Lymphoma Tumor Board
Friday, November 18, 2016
Plasmablastic lymphoma
Plasmablastic lymphoma - Background

- Aggressive lymphoma associated with HIV infection and other conditions associated with immune deficiency
- B-cell lineage, but CD20-negative
- Immunophenotype of tumor cells generally resembles that of plasma cells
- Median age at diagnosis is 40-60
- Predilection for the oral cavity, nasal cavity, gastrointestinal tract, skin, bone soft tissue, and lung
- Morphology resembles that of Burkitt lymphoma with a “starry sky” appearance
  - HHV-8 (KSHV) typically not detected
  - EBV positive in 75%
PBL biology: GC reaction in primary follicle


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PBL: Histopathologic features in HIV+ setting


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Immunophenotype of plasmablastic lymphoma

- Viewed as clinicopathologic variant of DLBCL
- Castillo *et al.* studied phenotypic variability within PBL to identify a specific IHC profile that would reliably distinguish it from DLBCL
- Markers studied:
  - CD20
  - PAX5
  - BCL6
  - CD10
  - GCET1
  - KLHL6
  - IRF4/MUM1
  - PRDM1/BLIMP1
  - XBP1
  - CD38
  - CD138
  - Ki-67(MIB-1)
  - p53
  - ISH for EBV EBER
- Plasmablastic lymphoma comprises two primary immunophenotypes
PBL immunophenotype: lack of expression of CD10 and CD20; reliable expression of IRF4/MUM1 and MYC; high Ki-67

Expression of PAX5, CD20, PRDM1/BLIMP1, XBP1 characterizes the immunophenotype of plasmablastic lymphoma
Phenotypic heterogeneity in plasmablastic lymphoma

<table>
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<tr>
<th></th>
<th>HE</th>
<th>CD20</th>
<th>PAX5</th>
<th>BLIMP1</th>
<th>XBP1</th>
<th>CD138</th>
<th>EBER</th>
<th>GCET1</th>
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Santiago Montes-Moreno et al. *Haematologica* 2010;95:1342-1349

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### Differential diagnosis of PBL and related lymphomas

#### Table 3. Differential diagnosis of PBL

<table>
<thead>
<tr>
<th></th>
<th>PBL</th>
<th>Plasmablastic myeloma</th>
<th>LBCL HHV-8-positive</th>
<th>IBL DLBLC</th>
<th>ALK-positive DLBCL</th>
<th>DLBCL ACI</th>
<th>PEL</th>
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<tr>
<td>Disease distribution</td>
<td>Extranodal</td>
<td>Bone marrow and extranodal</td>
<td>Nodal</td>
<td>Nodal</td>
<td>Nodal</td>
<td>Extranodal</td>
<td>Extranodal</td>
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<tr>
<td>HIV infection</td>
<td>~70%</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Pathogenesis</td>
<td>EBV, HIV, IL-10</td>
<td>IL-6</td>
<td>HHV-8, MCD</td>
<td>ALK</td>
<td>EBV, IL-10, IL-6</td>
<td>HHV-8</td>
<td></td>
</tr>
<tr>
<td>Positive markers</td>
<td>CD138, IRF-4/MUM-1, MYC</td>
<td>CD138, cytoplasmic Ig, MYC</td>
<td>CD20&lt;sup&gt;+&lt;/sup&gt;, CD138&lt;sup&gt;+/−&lt;/sup&gt;, IgM</td>
<td>CD20, PAX-5, CD4, CD45</td>
<td>CD20, CD4</td>
<td>IRF-4/MUM-1, CD30&lt;sup&gt;−/+&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Negative markers</td>
<td>CD20, PAX-5</td>
<td>CD20, PAX-5, BCL-6</td>
<td>CD138</td>
<td>CD20, CD30, MYC</td>
<td>ALK</td>
<td>PAX-5, CD20, CD138, Ig</td>
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<tr>
<td>Proliferation rate</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
<td>~80%</td>
<td>&gt;90%</td>
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<td>Cytoplasmic immunoglobulin</td>
<td>50%-70%</td>
<td>&gt;90%</td>
<td>IgA λ</td>
<td>Uncommon</td>
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<tr>
<td>EBV infection</td>
<td>Common</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Common</td>
</tr>
<tr>
<td>EBV latency pattern</td>
<td>I</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>III</td>
<td>I</td>
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<tr>
<td>HHV-8 infection</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Molecular genetics</td>
<td>MYC GR</td>
<td>Myeloma FISH abnormalities</td>
<td>Unmutated Ig</td>
<td>MYC GR</td>
<td>t(2;17)(p23;q23)</td>
<td>TP53 mutations</td>
<td>Hypermutated Is mutations</td>
</tr>
</tbody>
</table>

