Hemopoietic Progenitor Cell Collection in Tandem with Hemodialysis for Patients with M-Protein Disorders

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M-proteins and M-protein Disorders

• **M-protein**
  - Monoclonal immunoglobulin and/or free light chains
  - Produced by malignant clone of plasma cells

• **M-protein disorders**
  - Serum (plasma) M-protein
    - Renal impairment
    - Disordered Hemostasis
    - Altered plasma viscosity
  - Syndrome-specific clinical effects
    - Multiple myeloma
    - Amyloidosis
    - Waldenström’s macroglobulinemia
Multiple Myeloma

• Epidemiology
  – Median age 61♀, 62♂
  – 1-4 per 100,000 per year
  – 12,650 US deaths in 2016

• Renal Impairment
  – 20-40% at diagnosis
  – 10% need dialysis at diagnosis

• Median survival
  – Conventional treatment: 3-4 years
  – Auto HPC transplant: 5-7 years

• Apheresis in multiple myeloma
  – Many will receive plasma exchange while also receiving hemodialysis
  – All will be offered autologous HPC collection, including those receiving hemodialysis
Renal Impairment in Multiple Myeloma

- Nephrotoxic effects of monoclonal light chains (LC)
  - Cast nephropathy ("myeloma kidney") in 90% of cases
    - PCT light chain receptors (megalin and cubilin) overwhelmed
    - Light chains combine with Tamm-Horsfall protein in distal tubules
  - Amyloidosis
  - Light chain deposition: PCT
    - Local stimulation of IL-6, TNFα by LC
    - Interstitial fibrosis

- Contributing factors
  - Dehydration
  - Hypercalcemia
  - Hyperuricemia
  - Drugs (NSAIDs, antibiotics)
Survival after Transplants for Multiple Myeloma, 2003-2013

- Autologous (n=37,385)
  - 75% ± 1%
- Allogeneic (n=1,012)
  - 52% ± 2%

p < 0.001

By Donor Type
Can Peripheral Blood HPC Collection be Performed in Tandem with Hemodialysis?

What would be the effect on

- Efficacy of the hemodialysis procedure
- Collection efficiency of hemopoietic progenitor cells
- Engraftment
Case Report (LA)

- 72 y/o ♂ with κ light chain myeloma
- Myeloma kidney requiring hemodialysis
- Poor response to initial chemotherapy
- Offered high intensity treatment
  - Intensive chemotherapy x 2
  - Autologous transplantation
    - Mobilization from course #2
    - HPC collection by apheresis
Apheresis Considerations
- Spectra LRS Turbo ver 7.0
- WBFR 80-100 ml/min
- Blood volumes processed limited by the duration of HD
- Anticoagulant
  - ACD-A 500 mL bags
  - 0.8 mL/min/L patient blood volume
  - Heparin 3000 U/bag ACD-A
- No supplemental calcium

Hemodialysis Considerations
- Gambro Phoenix 2
- Fresenius polysulfone dialyzer
- Electrolytes (mEq/L)
  - Na⁺ 141
  - Ca²⁺ 2.5
  - HCO₃⁻ 35
  - K⁺ 2.0
- QB 300-400 ml/min
- 4 hour dialysis
- Laboratory parameters
  - BUN pre- and post-dialysis
  - [Ca]ᵢ pre- mid- and post-
Tandem HPC Collection and Hemodialysis
Outcome of Tandem HPC Collection and HD

Efficacy of hemodialysis (urea reduction ratio):

$$URR = 100 \times \frac{[BUN]_{\text{PRE}} - [BUN]_{\text{POST}}}{[BUN]_{\text{PRE}}}$$

Collection efficiency (CE) of hemopoietic progenitor cells:

$$CE = 100 \times \frac{[CD34^+]_{\text{PROD}} \times VOL_{\text{PROD}}}{[CD34^+]_{\text{BLOOD}} \times VOL_{\text{BLOODPROC}}}$$

