SH/EAHP WORKSHOP PRESENTATION

CASE: SH2017-0028
9-8-2017

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Clinical history

• 73 year old male with history of elevated immunoglobulin (IgM) diagnosed with monoclonal gammopathy of undetermined significance (MGUS) in 2009.

• At that time per report his bone marrow findings were within normal limits.

• Since then pt. had slow increase in IgM levels and minimal cytopenia

• Clinical symptoms were significant for fatigue and night sweats.

• Eventually diagnosed with low grade symptomatic LPL and treated with one dose of Rituximab. Patient was transferred to our institution for second opinion and treatment
Bone marrow aspirate & Bx - Significant for hypercellularity, trilineage dyspoiesis with mild monocytosis, small lymphoplasmacytic aggregates

Ancillary studies

- Flow cytometry – myeloid, lymphoid and plasma cell immunophenotype
- Cytogenetics
  - Karyotype
  - FISH analysis: MDS panel
- Molecular (foundation 1)
Dysmegakaryopoiesis
Dysgranulopoiesis

Mild dyserythropoiesis
~5% plasma cells

Small lymphoid aggregate
Hypercellular marrow

Blue-Lymphoid aggregate

Orange-Megakaryocyte
Case summary: Ancillary tests findings:

- Flow cytometry- Immunophenotype:
  - CD5 negative kappa light chain restricted B cell population (0.5% of all analyzed events)
  - Kappa restricted plasma cell population
  - No increase in myeloblasts (0.6% by flow with normal immunophenotype)
  - Mild increase in monocytes

Chromosomal analysis: normal male karyotype, and no evidence of an acquired clonal abnormality.

FISH: No evidence of numeric or structural abnormalities of chromosomes 5, 7, 8, 11, 13, or 20

NGS (F1) CD19 sorted-DNA: (genomic alterations in MYD88 L265P, ARID2 N156fs*3 and ASXL1 E635fs*15.)
Diagnosis:

- CHRONIC MYELOMONOCYTIC LEUKEMIA (CMML-o)
- LOW LEVEL INVOLVEMENT BY LYMPHOPLASMACYTIC LYMPHOMA
Case summary: Clinical correlation

Upon discussion with the clinician and with the concern for bone marrow involvement by CMML, the clinician mentioned noticing patients gum hyperplasia – which lead to gum biopsy.
Case summary: Gum biopsy

Gum biopsies from right, left and middle gum, all were received fresh and a repeat bone marrow biopsy

Ancillary studies

• Flow cytometry – Myeloid immunophenotype
• Cytogenetics
  • Karyotype
  • FISH analysis: MDS/AML panel
• Molecular (foundation 1)
Ancillary tests findings: Gum biopsy

- Chromosome analysis: Unsuccessful cell culture
- FISH: No evidence of monosomy 5, deletion 5q, t(8;21), t(11q23) or inv(16).
- NGS (F1) unsorted-DNA: Genomic alterations in STAG2 T244fs*7 and ASXL1 E635fs*15

- NGS performed on concurrent whole bone marrow aspirate showed:
  - NGS(F1) CD34 sorted-DNA: ASXL1 E635fs*15 and STAG2 T244fs*7
  - NGS( reference lab) unsorted-DNA: ASXL1 E635fs*15
Summary of NGS studies and points to discuss:

<table>
<thead>
<tr>
<th>Tissue</th>
<th>sample</th>
<th>lab</th>
<th>Results</th>
<th>VAF- %</th>
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</thead>
<tbody>
<tr>
<td>BM (at presentation)</td>
<td>CD19+ cells (low purity)</td>
<td>F1</td>
<td>ASXL1</td>
<td>28</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>ARID2</td>
<td>15</td>
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<td>MYD88</td>
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<tr>
<td>Gum( 4 weeks after presentation)</td>
<td>unsorted</td>
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<td>ASXL1</td>
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<tr>
<td></td>
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<td>STAG2</td>
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<tr>
<td>BM ( 4 weeks after presentation)</td>
<td>CD34+ cells</td>
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<td>STAG2</td>
<td>58</td>
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<tr>
<td>BM( 4 weeks after presentation)</td>
<td>unsorted</td>
<td>Reference lab*</td>
<td>ASXL1</td>
<td>NA</td>
</tr>
</tbody>
</table>

* The panel didn’t include MYD88, STAG2 and ARID2
Proposed Diagnosis:

ASXL1 positive Incidental myeloid sarcoma diagnosed in a patient with lymphoplasmacytic lymphoma (LPL).

Panel Diagnosis:

Occult myeloid sarcoma (in a patient with lymphoplasmacytic lymphoma).
Thank you