Lymphomas of the Head and Neck

Patrick Treseler, MD, PhD
University of California San Francisco

Head & Neck Lymphomas: Update on Distinctive Entities

1. Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
2. Extranodal NK/T-cell lymphoma, nasal type
3. Plasmablastic lymphoma

Distinctive Lymphomas of the Head & Neck

1. Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
2. Extranodal NK/T-cell lymphoma, nasal type
3. Plasmablastic lymphoma
MALT lymphoma of H&N

- Clinical features:
  - Typically arises in setting of lymphoid hyperplasia associated with autoimmune disorders (LESA, Hashimoto’s thyroiditis) or chronic infection (conjunctivitis due to *C. psittaci*)
  - Can present as mass/swelling or no symptoms
  - Most low stage (I/II) at presentation, good prog.
MALT lymphoma of H&N

- Immunophenotype:
  - Most have “B-cell, NOS” phenotype, but aberrant CD43 expression seen in nearly half of cases
  - Plasma cells monotypic in about one-third of cases
  - CD5+ cases rare but well described
**Differential Diagnosis**

**Benign:**
- Lymphoepithelial sialadenitis (LESA)
- Chronic sclerosing sialadenitis

**Malignant:**
- Lymphoplasmacytic lymphoma and other small B-cell lymphomas
- Extramedullary plasmacytoma

---

**Lymphoepithelial sialadenitis**

- Previously known as myoepithelial sialadenitis (MESA), benign lymphoepithelial lesion, & Mikulicz disease
- Characterized by marked infiltration of small lymphocytes (mainly T-cells) into atrophic salivary gland parenchyma
- May form mass or be asymptomatic
- LESA increase risk of salivary gland lymphoma up to 44-fold (most are MALT lymphomas)\(^4\)
Lymphoepithelial sialadenitis

Transformation to MALT lymphoma

Earliest histopathologic indicators:
- Monocytoid small B-cells not only in the LELs, but outside as well, forming broad halos or sheets
- Sheets of plasma cells (stain for kappa/lambda)
MALT lymphoma of H&N

Differential Diagnosis

- Benign:
  - Lymphoepithelial sialadenitis (LESA)
  - Chronic sclerosing sialadenitis

- Malignant:
  - Lymphoplasmacytic lymphoma and other small B-cell lymphomas
  - Extramedullary plasmacytoma

Chronic sclerosing sialadenitis

- Also known as Küttner tumor, and almost exclusively affects submandibular gland, producing large firm gland that mimics tumor
- One of the family of IgG4-related fibrosclerosing diseases that include autoimmune pancreatitis, but has been described in virtually every organ
- Major histopathologic features are 1) dense lymphoplasmacytic infiltrate, 2) storiform fibrosis, and 3) obliterative phlebitis, but latter two features can be absent in head & neck sites (salivary glands, lacrimal gland)!

IgG4-Related Disease of Salivary Gland

MALT lymphoma of H&N

Differential Diagnosis

- **Benign:**
  - Lymphoepithelial sialadenitis (LESA)
  - Chronic sclerosing sialadenitis
- **Malignant:**
  - Lymphoplasmacytic lymphoma and other small B-cell lymphomas
  - Extramedullary plasmacytoma

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>
</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>MZL/LPL</td>
<td>+</td>
<td>-</td>
<td>-/+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

(Cyclin D1)

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

MALT lymphoma of H&N

Differential Diagnosis

- **Benign:**
  - Lymphoepithelial sialadenitis (LESA)
  - Chronic sclerosing sialadenitis
- **Malignant:**
  - Lymphoplasmacytic lymphoma and other small B-cell lymphomas
  - Extramedullary plasmacytoma
**Extramedullary Plasmacytoma**

- Clonal tumor-forming neoplasm of plasma cells occurring outside the bone/bone marrow in the absence of a clinical evidence of myeloma at presentation
- 80% occur in upper aerodigestive tract, most commonly in nasal cavity, paranasal sinuses, nasopharynx, & oropharynx, usually good prognosis
- Composed of sheets of mature plasma cells, with typical plasma cell phenotype (CD20- CD138+ cIg+)
- But extranodal MZL can have variable proportions of mature plasma cells, occ. quite high, causing them to resemble EMP

**Kappa**  **Lambda**  **CD20**
Question Time!

Q: What is the difference between an extranodal marginal zone lymphoma with extensive/extreme plasmacytic differentiation and a plasmacytoma?

