Acute Myeloid Leukemia: The Aga Khan experience

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AML

- Characterized by an increase in the number of myeloid cells in the marrow and an arrest in their maturation

- Granulocytopenia, thrombocytopenia, or anemia

- Leukocytosis.
Epidemiology

- United States
  - Annual incidence - 2.4 per 100,000
  - 12.6 per 100,000 > 65 years
  - Median age approx. 25 to 30 years
  - 5YSR <65 yr less than 40%

<table>
<thead>
<tr>
<th>FAB Subtype</th>
<th>Common Name</th>
<th>Results of Staining</th>
<th>Associated Translocations and Rearrangements</th>
<th>Genes Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>Acute myeloblastic leukemia with minimal differentiation (3%)</td>
<td>−</td>
<td>−</td>
<td>inv(3q26) and t(3;3) (1%)</td>
</tr>
<tr>
<td>M1</td>
<td>Acute myeloblastic leukemia without maturation (15–20%)</td>
<td>+</td>
<td>+</td>
<td>t(8;21) (40%), t(6;9) (1%)</td>
</tr>
<tr>
<td>M2</td>
<td>Acute myeloblastic leukemia with maturation (25–30%)</td>
<td>+</td>
<td>+</td>
<td>t(15;17) (98%), t(11;17) (1%), t(5;17) (1%)</td>
</tr>
<tr>
<td>M3</td>
<td>Acute promyelocytic leukemia (5–10%)</td>
<td>+</td>
<td>+</td>
<td>11q23 (20%), inv(3q26) and t(3;3) (3%), t(6;9) (1%)</td>
</tr>
<tr>
<td>M4</td>
<td>Acute myelomonocytic leukemia (20%)</td>
<td>+</td>
<td>+</td>
<td>11q23 (20%), inv(16), t(16;16) (80%)</td>
</tr>
<tr>
<td>M4E0</td>
<td>Acute myelomonocytic leukemia with abnormal eosinophils (5–10%)</td>
<td>+</td>
<td>+</td>
<td>inv(16), t(16;16) (80%)</td>
</tr>
<tr>
<td>M5</td>
<td>Acute monocytic leukemia (2–9%)</td>
<td>−</td>
<td>−</td>
<td>11q23 (20%), t(8;16) (2%)</td>
</tr>
<tr>
<td>M6</td>
<td>Erythroleukemia (3–5%)</td>
<td>+</td>
<td>+</td>
<td>t(1;22) (5%)</td>
</tr>
<tr>
<td>M7</td>
<td>Acute megakaryocytic leukemia (3–12%)</td>
<td>−</td>
<td>−</td>
<td>t(1;22) (5%)</td>
</tr>
</tbody>
</table>

*Cells are positive for myeloid antigen (e.g., CD13 and CD33).
†Cells are positive for α-naphthylacetate and platelet glycoprotein IIb/IIIa or factor VIII–related antigen and negative for naphthylbutyrate.
AML

- **Primary**
- **Secondary**
  - From CMML
  - Myelodysplastic syndromes
  - Chemotherapy
  - Congenital neutropenia, Blooms syndrome, Fanconis anemia
Bone Marrow Audit: AKUH

- Feb 2003 to Feb 2006
- To determine the relative frequencies of hematological malignacies
- To establish the AML subtypes in our patients
Patients

- 356 pts
- 18 mo. To 91 yrs
- Male 180 (50.6%)
- Female 176 (49.4%)
Indications

- Anaemia 26.9%
- PUO 17.5%
- Pancytopenia 17.1%
- Possible leukemia 10.9%
- Leukoerythroblastic picture 7.5%
- Staging lymphomas 6.1%
- Monocytopenias 5%
- Undetermined 9%
## Findings

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myeloid leukemia</td>
<td>29</td>
<td>8.6%</td>
</tr>
<tr>
<td>Lymphoproliferative disorder</td>
<td>24</td>
<td>6.7%</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>20</td>
<td>5.6%</td>
</tr>
<tr>
<td>Myeloproliferative disorder/myelodysplastic syndrome</td>
<td>9</td>
<td>2%</td>
</tr>
<tr>
<td>Metastatic tumour</td>
<td>9</td>
<td>2%</td>
</tr>
<tr>
<td>Acute lymphoblastic</td>
<td>6</td>
<td>1.7%</td>
</tr>
</tbody>
</table>
AML: FAB subtypes

