Traveling the World in Pursuit of Experimental Therapy for Juvenile Primary Amyotrophic Lateral Sclerosis

Jessica A. Moore, DHCE
Case - GK

- Developed spasticity, elevated tone and development regression at age 8;
- Sinemet for dystonia – no imp.; progressive functional gait issues

- **Initial diagnosis:** Cerebral Palsy and Dyslexia
- Family history: 22q deletion syndrome, dyslexia, juvenile diabetes, toe walking, cerebral palsy, ADHD
Case - GK

- Toe walking,
- progressive dysarthria,
- dysphasia,
- dysconjugate gaze,
- contractures, and
- incontinence (baclofen pump age 10)

**Final Diagnosis:** Juvenile Primary Amyotrophic Lateral Sclerosis
- Cardiac Dysautonomia - age 13
Juvenile Amyotrophic Lateral Sclerosis (ALS2)

- Cytogenetic Location: 2q33.1

- Amyotrophic Lateral Sclerosis
- Infantile-onset Ascending Hereditary Spastic Paralysis
- Juvenile Primary Lateral Sclerosis

### Research Background

<table>
<thead>
<tr>
<th>Stem cells</th>
<th>Route of delivery</th>
<th>Number of Patients</th>
<th>Patients characteristics</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
<td>Autologous Bone marrow (BM)-derived hematopoietic progenitors</td>
<td>Laminectomy; cells injected to the anterior part of the spinal at the C1 – C2 level. (free hand?)</td>
<td>13</td>
<td>2 – 5 years from disease onset; age 34 – 71; ‘moderate or severe’ symptoms, three patients ventilation bounded</td>
<td>Nine patients ‘became much better’ (improved neck and limbs MRC; EMG findings of ‘regeneration’). One patient was stable. Three patients died (1.5, 2 and 9 months after), of lung infection or myocardial infarction</td>
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<tr>
<td>Autologous blood purified CD133+ stem cells</td>
<td>Bilateral implantation in frontal motor cortex, with stereotheathic or navigation guidance</td>
<td>10</td>
<td>Age 38 – 62; 18 – 42 months from diagnosis; no patients with severe bulbar involvement or malnutrition; occurrence of FVC values</td>
<td>Safe and well-tolerated (1 year follow-up). Patients survival significantly higher than control group (10 non-operated ALS patients)</td>
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**Table 2. Clinical trials of stem cells in ALS.** ALS-FRS: ALS-functional rating scale; FVC: Forced vital capacity; GVHD: Graft-versus-host disease; MSC: Mesenchymal stem cell; SC: Spinal cord.

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## Table 2. Clinical trials of stem cells in ALS.

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<td>Autologous MSC (from bone marrow)</td>
<td>Injection into the central part of thoracic SC after laminectomy and mielotomy</td>
<td>9</td>
<td>Spinal onset, FVC &gt; 50%, normal polisomnography, ambulation with assistance or wheelchair bound Age 32 – 75. Months from diagnosis 8 – 60</td>
<td>Safe and well-tolerated even in long-term (4 years)</td>
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<td>Peripheral blood stem cells (PBSC)</td>
<td>Mobilisation of autologous PBSC with GCSF</td>
<td>8</td>
<td>Seven patients had limb onset. Time interval from onset: 3 months to 4 years. Three patients wheelchair-bound and five ambulatory. Pre-treatment FVC range 50 – 150%</td>
<td>Safe and well tolerated. No significant changes in disease progression</td>
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<td>Allogenic hematopoietic stem cell (HSCT)</td>
<td>Intravenous infusion following total body irradiation; immuno-suppression</td>
<td>6</td>
<td>Spinal cord or bulbar onset, FVC &gt; 60%, Age 35 – 59; Months from diagnosis 5 – 30</td>
<td>Tolerated (three chronic GVHD). No clinical benefits. Autopsies: spinal cord engrafted with immune cells, probably donor-derived</td>
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</table>

• Many Countries and States age 10-12

• Medical Tourism: traveling to another country for medical care
  – Not this case
  – good study design and timely results
  – reputation for research and experienced investigators/clinicians
  – collaborations to extend access
Physician Request for a Single Patient IND for Compassionate or Emergency Use

- Request statement
- Brief Clinical History
- Proposed Treatment Plan
- Drug Supply Reference Statement
- Informed Consent Statement *
- Investigator Qualification Statement
- FDA Form 1571
- Contact telephone number and facsimile number.
Ethics Consult

Request for independent Ethics consultation

• Age 12
  – wheelchair bound,
  – PEG – tube/oral,
  – Bi-Pap at night,
  – Communicated with facial expressions and hand gestures,
  – Cognitively intact

• Advance Care Planning: no permanent, continuous ventilation
Ethics Consult

Request for independent Ethics consultation

- History, research, understanding, B/B discussions, honest emotions
Case Continued – Age 13

Day 1: Marrow harvested from posterior iliac crest, bilaterally

Day 2:
• Cervical laminectomy (C1-C2),
• Inject SC: anterior horn of spinal cord bilaterally,
• SC impreg. gelfoam: subdural/subarachnoid space,
• trans-dural injection: SC in spinal fluid
• IV SC injection

• Discharged home six days later
Outcomes

• Continued care with PCP
• 3 months post-procedure: disease stabilized
  – Improved phonation
  – Improved facial movements and swallowing
  – Some upper extremity improvement
  – Intermittent nocturnal spasms/clonus and pain Rt LE
• MDACC lost to follow-up
• Death @ 3 yrs. post procedure: age 15
  – Declined continuous ventilation or Bi-Pap for CO₂ retention
"If ever there is tomorrow when we're not together….

There is something you must always remember.
You are braver than you believe, stronger than you seem,
and smarter than you think.
But the most important thing is, even if we are apart…
I'll always be with you."

A.A. Milne
Special Thanks To:

Mary Kay Koenig, MD
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Ian McCutcheon, MD
Questions