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

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Hodgkin lymphomas

Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
“The non-classic one”

Indolent course
Diagnosed in early stages
Excellent prognosis of early-stage PFS/OS >90% after involved-field radiotherapy alone for stage IA (as an example)

Classic Hodgkin lymphoma (cHL)

Nodular sclerosis classic Hodgkin lymphoma
Mixed cellularity classic Hodgkin lymphoma
Lymphocyte-depleted classic Hodgkin lymphoma
Lymphocyte-rich classic Hodgkin lymphoma

Hodgkin lymphoma

- Nodular lymphocyte predominant Hodgkin lymphoma (LP cells)
- Classic Hodgkin lymphoma (RS cells*)

- CD30
- CD15
- CD45
- CD20
- PAX5
- OCT2
- BOB1
- BCL6
- MUM1

*RS cells=Reed-Sternberg cells

Hodgkin lymphoma

NLPHL

Lymphocyte-rich classic Hodgkin lymphoma

CD30
CD15
CD45
CD20
PAX5
OCT2
BOB1
BCL6
MUM1

T-cell/histiocyte-rich large B-cell lymphoma (THRLBL)

Low frequency of neoplastic large cells

De novo
THRLBL-like transformation

Lymphocyte-rich classic Hodgkin lymphoma

NLPHL

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


NLPHEL

The immuno-architectural patterns


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

NLPHL
Flow cytometry immunophenotypic findings
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


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


<table>
<thead>
<tr>
<th>Percentage</th>
<th>Condition</th>
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<tbody>
<tr>
<td>63%</td>
<td>NLPHL</td>
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<tr>
<td>5%</td>
<td>Progressive transformation of germinal centers</td>
</tr>
<tr>
<td>2%</td>
<td>in classic Hodgkin lymphoma</td>
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<tr>
<td>3%</td>
<td>in reactive lymphoid hyperplasia</td>
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</tbody>
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Morphologic assessment of NLPHL in core needle biopsy

Needle cores of a lymph node (representatively limited material). We are looking at randomly selected areas of a lymph node.
Sampling a histomorphologically heterogeneous disease: e.g. NLPHL

Case studies

Cases 15 and 16 (digital slide set)
Case 15
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)
• Excision was performed confirming NLPHL
• Mixed Patterns A and D

Staging bone marrow
“Bone marrow involvement correlated with a variant histologic pattern in lymph node and a higher rate of disease progression or relapse, but it did not impact OS”.  

Agbay et al. 2018
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

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