- Hemodynamic stability of patient during tandem procedures
- Ionized calcium during the procedures
- Number of CD34^+ cells collected
- Engraftment
## Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Gender</th>
<th>M-Protein Disorder</th>
<th>Indication for Hemodialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>72 y/o ♂</td>
<td>κ light chain multiple myeloma</td>
<td>Cast nephropathy</td>
</tr>
<tr>
<td>JC</td>
<td>59 y/o ♂</td>
<td>κ light chain multiple myeloma</td>
<td>Cast nephropathy</td>
</tr>
<tr>
<td>FR</td>
<td>74 y/o ♂</td>
<td>λ light chain multiple myeloma with plasma cell leukemia</td>
<td>Cast nephropathy</td>
</tr>
<tr>
<td>SM</td>
<td>60 y/o ♂</td>
<td>IgG κ multiple myeloma with amyloidosis</td>
<td>Hypertensive renal disease and cast nephropathy</td>
</tr>
</tbody>
</table>
## HPC Collection Parameters and Outcomes

<table>
<thead>
<tr>
<th>Pt</th>
<th>Blood Vol (L)</th>
<th>CD34⁺ Count (per µL)</th>
<th>Collection Time (min)</th>
<th>Blood Volumes Processed</th>
<th>Product Volume (mL)</th>
<th>CD34⁺ Collected (x10⁶/kg)</th>
<th>CD34⁺ CE (%)</th>
<th>URR (%)</th>
<th>Day of Engraftment</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>4.655</td>
<td>48</td>
<td>212</td>
<td>3.84</td>
<td>407</td>
<td>8.93</td>
<td>70.7</td>
<td>73.9</td>
<td>11</td>
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<tr>
<td>JR</td>
<td>4.473</td>
<td>80</td>
<td>216</td>
<td>4.33</td>
<td>417</td>
<td>11.7</td>
<td>53</td>
<td>§</td>
<td>10</td>
</tr>
<tr>
<td>FR</td>
<td>6.675</td>
<td>16</td>
<td>181</td>
<td>2.7</td>
<td>347</td>
<td>1.91</td>
<td>84</td>
<td>62.5</td>
<td>‡</td>
</tr>
<tr>
<td>FR</td>
<td>6.643</td>
<td>57</td>
<td>185</td>
<td>2.77</td>
<td>355</td>
<td>5.45</td>
<td>65</td>
<td>67.7</td>
<td></td>
</tr>
<tr>
<td>SM</td>
<td>3.350</td>
<td>88</td>
<td>244</td>
<td>4.63</td>
<td>366</td>
<td>6.38</td>
<td>27¶</td>
<td>73.4</td>
<td>‡</td>
</tr>
</tbody>
</table>

§ Not measured. BUN was 16 mg/dL on day of procedure.
‡ Expired while awaiting hospitalization for autologous transplantation.
¶ Peripheral WBC count was 148.6 x 10³/µL on the morning of collection procedure.
Pulse Rate Not Significantly Changed During Tandem HD/HPC Collection

Graph showing the pulse rate over procedure time for different patients (LA, JC, FR1, FR2, SM), with a significance level of $p=0.625$. The procedure time ranges from 0 to 250 minutes, and the pulse rate is measured in beats per minute.
Mean Arterial Pressure Remains Stable During Tandem HD/HPC Collection

$p = 0.188$
Ionized Calcium Remains Stable During Tandem HD/HPC Collection

Reference range: 4.6-5.3 mg/dl

\[ [\text{Ca}^{2+}]_{i} \text{ mg/dl} \]

Beginning    Midpoint    End

LA          JC          FR1         FR2          SM

\[ p=0.954 \]
Tandem HD/HPC Collection

- HPC collection can safely be performed in tandem with hemodialysis
- Tandem procedures do not compromise the efficiency of HPC collection or the efficacy of hemodialysis
- Tandem-collected HPC engraft as expected
- Ionized calcium homeostasis is maintained by the hemodialysis