- M0 – 2 (6.7%)
- M1 – 7 (23%)
- M2 – 11 (36%)
- M3 – 2 (6.7%)
- M4 – 5 (16%)
- M5 – 3 (10%)
- M6 – 1 (3.3%)
- M7 – 0
AML: Patients characteristics

- Male – 18 (60%)
- Female – 12 (40%)
- Avg. age – 45yrs (22 – 85yrs)
Outcomes

- Declined treatment – 10
- Died while undergoing treatment – 8
- On follow up – 1
- Lost to follow up - 10
Outcomes

- Average hospital stay – 30 days
- Cost – avg Sh. 1.2m (564,000 – 2.6m)
Complications

- Severe thrombocytopenia
- Febrile neutropenia
- Cellulitis
- Metrorrhagia
- Blood reaction
- Depression
- Diarrhoea
Complications

- Purulent conjunctivitis
- UTI
- Anemia
- Alopecia
Treatment

- Complete remission approx 0.65%
- Decreases with increasing age and the presence of unfavorable cytogenetic abnormalities.
- With postremission therapy, disease-free survival at five years ranges from 10 to 15% with low-dose maintenance therapy to 25 to 35% with intensive courses of chemotherapy.
Chemotherapy

Adriamycin 70mg od *3/7
Cytosine arabinoside Ara-C 300mg od *5/7

Then

• Ara C 2g IV infusion x2/7
Complete Remission

- Blood neutrophil > 1500
- Plt > 100,000
- No blasts in circulation
- Bone marrow
  - >20% trilineage maturation
  - <5% blasts
Bone marrow transplant

• Allogeneic or autologous bone marrow transplant may not give any additional benefit to high dose cytarabine
• 740 pts, 70% went into remission
• More studies on the pipeline

• Nejm Volume 339:1649-1656
• 1998
Figure 1. Probability of Disease-free Survival According to Postremission Therapy.
<table>
<thead>
<tr>
<th>Factors Used to Predict Response to Induction Chemotherapy</th>
<th>Factors Used to Predict Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfavorable karyotype</td>
<td>Unfavorable karyotype</td>
</tr>
<tr>
<td>Age &gt; 60 yr</td>
<td>Age &gt; 60 yr</td>
</tr>
<tr>
<td>Secondary AML</td>
<td>Delayed response to induction</td>
</tr>
<tr>
<td>Poor performance score*</td>
<td>chemotherapy</td>
</tr>
<tr>
<td>Features of multidrug resistance</td>
<td>Features of multidrug resistance</td>
</tr>
<tr>
<td>White-cell count of &gt; 20,000/mm³</td>
<td>White-cell count of &gt; 20,000/mm³</td>
</tr>
<tr>
<td>Unfavorable immunophenotype</td>
<td>Female sex</td>
</tr>
<tr>
<td>CD34 positivity†</td>
<td>Elevated lactate dehydrogenase</td>
</tr>
<tr>
<td></td>
<td>level</td>
</tr>
<tr>
<td></td>
<td>Autonomous growth of leukemic</td>
</tr>
<tr>
<td></td>
<td>cells</td>
</tr>
</tbody>
</table>

*The extent of a patient’s disabilities are assessed according to a well-defined set of criteria.\(^{50}\)

†Unlike the other factors listed, this factor is considered to be minor.
### Table 4. Patients Completing Assigned Therapy in Randomized Trials of Bone Marrow Transplantation for Acute Myeloid Leukemia.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients Remaining in the Study after Complete Remission</th>
<th>Patients Assigned to Therapy Who Completed the Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Autologous Bone Marrow Chemotherapy*</td>
</tr>
<tr>
<td></td>
<td>Number</td>
<td>Number (percent)</td>
</tr>
<tr>
<td>Current study</td>
<td>346/518</td>
<td>106/117 (91)</td>
</tr>
<tr>
<td>Zittoun et al.15</td>
<td>422/623</td>
<td>104/126 (83)</td>
</tr>
<tr>
<td>Burnett et al.16</td>
<td>759/1509</td>
<td>186/191 (97)</td>
</tr>
<tr>
<td>Harousseau et al.17</td>
<td>252/367</td>
<td>71/78 (91)</td>
</tr>
<tr>
<td>Ravindranath et al.18</td>
<td>321/552</td>
<td>113/117 (97)</td>
</tr>
</tbody>
</table>

* Patients were randomly assigned to therapy.

† Patients were assigned to therapy on the basis of the availability of a suitable donor. NA denotes not available.
Thank You