Bone Marrow Transplant for Acute Leukaemia in Childhood: Experience in Singapore.

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The percentage of long term leukaemia-free survival in "good prognosis" childhood acute leukaemia is at least 50% \(^1\). The cure rate for the high risk acute lymphoblastic leukaemia (ALL) and acute non-lymphoblastic leukaemia (ANLL) is poorless than 20% \(^2\). Experience to date indicates that bone marrow transplant (BMT) is an acceptable mode of curative therapy for acute leukaemia \(^3\)\(^-\)\(^4\). BMT allows two potential therapeutic advantages over standard therapy. One, it allows high intense chemotherapy for cytoreduction of leukaemic cells as infusion of marrow "rescues" the patient from a potentially lethal therapy. Secondly, the graft-versus-host effect post-transplant may provide an immune effect against residual leukaemic cells. The best results of BMT were in patients transplanted with histocompatible allogeneic bone marrow and in first remission \(^5\).

In Singapore, we have initiated a transplant program and five children had been transplanted for curative therapy of their acute leukaemia or CML.

The demographic and clinical data of these children are given in Table 1. They were 15 years and younger and underwent BMT for ALL, ANLL or CML in blast crisis (BC). Two of them were given syngeneic marrow and the rest HLA-matched and MLR non-reactive allogeneic marrow. The patients were prepared for allogeneic or syngeneic BMT with cyclophosphamide (CY), 50mg/kg/d on each of two consecutive days starting day -5 (Fig. 1). This was followed by fractionated total body irradiation (TBI) delivered at 20Gy/fraction over three days. The child with CML in BC was given high dose busulphan (4mg/kg/d) on each consecutive 4 days instead of TBI and followed by 4 days of CY 50mg/kg/d. Except for the first two transplants, subsequent BMT patients were given mesna as prophylaxis against hemorrhagic cystitis. The last three patients were given high dose intravenous immunoglobulin containing high titre antibodies against CMV. Allogeneic recipients were given methotrexate (MTX), 10mg/m\(^2\) on day 1,3,5,7 and 11, cyclosporin A (CSP) mg/kg for GVHD prophylaxis at least 6 months. CSP dose was tapered after 2 months. Patients were nursed with strict reverse barrier techniques with all procedures.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Dx</th>
<th>Status</th>
<th>BMT Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>12</td>
<td>T-ALL</td>
<td>Remission 1</td>
<td>Syngeneic</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>12</td>
<td>ANLL (M1)</td>
<td>Remission 1</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>12</td>
<td>ANLL (M4)</td>
<td>Remission 1</td>
<td>Allogeneic</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>8</td>
<td>C-ALL</td>
<td>Remission 3</td>
<td>Syngeneic</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>15</td>
<td>CML</td>
<td>Early BC</td>
<td>Allogeneic</td>
</tr>
</tbody>
</table>
BMT PREPARATIVE REGIMEN - ACUTE LEUKAEMIA

<table>
<thead>
<tr>
<th>CY 60mg/kg</th>
<th>TBI 120 Gy total</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ ↓ ↓ ↓ ↓ ↓</td>
<td>↓ ↓ ↓ ↓ ↓ ↓</td>
</tr>
<tr>
<td>-5 -4 -3 -2 -1 0 1 2 3 4 5</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. BMT prepalative regimen-Acute leukemia
done aseptically. No oral gut decontamination
was done. Engraftment was considered to have
occurred when neutrophil count exceeds $5 \times 10^8$
/ l. The outcome and complicatins of these B
MTs are summarised in Table II.

Syngeneic BMT.
Two children received syngeneic BMT. Both
had ALL, one T-ALL and the other C-ALL in
third remission. Both are alive, however, the
one with C-ALL relapsed after 9 months. He is
now in remission after a further course of che-
motherapy. A second BMT was considered from
a HLA-compatible allogeneic sib but none was
found. Both suffered from fever and mild to
moderate mucositis but these symptoms sub-
sided in the second week when engraftment
took place. The boy with T-ALL developed Her-
pes Zooster (HZ) on day 11 which resolved with
intravenous acyclovir. There were no other
complications.

Allogeneic BMT
Three children received allogeneic marrow
from their sibs. All three patients have died.
The first allogeneic BMT (child 2) developed
interstitial pneumonitis (IP) on day 105. His lung
function deteriorated rapidly despite resusi-
tative measures. A limited post-mortem confirmed
presence of a IP. There was no patholog-
evidence of CMV but culture grew CMV.
Child number 4 relapsed after a year in the CN S
with subsequent relapse in the marrow. He
was reinduced with high dose Ara-C and dauno-
rubicin. He went into a partial remission (10% blasts). This was followed by high dose
busulphan/CY and BMT from the original do-
nor. Marrow engrafted but he relapsed after a
month. Subsequent reinduction with chemother-
rapy was unsuccessful. The third allogeneic
BMT was performed on a girl with CML in
blast crisis. She developed BC one year post-
diagnosis of CML. Remission was induced with
vincristine/prednisolone and daunorubicin. She
died of complications of BMT on day 9 : acute
GVHD and CY/daunorubicin cardiomypathy.

Graft-versus-host disease
GVHD did not develop in the syngeneic B
MT as expected. The two patients with ANLL
developed mild Grade I skin GVHD which resol-
ved with oral prednisolone. The girl developed
Grade III GVHD with the main manifestation
in the skin. Mild diarrhea and mild elevation
of liver enzymes were noted. She was treated
with intravenous methylprednisolone 10mg/kg
infused over 1 hour. She died before complete
resolution of the GVHD. A limited post-mortem
confirmed GVHD and marrow engraftment.

IN SUMMARY
In our limited experience, we note that BMT
in children is associated with minimal compli-

Table 2. BMT Complications and outcome

<table>
<thead>
<tr>
<th>Patient</th>
<th>Acute GVHD</th>
<th>Chronic GVHD</th>
<th>Infections</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>nil</td>
<td>nil</td>
<td>HZ-D11</td>
<td>Remission years</td>
</tr>
<tr>
<td>2</td>
<td>Grade 1-skin</td>
<td>Grade 1-Skin</td>
<td>IP-D105</td>
<td>Death-D105</td>
</tr>
<tr>
<td>3</td>
<td>nil</td>
<td>Facial-grade 1</td>
<td>nil</td>
<td>Relapsed 1 year</td>
</tr>
<tr>
<td>4</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>Remission 9 mths</td>
</tr>
<tr>
<td>5</td>
<td>Grade 3-skin</td>
<td>nil</td>
<td>nil</td>
<td>Death-D15</td>
</tr>
</tbody>
</table>
cations. Only one developed moderate GVHD. Except for an incidence of HZ, there was no severe bacterial or fungal infections. The children tolerated the preparative regime well. Engraftment occurred in all patients. Two deaths were related to complications of BMT: IP and acute GVHD and chemotherapy cardiomyopathy. One death was due to leukaemia relapse.

REFERENCES


