The story of the two headed monster

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Once upon a time...

- 72 year old, previously healthy man.
- Hospitalized on June 2019 for investigation of newly diagnosed pancytopenia, seen on routine blood tests. (previous test on 2016 was normal).

- Blood count:
  - WBC 1.3K
  - 5% blasts
  - 27% neutrophils – abs 350

- Hb 8.5, anisocytosis, poikilocytosis, tear drops
- PLT 73K
Bone marrow 1–16/6/2019

- **Cytology** – prominent dysplastic changes 5% blasts.

- **Biopsy results** (mid July)
  * 60% cellularity
  * myeloid lineage – left shift, almost without maturation.
  15% blasts (MPO, CD117)
  * Dysplastic changes on red cell lineage and megakaryocytes.

- Biopsy is pending. The patient is well, blood counts are stable.

- **MDS with excess of blasts II.**
- **IPSS high risk**
- **Hypomethylating agent (+HSC donor search)**
24/7/2019

• Severe and sudden clinical deterioration (weak, weight loss, ascites, bilateral leg edema, pleural effusion).

• Blood counts are stable.

• Albumin 3.4 → 2.7
LDH 1000 → 3300
uric acid 6.0 → 10.3
Bone marrow 2– 25/7/2019

- **Cytology –**
  * Hypercellular bone marrow
  * Severe dysplastic changes
  * **18% Blasts** (only half have myeloid immunophenotype. The other half - ?)

- **Pathology –**
  * Severe dysplastic changes – trilineage.
  * **Almost 20% myeloblasts**

**MDS in leukemic transformation?**
• NPM1, FLT3, INV16, t(8;21) – neg

• NGS – positive for U2AF1  VAF 33%
But something else is lurking...

• Cytology –
  Lymphocytic infiltrate, pathologic, clonal B cells
  CD19  CD20  KAPPA

• pathology –
  CD20 and BCL6 demonstrate groups of large and small lymphocytes – consistent with lymphoma.
• Lymphadenopathy:
  - mediastinal
  - supra diaphragmatic
  - axillary
  - celiac
  - retroperitoneal
  - iliac
  - inguinal

• Omental implants

• Ascites, pleural effusion, pericardial effusion.

• Needle biopsy from inguinal lymph node –
  DLBCL, non-GCB, high proliferation index
MDS IN LEUKEMIC TRANSFORMATION

DLBCL, non-GCB, high proliferation index
Time for battle

• Seems like the **lymphoma** is the more aggressive disease.
• Starting treatment with R-CHOP, very reduced dose.

• **After one cycle** – dramatic improvement in the patient’s general condition.
  - Ascites, leg edema and pleural effusion are receding.
  - LDH $7300 \rightarrow 360$
  - Albumin $2.7 \rightarrow 3.5$
  - Blood counts are stable
Time for battle

• Continuing treatment with R-CHOP, gradually increasing doses. **No treatment related complications.**

• Blood counts are improving:
  
  WBC 4000
  Hb 12.4
  plt 197
Reassessment

• PET-CT (after cycle 5):
  - The lymphoadenopathy receded.
  - No FDG uptake
  - The ascites, pleural effusion and pericardial effusion receded.

• No sigh of active lymphoma.
Reassessment

• Bone marrow (27/10, after cycle 4):
  • **Cytology:** Hypercellular bone marrow, normal morphology.
  • **Pathology:** Hypercellular bone marrow (60%), -- myeloid hyperplasia (GCSF) with less than 4% blasts. Normal maturation of the myeloid lineage. -- Erythroid lineage and megakaryocytes are normal (some dysplastic megakaryocytes). -- No lymphoproliferative infiltrate.
The table shows the karyotype analysis results:

<table>
<thead>
<tr>
<th>G-Banding</th>
<th>46, XY</th>
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<tbody>
<tr>
<td>Metaphase</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td></td>
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<tr>
<td>10</td>
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</tbody>
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The karyotype is 46, XY, indicating a normal male karyotype.
Clinical significance of cytogenetic aberrations in bone marrow of patients with diffuse large B-cell lymphoma: prognostic significance and relevance to histologic involvement


<table>
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<tr>
<th>Chromosome</th>
<th>Description</th>
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<tbody>
<tr>
<td>45, X0</td>
<td>del(4)(q34), del(6)(q12q23), inv(13), add(14)(q32)</td>
</tr>
<tr>
<td>46, XY</td>
<td>+18, del(6)(q12q23), add(14)(q32)</td>
</tr>
</tbody>
</table>

**Clinical Abnormalities**

- Good: Normal, del(17q), del(5q), del(12p), del(20q), double including del(5q)
- Intermediate: -7/7q-, +8, i(17q), +19, +21, any other single, double, independent clones
- Poor: der(3)(q21)/der(3)(q26), double including -7/7q-, complex (three abnormalities)
- Very poor: complex (more than three abnormalities)

The most frequently involved chromosomal abnormalities (n = 150) were trisomy 18. The predominant specific cytogenetic aberrations were trisomy 18, -7, -7q-, +8, +19, +21, any other single, double, or independent clones. The well-known oncogenes and lymphoma-
Time for round two

- January 2020 – HDMTX
- February 2020 – blood counts are dropping: WBC 2K, Hb 10.7, plt 125
- Peripheral blood Blasts counts is rising to 20%.

- Bone marrow cytology: no excess of blasts (?)
- Pathology is pending.
- Normal karyotype.