ACI, associated with chronic inflammation; ALK, anaplastic lymphoma kinase; FISH, fluorescence in situ hybridization; GR, gene rearrangement; IBL, immunoblastic; IL, interleukin; IRF-4/MUM-1, interferon regulatory factor 4/multiple myeloma 1; LBCL, large B-cell lymphoma; NA, not available; PEL, primary effusion lymphoma.
Treatment of plasmablastic lymphoma

• Progosis is generally poor
• MYC rearrangements have been shown to be associated with shorter OS
• CHOP, infusional EPOCH, hyperCVAD, and CODOX-M/IVAC are mainstays of therapy
• Intrathecal prophylaxis should be considered
• In the US, “first-line treatment of PBL is 6 cycles of infusional dose-adjusted EPOCH (with or without bortezomib) with intrathecal prophylaxis with each cycle of EPOCH and consideration of consolidative HDC followed by autologous SCT in first remission for appropriate candidates.”
• HIV+ individuals should be started on cART and optimized to ensure there are no interactions between anticancer agents and cART
Treatment of plasmablastic lymphoma - NCCN

### NCCN Guidelines Version 4.2014
AIDS-Related B-Cell Lymphomas

#### TREATMENT

**Antiretrovirals** can be administered safely with chemotherapy; however, some regimens have recommended discontinuation. Any change in antiviral therapy should be done in consultation with an infectious disease specialist.

- **Suggested regimens:**
  - CODOX-M/IVAC (modified)
  - Dose-adjusted EPOCH
  - HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine)
  - Standard CHOP is not adequate therapy

**Plasmablastic lymphoma**

- Consider high-dose methotrexate
- Consider RT alone
- For select patients with good performance status on HAART, see [NCCN Guidelines for CNS- Primary CNS Lymphoma](#)
- Best supportive care (See [NCCN Guidelines for Palliative Care](#))

**Primary CNS lymphoma**

- Consider prophylaxis for tumor lysis syndrome (See [NHODG-B](#))
- See monoclonal antibody and viral reactivation (NHODG-B)

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<sup>See references for regimens (AIDS-A).</sup>

<sup>Management can also apply to HIV-negative plasmablastic lymphoma.</sup>
Survival in plasmablastic lymphoma vs. DLBCL

Santiago Montes-Moreno et al. Haematologica 2010;95:1342-1349
Significance of PRDM1/BLIMP1 expression in DLBCL and plasmablastic lymphoma

Santiago Montes-Moreno et al. Haematologica 2010;95:1342-1349

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Significance of EBV in plasmablastic lymphoma

A
Kaplan-Meier Curve in all PL patients

B
Kaplan-Meier Curve in EBV+PL versus EBV- patients

Camille Laurent et al. Haematologica 2016;101:976-984
Summary – Plasmablastic lymphoma

• Uncommon subtype of B-cell lymphoma
• No well-recognized standard of care
• Poor prognosis
• Intrathecal agents should be used to minimize the risk of CNS involvement/relapse
• New immunohistochemical profiles have been studied for better characterization of plasmablastic lymphoma
• Chemotherapy with CHOP, infusional EPOCH, hyperCVAD, and CODOX-M/IVAC are commonly used for treatment at this time
• Current treatment is inadequate and better regimens are needed
References


• NCCN Guidelines: https://www.nccn.org/professionals/physician_gls/f_guidelines.asp#nhl

• ASH Image Bank: http://imagebank.hematology.org/

• https://en.wikipedia.org/wiki/Plasmablastic_lymphoma

• Cover Image: http://www.dovemed.com/diseases-conditions/plasmablastic-lymphoma/