A: Maybe nothing (at least in some cases)

Extramedullary Plasmacytoma: A Form of Extranodal MZL?

Hussong et al. AJCP 111:111; 1995

Extra-osseous plasmacytomas can share many features with MALT lymphoma:
- Predilection for mucosa surfaces
- Often have some monocytoid or CCL cells
- Often form LELs if epithelium present
- Some have classic extranodal MZL before or after dx EMP
- Do well with conservative therapy, no progression to myeloma

"We hypothesize that EMPs not associated with MM, whether in mucosal sites or LNs, may represent MZL with extensive plasmacytic differentiation"
Distinctive Lymphomas of the Head & Neck

1. Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
2. Extranodal NK/T-cell lymphoma, nasal type
3. Plasmablastic lymphoma

Extranodal NK/T-cell Lymphoma, Nasal Type

Key Features:
- Malignant lymphoma that typically co-expresses:
  - NK-cell marker CD56, T-cell markers (CD2, CD43, CD45RO, and sometimes CD7), & cytotoxic proteins (TIA-1, etc.)
  - But usually not CD5, CD4, CD8, TCRαβ, or TCRγδ.
- Surface CD3- (flow), but cytoplasmic CD3ε+ (IHC)
- Almost universally EBV+ by ISH (“diagnosis should be accepted with some skepticism if EBV is negative”)
- Most are NK-cells (TCR germline), minority are T-cells (TCR rearranged), but behavior & treatment are similar
- Nasal cavity, nasopharynx, palate most common sites
- Cytologic composition highly variable, often angiocentric

"Settled Law" in the DDx of NK/T-Cell Lymphoma (per 2008 WHO)

- If a CD3ε+ lymphoma is CD56 negative, it can still be NK/T-cell lymphoma, provided it is positive for both:
  - EBV (i.e., EBER), and
  - Cytotoxic proteins (i.e., TIA-1, granzyme B, perforin)
- But if negative for either EBV or cytotoxic granule proteins (while still CD3ε+), it goes to category of PTCL, NOS

Remember, many of these lymphomas are clonal T-cell neoplasms, and they can lack NK marker CD56, but still need to be cytotoxic T-cells (and probably EBV+ too)!
CD5

CD56

EBV-ISH

EBV-ISH
Q: Can you have an extranasal extranodal nasal-type NK/T-cell lymphoma?
A: Yes, well described in skin, GI tract, lung, testis, eye, other sites per WHO.

Q: Are there NK/T-cell lymphomas other than nasal-type?
A: Apparently not. NK-cell neoplasms in 2008 WHO are:
- Extranodal NK/T-cell lymphoma, nasal type
- Aggressive NK-cell leukemia
- Chronic lymphoproliferative disorder of NK cells
- NK lymphoblastic leukemia/lymphoma

Q: Can you have a nodal extranodal nasal-type NK/T-cell lymphoma?
A: Yes, 2008 WHO cites rare reports of primary lymph node disease in the absence of extranodal disease (but “extranodal” part of official WHO name)
**NK/T-cell Lymphoma**

**Differential Diagnosis:**

- **Benign:**
  - Reactive lymphoid hyperplasia

- **Malignant:**
  - Peripheral T-cell lymphoma, NOS
  - Other NK-cell malignancies
  - Other CD56+ malignancies

---

**Reactive Lymphoid Hyperplasia**

- Mimics NK/T-cell lymphoma because:
  - Extranodal reactive lymphoid cells often mildly atypical, form dense and monomorphc infiltrates that are mixture of T-cells and NK-cells with few B-cells
  - In Wegener’s, may be angiocentric with necrosis

- **Not** NK/T-cell lymphoma because:
  - Reactive hyperplasia will not show sheet-like growth of CD3ε+ CD56+ TIA-1+ EBER+ cells
  - Typically lacks destructive infiltration of mucosa, ulceration, high mitotic rate often seen in NK/TCL
  - Never show high-grade cytologic atypia of virtually all cells seen in many cases of NK/TCL

