Mimics of Lymphoma in Routine Biopsies

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Types of Lymphoid Hyperplasia

- Follicular hyperplasia (B-cells)
- Paracortical hyperplasia (T-cells) (interfollicular immunoblastic hyperplasia)
- Mixed hyperplasia

Mixed follicular and paracortical hyperplasia
Follicular Hyperplasia

Mixed Follicular Hyperplasia and Paracortical Hyperplasia

CD3

CD20
The “Panel o’ Three” (for assessment of lymphoid infiltrates)

- CD20
- CD3
- CD21
Small B-Cell Lymphomas

Basic Immunophenotypes

<table>
<thead>
<tr>
<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>
</tr>
</thead>
<tbody>
<tr>
<td>CLL/SLL</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>
</tr>
<tr>
<td>Follicular</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Marginal</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
</tbody>
</table>

Proportion of cases positive: + >90%, +/- 50-90%, +/- 10-50%, - <10%

The “Panel o’ Nine”
(for diagnosis of small B-cell lymphomas)
- CD20
- CD3
- CD43
- CD5
- 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

**CD3**
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

Slide courtesy of Dr. Dan Arber, Stanford Univ.

EBV-ISH

CD30

Infectious Mono

CD20

Infectious Mono
Classical Hodgkin lymphoma

**HRS Cell Immunophenotype**
(Basic Panel for Dx of CHL)

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

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

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**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)
“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?

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

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases Positive</th>
</tr>
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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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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.