Topic: Myeloid Neoplasms with TP53 mutation

Discussants:  
Dr. Robert Hasserjian  
Dr. Joseph Khoury

Case presented and session moderated by:  
Dr. Xueyan Chen  
SH Education Committee

11/28/2023 11 AM EST
Clinical Information

- 70 year old male with a history of DLBCL post chemotherapy
- Presented with cytopenias.
- Work-up for nutritional deficiency was negative.
- Feeling more fatigued than usual.
Peripheral blood findings

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blasts</td>
<td>2</td>
</tr>
<tr>
<td>Promyelocytes</td>
<td>2</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>1</td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>1</td>
</tr>
<tr>
<td>Band Neutrophils</td>
<td>1</td>
</tr>
<tr>
<td>Seg. Neutrophils</td>
<td>70</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0</td>
</tr>
<tr>
<td>Basophils</td>
<td>0</td>
</tr>
<tr>
<td>Monocytes</td>
<td>11</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>13</td>
</tr>
<tr>
<td>Atypical Lymphs</td>
<td>3</td>
</tr>
<tr>
<td>Other Cells</td>
<td></td>
</tr>
<tr>
<td>Erythroblasts (NRBCs)</td>
<td>0</td>
</tr>
</tbody>
</table>

WBC: 3.8/k/uL
Hemoglobin: 9.6 g/dL
Hematocrit: 26.8%
MCV: 90 fL
Platelets: 111/k/uL
Details of Microscopic Findings (bone marrow biopsy)

13% blasts aspirate differential
Details of Microscopic Findings (bone marrow biopsy)
Immunophenotype (flow cytometry)

- Positive for CD13, CD33, CD34, CD117, CD4, CD64, CD11c, CD123, CD11b, HLA-DR, cMPO
- Negative for CD14, CD15, CD56, cCD3, CD19
Cytogenetics

- **Karyotype:**
  - 47,XY,+Y,-3,del(5)(q13q33),del(7)(q11.2),-17,add(20)(q11.2),+r,+mar[18]/47,idem,add(19)(q13.1)[2]/46,XY[1]

- **FISH:**
  - The AML/MDS panel of probes showed loss of EGR1(5q) in 79% of cells, loss of one copy of D7S486(7q) in 85% of cells, loss of one copy of TP53(17p) in 75% of cells and a loss of one copy of both signals on 20q in 84% of the cells.
## Trusight Myeloid Panel Results

<table>
<thead>
<tr>
<th>Gene</th>
<th>Variant</th>
<th>VAF</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETV6</td>
<td>c.799C&gt;T (p.Q267*)</td>
<td>37%</td>
<td>Tier I: Strong clinical significance</td>
</tr>
<tr>
<td>TP53</td>
<td>c.371dupG (p.C124Wfs*25)</td>
<td>66%</td>
<td>Tier I: Strong clinical significance</td>
</tr>
</tbody>
</table>
Questions posed to the discussants

- What is your diagnosis for this case?
CASE 2 PRESENTATION
Clinical Information

- 62 year old female presented with tachycardia when hiking.
- She was found to have anemias and transfused 2 units of RBCs.
- She had no significant past medical history.
- A bone marrow biopsy was performed.
Peripheral Blood

- CBC data
  - WBC 3.0 K/ul
  - Hgb 7.3 g/dL
  - Hct 22%
  - MCV 106 fL
  - RDW 18.9%
  - PLT 222 K/uL
- WBC Differential
  - Neutrophils 41%
  - Lymphocytes 49%
  - Monocytes 3%
  - Eosinophils 4%
  - Basophils 3%
Bone Marrow Aspirate

- Differential
  - Myeloid: 73%
  - Erythroid: 9%
  - Blasts: 1%
  - Lymphocytes: 15%
  - Plasma cells: 2%
  - M:E ratio: 8:1
Bone Marrow Biopsy
Immunophenotype

• Myeloid blasts are 1.3% of white blood cells with expression of CD34, CD117, HLA-DR, CD38, CD33, CD13 (decreased), partial/low-level CD11b, and partial/low-level CD7 without expression of other markers tested.

• No abnormal myelomonocytic maturation.

• No abnormal B cell population identified.
Cytogenetics

- Karyotype:
  - 46,XX,del(5)(q11.2),der(12;13)(q10;q10),+13[14]/46,XX[6]

- FISH:
  - Deletion of 5q in 60% nuclei analyzed
  - Del(7q), trisomy 8, del(17p), del(20q) not detected
Molecular Studies

• Mutations with functional impacts:
  – DNMT3A p.Glu814* (NM_022552.4:c.2440G>T), VAF 2%
  – TP53 p.Gly245Ser (NM_000546.5:c.733G>A), VAF 30%

• Other variants: No other mutations detected.

• GENES IN PANEL:
  – ABL1, ANKRD26, ASXL1, BCOR, BRAF, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A, ETNK1, ETV6, EZH2, SF3B1, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2
Questions posed to the discussants

- What is your diagnosis for this case?