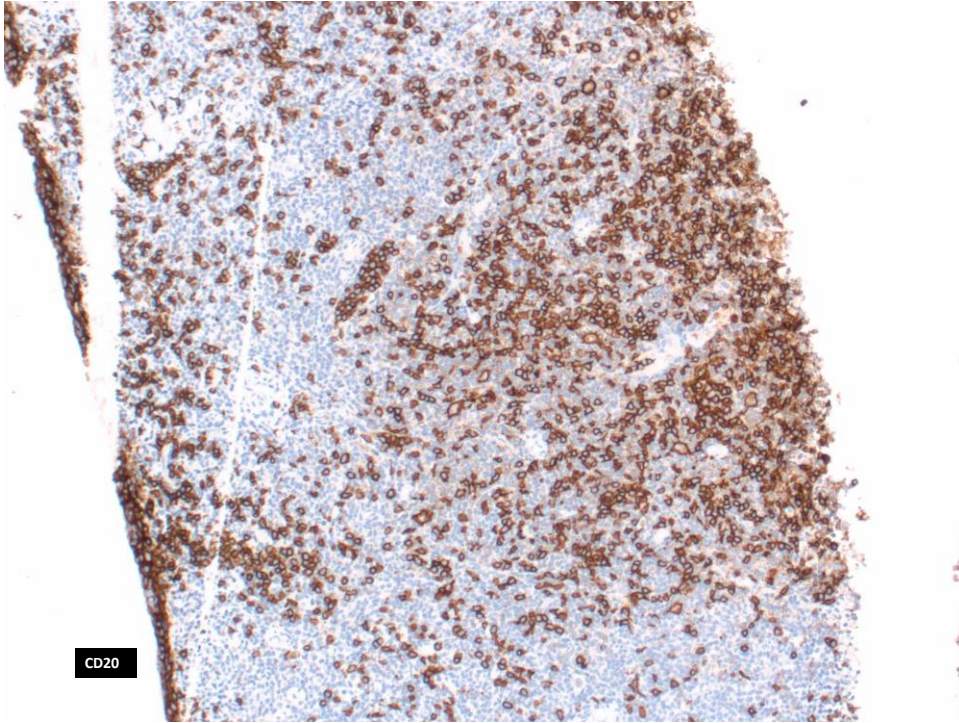
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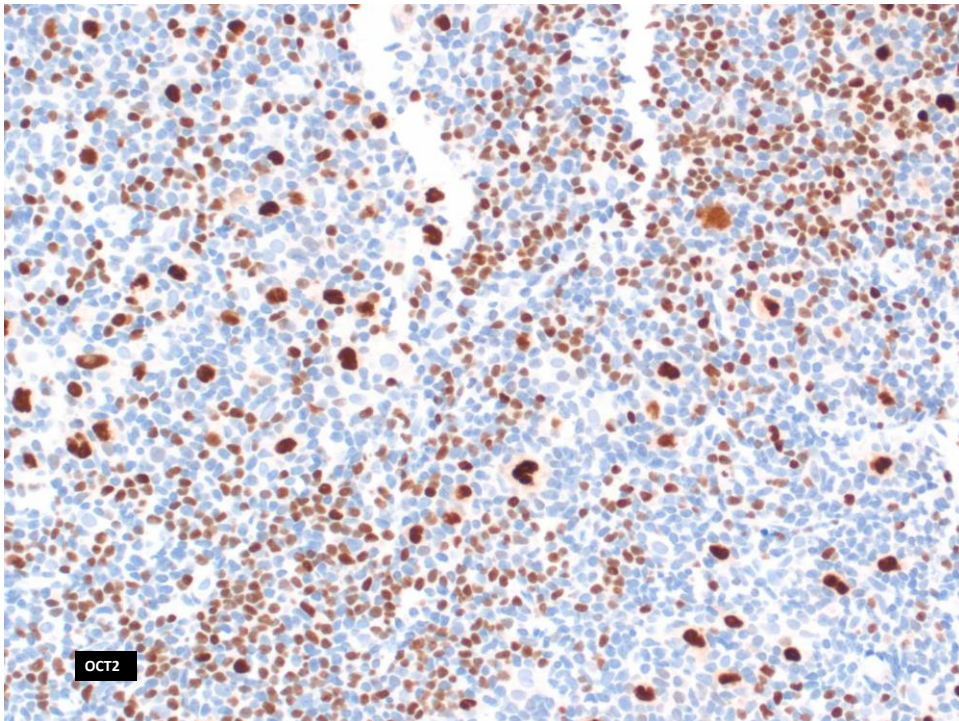
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## Concluding thoughts-I

- NLPHL should be considered in the differential diagnosis of lymphocyte-rich lymph node sample with:
  - atypical large cells
  - disarrayed histomorphology (based on CD3 and CD20 staining)
  - and adequate flow cytometry testing:
    - Negative for conventional B/T lymphomas with preferably double positive CD4+/CD8+ T-cell subset
- **Negative flow** → **CD20/CD3** immunostains could be a good start → **OCT2/PD1** immunostains could be a helpful add-on
- **No flow** → Consider expanding IHC W/U

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## Concluding thoughts-II

- Even if NLPHL diagnosis is rendered on core, excision may be still indicated to exclude variant patterns and/or THRLBL-like transformation
- It is always helpful to discuss with clinician when assessing limited tissue to fine tune the work-up

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