Mimics of Lymphoma in Routine Biopsies

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I have nothing to disclose regarding the information to be reported in this talk.

Types of Lymphoid Hyperplasia

• Follicular hyperplasia (B-cells)
• Paracortical hyperplasia (T-cells) (interfollicular immunoblastic hyperplasia)
• Mixed hyperplasia
Mixed follicular and paracortical hyperplasia

Pure Reactive Follicular Hyperplasia

Reactive Follicular Hyperplasia and Paracortical Hyperplasia

CD3
The “Panel o’ Three”
(for assessment of lymphoid infiltrates)

- CD20
- CD3
- CD21
Small B-Cell Lymphomas

Basic Immunophenotypes

<table>
<thead>
<tr>
<th></th>
<th>CD20</th>
<th>CD5</th>
<th>CD43</th>
<th>CD23</th>
<th>BCL1</th>
<th>BCL6</th>
<th>CD10</th>
<th>Cyclin D1</th>
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</thead>
<tbody>
<tr>
<td>CLL/SLL</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mantle cell</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Follicular</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-/+</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
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<tr>
<td>Marginal</td>
<td>+</td>
<td>-</td>
<td>-/+</td>
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</tbody>
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Proportion of cases positive: + >90%, +/- 50-90%, -/+ 10-50%, - <10%

B-LPD
The “Panel o’ Nine”  
(for diagnosis of small B-cell lymphomas)
- CD20
- CD3
- CD5
- CD43
- CD10
- CD21
- CD23
- BCL-1 (cyclin D1)
- BCL-6

Paracortical hyperplasia

Differential diagnosis
- Drug reaction
- Other hypersensitivity reaction
- Viral infection
- Post-vaccination
- No clear etiology
Florid paracortical hyperplasia (e.g., infectious mononucleosis) can mimic:

- Diffuse large B-cell lymphoma, NOS
- Classical Hodgkin lymphoma
- T-cell/histiocyte-rich large B-cell lymphoma
- EBV+ diffuse large B-cell lymphoma of the elderly
- Peripheral T-cell lymphoma
“One should think twice and thrice before rendering a diagnosis of DLBCL in a patient younger than 20 years. Infectious mononucleosis in particular has to be suspected when ... there are many admixed large T-cells and Waldeyer’s ring is involved.”

ACL Chan & JKC Chan, 2011
Diffuse large B-cell lymphoma, in Hematopathology (Saunders/Elsevier)
**Infectious Mono**

- **CD30**: + >90%
- **CD15**: +/- ~80%
- **CD20**: -/+ ~20% (focal, weak)*
- **Oct2**: - ~60% (focal, weak)*
- **Pax-5**: + >90% (often focal, weak)*
- **CD3**: - <10%

*Based on data from García-Cosío et al. Mod Pathol 17: 1531; 2004

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**Classical Hodgkin lymphoma**

**HRS Cell Immunophenotype**

*(Basic Panel for Dx of CHL)*

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- **CD15**: +/- ~80%
- **CD20**: -/+ ~20% (focal, weak)*
- **Oct2**: - ~60% (focal, weak)*
- **Pax-5**: + >90% (often focal, weak)*
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Proportion of cases positive: + >90%, +/- 50-90%, -/+ 10-50%, - <10%

*Based on data from García-Cosío et al. Mod Pathol 17: 1531; 2004*
T-cell/histiocyte-rich large BCL

Diagnostic criteria (WHO 2008)

- Large B-cells (may resemble immunoblasts, LP cells, or HRS cells) present only as dispersed cells (<10% cells), no aggregates or sheets
- Background cells are small lymphocytes and histiocytes, no eos or plasma cells
- Background small lymphs “nearly all” T-cells
- No nodules typical of NLPHL
- Most patients present with high-stage disease, B-symptoms

CD20

T-cell/histiocyte-rich large BCL

Boudová et al. (Blood 102: 3753; 2003)

Ratio of small to large B-cells

- TCHRLBCL: 0.7:1 (range 0.3 – 1.5)
- DLPHL: 6:1
- NLPHL: 20-50:1
“There are aggressive B-cell lymphomas, rich in reactive T-cells, in which the neoplastic cells are sparse, and are EBV-positive. In such cases, the neoplastic cells may exhibit a Hodgkin-like morphology. Such cases should not be classified as THRLBCL, and should be considered within the spectrum of EBV-positive DLBCL.”

WHO Classification (2008), p. 238
EBV+ DLBCL of the Elderly

Why not infectious mono?

*EBV uniformly present in large cells, absent or virtually absent in small cells*
Peripheral T-cell lymphoma, NOS?

Clues that a dense T-cell infiltrate might be a T-cell lymphoma...

- Characteristic morphologic features
- Aberrant immunophenotype, e.g.,
  - CD56+ EBV+ (NK/T-cell lymphoma)
  - Loss of pan T-cell antigen other than CD7
- Overtly destructive tissue infiltration (difficult to assess in small)
- Nothing (in some cases)

Follicular hyperplasia

Follicular hyperplasia Follicular lymphoma
Follicular lymphoma grade 3A

CD20

BCL-2

Follicular hyperplasia

Follicular lymphoma
**BCL-2 Expression in Follicular Lymphoma**  
*Guo et al. (Leukemia 19:1058; 2005)*

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases Positive</th>
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<tbody>
<tr>
<td>Grade 1</td>
<td>97%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>96%</td>
</tr>
<tr>
<td>Grade 3A</td>
<td>80%</td>
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<tr>
<td>Grade 3B</td>
<td>71%</td>
</tr>
<tr>
<td>Total</td>
<td>91%</td>
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</table>
Densely aggregated poorly formed B-cell follicles

Differential Diagnosis
- Follicular lymphoma
- Follicular pattern mantle cell lymphoma
- Nodular lymphocyte predominant Hodgkin lymphoma
- Nodular lymphocyte-rich classical Hodgkin lymphoma

References
- Guo Y et al. Low-grade follicular lymphoma with t(14;18) presents a homogeneous disease entity otherwise the rest comprises minor groups of heterogeneous disease entities with Bcl2 amplification, Bcl6 translocation or other gene aberrances. Leukemia. 2005 Jun;19(6):1058-63.