Single Center Experience with Hematopoietic Cell Transplantation in Young Children with Chronic Granulomatous Disease

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Introduction

• Chronic granulomatous disease (CGD) is a primary immune deficiency caused by defects in the NADPH oxidase subunits.
• The only potentially curative option for CGD is hematopoietic cell transplantation (HCT).
• Risks of HCT, including graft-versus-host disease (GvHD), complications of chemotherapy, and death, have often deterred physicians and patients from pursuing HCT early.1
• We reviewed the outcomes of HCT for CGD patients performed at our institution between August 2005 – October 2018.

Results

• Eight patients underwent HCT: 6 X-linked, 2 autosomal recessive
• Median age of transplant: 2.2 y
• Pretransplant infectious complications:
  • Pneumonia in 3 patients (#3, 6, 8), lobectomy in 2 (#6, 8)
  • Lymphadenitis/skin abscesses in 3 (#1, 4, 5)
• Pretransplant inflammatory complications:
  • Lung granulomas in 2 patients (#1, 7)
  • Autoimmune hepatitis in 3 (#1, 2, 4)
  • Colitis in 2 (#2, 3)
• 3 received myeloablative conditioning, 5 received reduced intensity/toxicity conditioning
• All received 10/10 matched HCT, 4 related donors and 4 unrelated.
• Median neutrophil engraftment: 18.5 days
• All achieved primary engraftment, 1 had secondary graft failure at 1 yr s/p HCT
• 42% (3/7) maintain full donor chimerism, median follow-up 4.3 yr
• 42% (3/7) are mixed chimeria, median follow-up 1.4 yr
• Overall survival: 87.5%

Discussion

• Majority of published transplant cohorts involve older children, adolescent, and adult patients. 1,2,3
• Our institution’s experience demonstrates safety and efficacy with early HCT in patients with CGD.
• RTC using Bu/Flu/ATG appears to be well tolerated, even in very young children.

Table 1. Patient Characteristics and Outcomes of HCT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Gene</th>
<th>Age at diagnosis</th>
<th>Age at transplant</th>
<th>Donor</th>
<th>Pre-Conditioning</th>
<th>Outcome (length of follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>CYBB</td>
<td>2.5 y</td>
<td>4.16 y</td>
<td>10/10 MUD</td>
<td>Bu/Flu/ATG (MAC)</td>
<td>Full donor chimerism (8.3 y)</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>CYBA</td>
<td>&lt;1 mon</td>
<td>4.25 y</td>
<td>10/10 MRD</td>
<td>Mel/Flu/Thio/ATG (MAC)</td>
<td>Deceased, disseminated Trichosporon day +21</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>CYBB</td>
<td>2 mon</td>
<td>1.83 y</td>
<td>10/10 MRD</td>
<td>Bu/Cytosan (MAC)</td>
<td>Full donor chimerism (4.3 y) Grade I GvHD, Pericarditis, Hypothyroidism</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>CYBA</td>
<td>4 mon</td>
<td>2.5 y</td>
<td>10/10 MRD</td>
<td>Mel/Flu/Camphath (RIC)</td>
<td>Secondary graft failure at 1 y Granulomatous pneumonitis, uveitis, CGD-colitis</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>CYBB</td>
<td>3 mon</td>
<td>1.08 y</td>
<td>10/10 MUD</td>
<td>Bu/Flu/ATG (RTC)</td>
<td>Full donor chimerism (4 y) AIHA, ITP</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>CYBB</td>
<td>21 mon</td>
<td>3.75 y</td>
<td>10/10 MRD</td>
<td>Bu/Flu/ATG (RTC)</td>
<td>Mixed chimera, 93% (1.4 y)</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>CYBB</td>
<td>8 mon</td>
<td>1.58 y</td>
<td>10/10 MUD</td>
<td>Bu/Flu/ATG (RTC)</td>
<td>Mixed chimera, 60% (1.0 y)</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>CYBB</td>
<td>15 mon</td>
<td>1.66 y</td>
<td>10/10 MUD</td>
<td>Bu/Flu/ATG (RTC)</td>
<td>Mixed chimera, 70% (1.4 y) Grade I GvHD, EBV viremia</td>
</tr>
</tbody>
</table>

MUD = matched unrelated donor; MRD = matched related donor; Bu = busulfan, Flu = fludarabine, ATG = anti-thymocyte globulin, Mel = melphalan, Thio = thiotepa

References