---

**NK/T-cell Lymphoma**

**Differential Diagnosis:**

- **Benign:**
  - Reactive lymphoid hyperplasia

- **Malignant:**
  - Peripheral T-cell lymphoma, NOS
  - Other NK-cell malignancies
  - Other CD56+ malignancies
Peripheral T-cell lymphoma

- Lack of CD56 and both EBV and cytotoxic proteins puts them in category of PTCL, NOS per current WHO criteria
- “Gray zone” could exist for cases showing expression of multiple T-cell markers not typical of NK/TCL (CD5, CD4, CD8, TCRαβ, and/or TCRγδ), particularly if EBV negative
- PTCL, NOS can show variable expression of CD56, EBV, and cytotoxic proteins, but in isolation these are insufficient for NK/TCL dx

NK/T-cell Lymphoma

Differential Diagnosis:

- Benign:
  - Reactive lymphoid hyperplasia
- Malignant:
  - Peripheral T-cell lymphoma, NOS
  - Other NK-cell malignancies
  - Other CD56+ malignancies

Other NK-cell malignancies

- WHO recognizes three such disorders, all rare:
  - Aggressive NK-cell leukemia (EBV+)
  - Chronic lymphoproliferative disorder of NK-cells
  - NK-lymphoblastic leukemia/lymphoma
- Tissue infiltrates could mimic NK/T-cell lymphoma because of NK-cell phenotype
- All distinguishable from NK/T-cell lymphoma on basis clinical features (presentation as aggressive leukemia) and/or phenotype (weak to absent CD56, absent EBV)

NK/T-cell Lymphoma

Differential Diagnosis:

- Benign:
  - Reactive lymphoid hyperplasia
- Malignant:
  - Peripheral T-cell lymphoma
  - Other NK-cell malignancies
  - Other CD56+ malignancies
**Other CD56+ malignancies**

- Many high-grade malignancies can appear vaguely lymphoid and express CD56, sometimes along T-cell markers, and arise in head and neck, principally:
  - Myeloid sarcoma/acute myeloid leukemia
  - Blastic plasmacytoid dendritic cell neoplasm
  - Plasmacytoma/myeloma
  - Ewing sarcoma/PNET
  - Rhabdomyosarcoma
- All distinguishable from NK/T-cell lymphoma on basis clinical features and/or phenotype

---

**Plasmablastic Lymphoma**

**Key Features:**

- Aggressive variant of diffuse large B-cell lymphoma
- Composed of large cells +/- plasmacytoid differentiation
- CD20 and Pax-5 expression generally negative but weak staining (<25% of cells) in some cases, CD45- or weak
- Often presents in oral cavity, but can also involve other mainly extranodal sites
- Patients mainly HIV+, other immunocompromised
- Frequently EMA+, rare keratin+ cases reported
- Very poor prognosis, median survival 6-7 months

---

**Distinctive Lymphomas of the Head & Neck**

1. Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
2. Extranodal NK/T-cell lymphoma, nasal type
3. Plasmablastic lymphoma
Plasmablastic Lymphoma

Subtypes per Colomo et al. (AJSP 28:736; 2004)

- Plasmablastic lymphoma, oral mucosa type
- Plasmablastic lymphoma with plasmacytic differentiation

