Lymphocyte Predominant Hodgkin’s Lymphoma

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Case Presentation
32 yo male, diagnosed with stage IIIA lymphocyte predominant Hodgkin’s lymphoma 3 years prior, s/p ABVDx6 yielding a CR.

• new 6 cm mass in the L neck
• Biopsy: relapsed lymphocyte predominant Hodgkin’s lymphoma.
• Staging: Bulky mass L neck, asymptomatic.

How would you treat the patient?

1. Salvage chemo +/- radiotherapy
2. Salvage chemo followed by autologous transplant
3. Radiotherapy alone
4. Rituximab
5. Rituximab plus radiotherapy
6. Rituximab plus chemotherapy
Classification of Hodgkin’s Lymphoma

- Classical Hodgkin’s lymphoma (95%)
  - Nodular sclerosing
  - Mixed lymphocyte
  - Lymphocyte - rich
  - Lymphocyte - depleted
- Nodular Lymphocyte Predominant Hodgkin’s lymphoma (5%, LPHL)

Pathological Features

- Lymph Nodes: nodular or nodular and diffuse pattern
- LP cells (Popcorn cells): large, multi-lobed cells
- Immunophenotype of LP cells:
  - CD30/CD15 negative; strongly express CD20 and other B cell markers
- Difficult to dx: 30-50% historical cases reclassified upon expert review

LPHL: Clinical Characteristics

- Represents 5% of all Hodgkin’s lymphomas
- Male predominance: 70-80%
- Median age: 35 yo
- Early stage disease: Stage I/II 65-80%
- B symptoms are rare
- Bone marrow and extranodal involvement uncommon

LPHL: Clinical Outcome

- Responsive to treatment: CR1 rate 85 - 90%
- OS is favorable: 80-90% in 10 years
- Late and continuous relapses occur
- Transformation to diffuse large B cell lymphoma
- Cause of death: treatment complications, especially secondary malignancies, caused more death than refractory LPHL

Diehl, et al., JCO, 1999; Orlandi, et al., Leukemia and Lymphoma 1997; Nogova, et al., JCO 2008; Al-Mansour, et al., JCO 2010; Chen et al., JCO 2010

Comparing LPHL with Classical HL

German Hodgkin's Study Group 1988 - 2002

<table>
<thead>
<tr>
<th>%</th>
<th>LPHL</th>
<th>cHL</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yrs</td>
<td>37</td>
<td>33</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>75</td>
<td>56</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Early favorable stage</td>
<td>64</td>
<td>24</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Early unfavorable stage</td>
<td>16</td>
<td>38</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Advanced stage</td>
<td>21</td>
<td>39</td>
<td>&lt; 0.0001</td>
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<tr>
<td>CR/CRu</td>
<td>87.5</td>
<td>81.7</td>
<td>0.0034</td>
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<tr>
<td>FFTF</td>
<td>88</td>
<td>82</td>
<td>0.0092</td>
</tr>
<tr>
<td>CR</td>
<td>86</td>
<td>82</td>
<td>0.0156</td>
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<tr>
<td>Relapse</td>
<td>8.1</td>
<td>8.0</td>
<td>0.9442</td>
</tr>
<tr>
<td>Early relapse (&lt;1 yr)</td>
<td>0.8</td>
<td>3.2</td>
<td>0.0037</td>
</tr>
<tr>
<td>Late relapse (&gt;1 yr)</td>
<td>7.4</td>
<td>4.7</td>
<td>0.0226</td>
</tr>
</tbody>
</table>

Nogova, et al., JCO 2008

LPHL: Late and Continuous Relapses

Diehl, et al., JCO 1999
LPHL: Late and Continuous Relapses: Regardless of the initial stage

Treatment 1988-2002
Early: RT alone
Intermediate: chemo + RT
Advanced: chemo +/- RT
Chemo = COPP/ABVD, ABVD, BEACOPP

N = 394

LPHL: Transformation

- Tendency to develop aggressive NHL (typically diffuse large B cell lymphoma) either concurrently or subsequently
- Incidence 0.6 to 9.8%
- Time to transformation is variable, can be years later
- Long term remission after transformation has been reported

Transformation to Aggressive NHL: the Vancouver study

- Patients: n = 95 from 1965 to 2006
- Pathology reassessment performed
- Stage I/II: n = 64, advanced stage: n = 31
- PFS: 86% at 5 yrs, 73% at 10 yrs
- OS: 94% at 5 yrs, 91% at 10 yrs
- Most common cause of death is secondary NHL: n = 5 (33%)
- No death from refractory LPHL
- Splenic involvement with LPHL is a risk factor for future NHL transformation

Al-Mansour, et al., JCO 2010
LPHL: Risk of Transformation and Outcome

Al-Mansour, et al., JCO 2010

Time to Transformation

OS and PFS after transformation (Median f/u after transformation 8.1yrs)

| Total N = 95 | Transformed n = 13 (14%) |

LPHL: Treatment Approaches

- Early stage:
  - Watchful waiting
  - Radiotherapy alone
  - Chemo + radiotherapy
- Advanced stage
  - chemo +/- radiotherapy
- Experimental treatment
  - Rituximab

LPHL: Treatment Approaches

Pellergrino et al., JCO 2003

No therapy: 7/13 relapsed
With therapy: 2/14 relapsed

Treatment: Watchful Waiting in Children

Pellergrino et al., JCO 2003
RT for Early Stage LPHL:
Involved field is the standard

Nogova, et al., Annals of Oncology 2005

Prospective Studies of Rituximab in LPHL

<table>
<thead>
<tr>
<th>Prospective Study</th>
<th>Rituximab schedule</th>
<th>No. pts</th>
<th>Disease status</th>
<th>ORR/CR %</th>
<th>PFS/mFU months</th>
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<tbody>
<tr>
<td>Rehwald, 2003</td>
<td>standard</td>
<td>10</td>
<td>relapsed</td>
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<td>relapsed</td>
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<td>33/63</td>
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<td>Ekstrand, 2003</td>
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<td>22</td>
<td>10 relapsed</td>
<td>100/41</td>
<td>10.2/13</td>
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<tr>
<td></td>
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<td>23</td>
<td>11 relapsed</td>
<td>97/56</td>
<td>24/72</td>
</tr>
<tr>
<td></td>
<td>extended</td>
<td>16</td>
<td>9 untreated</td>
<td>97/88</td>
<td>NR/30</td>
</tr>
</tbody>
</table>

* Extended: wkly x 4, q6mos for 2 yrs


Summary

• LPHL is a distinct entity and differs from classical HL
• Indolent clinical course, high response rate and favorable survival
• Late relapses are not uncommon
• Transformation to diffuse large B cell lymphoma
• IF Radiotherapy for early stage disease
• Chemotherapy +/- RT for advanced disease
• Rituximab has excellent activity and should be considered in the setting of clinical trials
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6. Rituximab plus chemotherapy

Pt has been in CR2 for 2+ yrs

Thank You

Dr. Thomas Hodgkin
1798 - 1866
Radiotherapy for Early Stage LPHL: Long-term follow-up

Chen, et al., JCO 2010

N = 113
FU 136 mos

LPHL: Late and continuous relapses regardless of initial stage

Orlandi, et al., Leukemia and Lymphoma 1997