Case SH2017-0068

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• Nothing to disclose
Clinical History

• A 46 year-old male with CML for 3 years presented with abdominal pain and laboratory findings concerning for blast crisis

• PMH:
  – The patient had been in chronic phase for 3 years
  – BCR-ABL+
  – Initially was treated with nilotinib; complicated by pancreatitis
  – Switched to imatinib; no hematologic response
  – Non compliant; ultimately switched to dasatinib
Peripheral Blood

- WBC: 88.47 th/ μL (H)
- ANC: 18.99 th/ μL (H)
- HGB: 7.8 g/dL (L)
- PLT: 65 th/ μL (L)
Preliminary Diagnosis

• Chronic myeloid leukemia, blast phase (myeloid)
Clinical Course

• The patient received induction chemotherapy with high dose cytarabine and mitoxantrone

• Day 13 BMBx: Marked hypocellular marrow (5%) with fibrosis and scattered maturing granulocytes and occasional atypical immature cells
Blood(spec): 46,XY,t(9;22),t(15;17)
FISH: Positive for RARA and BCR-ABL gene rearrangements
Final Diagnosis

Chronic myeloid leukemia, BCR-ABL1+, in blast phase, with PML-RARA+
Clinical Course - Continue

• Day 40 BMBx: Relapsed APL (90% cellular; 20% blast)
• Arsenic, ATRA in addition to dasatinib were started
  – Course complicated by possible differentiation syndrome, for which the patient received 3 day course of dexamethasone
• Day 99 BMBx: Remission from APL, but continued chronic phase CML
After the 3rd cycle of arsenic

- The patient presented with severe bilateral frontal headaches associated with nausea, vomiting, photophobia, and dizziness
- CSF fluid: Positive for APL by cytomorphology, flow cytometry, and qRT-PCR
Clinical Course – Continue

• The patient was hospitalized for a total of 102 days in 9 months
• CNS disease did not respond to IT chemotherapy or PETHEMA consolidation (idarubicin, ATRA, and cytarabine)
• The patient died after 7 months of CNS involvement
Discussion

• Our patient never achieved remission from CML
• ABL1 kinase mutation was negative
• Duration from chronic phase to promyelocytic crises: 3 years
• The patient died 17 months after APL was first diagnosed
Review of the literature

• Promyelocytic blast crisis of CML with PML-RARA+ was first reported by Berger et al. in 1983
• Only 12 cases have been reported in the literature
• Age range: 22-85 years (mean: 51)
• M>F
• Duration from chronic phase to blastic crisis: 6 months - 3 years
• Chung et al. and Kashimura et al. reported remission with imatinib in combination with ATRA and arsenic trioxide
<table>
<thead>
<tr>
<th>Case/year of pub</th>
<th>age/sex</th>
<th>Duration from CML to blast crisis</th>
<th>Immunophenotyping</th>
<th>Extramedullary APL</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>1/1983</td>
<td>37/M</td>
<td>8 months</td>
<td>-</td>
<td>Skin</td>
<td>Died of APL relapse after 16 months</td>
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<tr>
<td>2/1984</td>
<td>38/M</td>
<td>24 months</td>
<td>-</td>
<td>Lymph node</td>
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<td>3/1987</td>
<td>85/F</td>
<td>10 months</td>
<td>-</td>
<td>-</td>
<td>Died of DIC in 2 days</td>
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<tr>
<td>4/1987</td>
<td>31/M</td>
<td>26 months</td>
<td>-</td>
<td>-</td>
<td>Died of DIC within 3 months</td>
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<tr>
<td>5/1990</td>
<td>50/M</td>
<td>3 yrs</td>
<td>-</td>
<td>-</td>
<td>Unknown</td>
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<tr>
<td>6/1995</td>
<td>52/F</td>
<td>3 yrs</td>
<td>-</td>
<td>-</td>
<td>Died of septic shock after 6 weeks</td>
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<tr>
<td>7/1995</td>
<td>55/M</td>
<td>2 yrs</td>
<td>CD13+, HLA-DR partial (23%); neg for other myeloid and lymphoid markers</td>
<td>-</td>
<td>CML chronic phase; loss f/u</td>
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<tr>
<td>8/1997</td>
<td>60/M</td>
<td>3 yrs</td>
<td>CD45+, CD13+, CD33+, CD34+, CD9+, CD14+ HLA-DR-</td>
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<td>Died of septic shock within 3 weeks</td>
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<td>9/2003</td>
<td>22/M</td>
<td>Unknown</td>
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<td>“CNS Leukemia”</td>
<td>CML chronic phase</td>
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<td>10/2008</td>
<td>32/M</td>
<td>6 months</td>
<td>CD13+, CD33+, CD117+; CD34-, HLA-DR-</td>
<td>-</td>
<td>Remission</td>
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<td>11/2010</td>
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<td>7 months</td>
<td>CD13+, CD33+ CD34-, HLA-DR-</td>
<td>-</td>
<td>Remission</td>
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<tr>
<td>12/2014</td>
<td>82/F</td>
<td>2 yrs</td>
<td>Unknown</td>
<td>-</td>
<td>Unknown</td>
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</table>
References


• Castaigne, Sylvie, et al. "Promyelocytic blast crisis of chronic myelocytic leukemia with both t (9; 22) and t (15; 17) in M3 cells." Cancer 54.11 (1984): 2409-2413.


Final Panel Diagnosis

Chronic myeloid leukemia, BCR-ABL1+, in blast phase, with PML-RARA+