PBL, oral mucosa type


<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex/Age/O</th>
<th>Primary Localization</th>
<th>Other Sites of Involvement</th>
<th>Immunosuppression</th>
<th>EBV</th>
<th>LMP-1</th>
<th>Stage</th>
<th>Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/22</td>
<td>Oral mucosa</td>
<td>CNS</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>I</td>
<td>Dead (26)</td>
</tr>
<tr>
<td>2</td>
<td>M/37</td>
<td>Oral mucosa</td>
<td>CNS</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>I</td>
<td>Dead (7)</td>
</tr>
<tr>
<td>3</td>
<td>M/41</td>
<td>Oral mucosa</td>
<td>Orbital, eyelid, skin,</td>
<td>HIV+</td>
<td>-</td>
<td>-</td>
<td>IV</td>
<td>Dead (44)</td>
</tr>
<tr>
<td>4</td>
<td>F/41</td>
<td>Oral mucosa</td>
<td>Muscularis, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M/35</td>
<td>Oral mucosa</td>
<td>Bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M/75</td>
<td>Oral mucosa</td>
<td>Bone marrow, LN</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M/19</td>
<td>Oral mucosa</td>
<td>Bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>F/36</td>
<td>Oral mucosa</td>
<td>Bone marrow, LN</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M/54</td>
<td>Oral mucosa</td>
<td>Bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>M/49</td>
<td>Oral mucosa</td>
<td>Bone marrow, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>M/49</td>
<td>Oral mucosa</td>
<td>Bone marrow, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>M/45</td>
<td>Bone marrow</td>
<td>Bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>M/55</td>
<td>Bone marrow</td>
<td>Bone marrow, LN</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>M/50</td>
<td>Bone marrow</td>
<td>Bone marrow, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>M/55</td>
<td>Bone marrow</td>
<td>Bone marrow, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>M/55</td>
<td>Bone marrow</td>
<td>Bone marrow, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>F/11</td>
<td>Bone marrow</td>
<td>Bone marrow, bone marrow</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>M/57</td>
<td>Lymph node</td>
<td>Plasmacytic nodular</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>M/57</td>
<td>Lymph node</td>
<td>Plasmacytic nodular</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>M/37</td>
<td>Lymph node</td>
<td>Plasmacytic nodular</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>M/32</td>
<td>Lymph node</td>
<td>Plasmacytic nodular</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>M/36</td>
<td>Lymph node</td>
<td>Plasmacytic nodular</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>M/41</td>
<td>Lymph node</td>
<td>Plasmacytic nodular</td>
<td>HIV+</td>
<td>+</td>
<td>-</td>
<td>IV</td>
<td></td>
</tr>
</tbody>
</table>

Oct-2
PBL, with plasmacytic diff.


<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex/Age (yr)</th>
<th>Localization</th>
<th>Immunosuppression</th>
<th>EBV</th>
<th>EBER</th>
<th>LMP-1</th>
<th>Stage</th>
<th>Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>M/42</td>
<td>Oral mucosa</td>
<td>HIV−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>IV</td>
<td>Alive (4)</td>
</tr>
<tr>
<td>25</td>
<td>F/44</td>
<td>Oral mucosa</td>
<td>HIV−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>IV</td>
<td>Alive (6)</td>
</tr>
<tr>
<td>26</td>
<td>M/37</td>
<td>Lymph node</td>
<td>HIV−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>II</td>
<td>Dead (5)</td>
</tr>
<tr>
<td>27</td>
<td>M/35</td>
<td>Lymph node</td>
<td>No</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>III</td>
<td>Dead (8)</td>
</tr>
<tr>
<td>28</td>
<td>F/47</td>
<td>Lymph node</td>
<td>No</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>III</td>
<td>Dead (5)</td>
</tr>
<tr>
<td>29</td>
<td>F/65</td>
<td>Lymph node</td>
<td>No</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>III</td>
<td>Dead (5)</td>
</tr>
<tr>
<td>30</td>
<td>M/52</td>
<td>Gastrintestinal tract</td>
<td>HIV−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>IV</td>
<td>Dead (1)</td>
</tr>
<tr>
<td>31</td>
<td>F/51</td>
<td>Lymph node</td>
<td>No</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>I</td>
<td>Alive (12)</td>
</tr>
<tr>
<td>32</td>
<td>M/66</td>
<td>Rectum</td>
<td>No</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>II</td>
<td>Dead (6)</td>
</tr>
<tr>
<td>33</td>
<td>M/55</td>
<td>Testicular</td>
<td>No</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>M/60</td>
<td>Nasal cavity</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>F/66</td>
<td>Skin</td>
<td>No</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>M/30**</td>
<td>Soft tissue, sacrum</td>
<td>HIV−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>I</td>
<td>Alive (40)</td>
</tr>
<tr>
<td>37</td>
<td>F/30</td>
<td>Small and large bowel</td>
<td>Crohn’s disease</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>M/55</td>
<td>Lymph node</td>
<td>No</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>F/71</td>
<td>Lymph node</td>
<td>No</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

*10–25% EBV+ cells by ISH.

Secondary Extramedullary Plasmablastic Tumor (EPT)
Colomo et al. AJSP 28:736.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex/Age (yr)</th>
<th>Localization</th>
<th>Immunosuppression</th>
<th>EBV</th>
<th>EBER</th>
<th>LMP-1</th>
<th>Associated Plasma Cell Disorder</th>
<th>Follow-up (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>M/34</td>
<td>Soft tissue, bone marrow transplant</td>
<td>Bone-marrow transplant</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM treated with BM transplant, 6 months before</td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>M/39</td>
<td>Testicular</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM, previous EBV+ nasal</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>M/51</td>
<td>Lymph node</td>
<td>No</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>Plasmacytoma, 2 years before</td>
<td>Dead** (1)</td>
</tr>
<tr>
<td>43</td>
<td>M/67</td>
<td>Lymph node</td>
<td>No</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>Vertebral plasmacytoma—MM, 4 years and 9 months</td>
<td>Dead (6)</td>
</tr>
<tr>
<td>44</td>
<td>M/39</td>
<td>Soft tissue, bone marrow transplant</td>
<td>Bone-marrow transplant</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM, multisite</td>
<td>Dead (18)</td>
</tr>
<tr>
<td>45</td>
<td>F/35</td>
<td>Breast</td>
<td>No</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM, previous</td>
<td>Dead (18)</td>
</tr>
<tr>
<td>46</td>
<td>M/31</td>
<td>Skin, skull, bone marrow</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM, unusual</td>
<td>AWD (4)</td>
</tr>
<tr>
<td>47</td>
<td>M/77</td>
<td>Skin</td>
<td>No</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM, 4 years before</td>
<td>Dead (4)</td>
</tr>
<tr>
<td>48</td>
<td>M/98</td>
<td>Bladder</td>
<td>No</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>MM, 2 months before</td>
<td>AWD (2)</td>
</tr>
</tbody>
</table>

MM, multiple myeloma; BM, bone marrow; AWD, alive with disease.
**Death of another cause.
Plasmablastic lymphoma

Differential Diagnosis:

- Malignant:
  - Anaplastic plasmacytoma
  - ALK+ diffuse large B-cell lymphoma
  - Poorly differentiated non-lymphoid malignancies, esp. undifferentiated nasopharyngeal ca, Schmincke pattern

*Original term used for tumor that would today be called PBL*¹⁴

Plasmablastic lymphoma

Differential Diagnosis:

- Malignant:
  - Anaplastic plasmacytoma*
  - ALK+ diffuse large B-cell lymphoma
  - Poorly differentiated non-lymphoid malignancies, esp. undifferentiated nasopharyngeal ca, Schmincke pattern

ALK+ large B-cell lymphoma

Differential Diagnosis:

- Malignant:
  - Anaplastic plasmacytoma
  - ALK+ diffuse large B-cell lymphoma
  - Poorly differentiated non-lymphoid malignancies, esp. undifferentiated nasopharyngeal ca, Schmincke pattern

- Very rare variant of DLBCL (<40 cases reported)
- Wide age range pediatric → adult
- Typically presents in lymph nodes, but some extranodal (including nasopharynx, tongue), often advanced stage
- Tumor cells resemble immunoblasts or plasmablasts, but can be RS-like, and typically infiltrate lymph node sinuses
- Has CD20- Pax5- Oct2+ plasma cell phenotype, CD45- or weak (overlap with plasmablastic lymphoma).
- Some cases EMA+ and keratin+
- ALK staining typically cytoplasmic & granular, and due to t(2;17) linking ALK with CLTC gene.
- Median surv. 11 mo. (some pediatric long-term survivors)
**Plasmablastic lymphoma**

*Differential Diagnosis:*
- Malignant:
  - Anaplastic plasmacytoma
  - ALK+ diffuse large B-cell lymphoma
  - Poorly differentiated non-lymphoid malignancies, esp. undifferentiated nasopharyngeal ca, Schmincke pattern

---

**UNPC, Schmincke Pattern**

- UNPC is a subtype of non-keratinizing nasopharyngeal carcinoma in 2005 WHO Classification
- Typically small primary with cervical lymph LN metastases
- Tumor cells large cells and loosely cohesive (“syncytial growth pattern”) mimicking large lymphoid cells, with heavy background infiltrate of small lymphocytes
- In Schmincke pattern, tumor cells present as single cells, small clusters, or ill-defined sheets, mimicking lymphoma (Regaud pattern has more obvious epithelial aggregates and sheets).
- Tumor cells EBV+, up to 20% keratin-negative, creating further confusion with large cell lymphomas such as PBL
References

References
