COMPLICATIONS FOLLOWING STEM CELL TRANSPLANT AND THE IMPACT ON OCCUPATIONAL PERFORMANCE IN PEDIATRIC ONCOLOGY CLIENTS

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Disclaimer

These presenters have no conflict of interest to report regarding any commercial product and/or manufacturer that may be referenced during this presentation.

Objectives

- Identify types of stem cell transplant (SCT) and phases of the transplant process used to treat pediatric clients
- Discuss the medical complications and long-term side effects commonly seen in pediatric oncology clients as a result of SCT, which negatively impact occupational performance and participation in life roles
- Identify the important role of occupational therapy with pediatric oncology clients following SCT to maximize improved occupational performance and client-centered care

Short Course Outline

- Stem Cell Transplant in Pediatric Clients
  - Indications for Autologous vs. Allogeneic Transplant
  - Phases of SCT
- Short and Long Term Effects following SCT
  - Medical Complications
  - Functional Implications Affecting Occupational Performance
- Role of Occupational Therapy
  - Preventative Programming
  - Multi-disciplinary Approach
  - Therapeutic Interventions

Pediatric Cancer and Transplant Cases

- About 10,450 children under the age of 15 will be diagnosed with cancer in 2014 (American Cancer Society, 2014)
- Approximately 2,495 pediatric clients were transplanted in 2011 (Pasquini & Wang, 2013)
- MSKCC performs approximately 50-55 transplants in pediatric patients per year (Blood & Marrow Transplant Information Network, 2013)
Hematopoietic Stem Cell Transplant

- **Hematopoietic** – blood forming cells
- All blood cells including red blood cells (RBC), white blood cells (WBC) and platelets start off as stem cells
- Stem cell transplants (SCT) are used to restore the stem cells when the bone marrow has been destroyed by disease, chemotherapy or radiation
  (American Cancer Society, 2013)
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Allogeneic Transplant

Preparation for stem cell harvest with cytokines and growth factors

Healthy donor

Stem cells are isolated from bone marrow or peripheral blood

Processed stem cells are preserved by freezing at -196°C and shipped for storage

Stem cells are reinfused into the recipient in order to repopulate bone marrow

Diagnoses Indicated for Allogeneic SCT

- Hematologic Malignancies (Cancers of the Blood)
  - Acute Lymphoblastic Leukemia (ALL)
  - Acute Myelogenous Leukemia (AML)
  - Chronic Myelogenous Leukemia (CML)
  - Juvenile Myelomonocytic Leukemia (JMML)
  - Myelodysplastic Syndromes (MDS)
  - Non-Hodgkin's Lymphoma (NHL)

Diagnoses Indicated for Allogeneic SCT (continued)

- Other Blood Disorders
  - Amegakaryocytic Thrombocytopenia
  - Aplastic Anemia
  - Diamond Blackfan Anemia
  - Hemophagocytic Lymphohistiocytosis (HLH)

Diagnoses Indicated for Allogeneic SCT (continued)

- Genetic Diseases
  - Hemoglobinopathies
    - Sickle cell disease; thalassemia
  - Severe Combined Immune Deficiency Syndrome (SCIDS)
  - Fanconi's Anemia
  - Wiskott-Aldrich Syndrome

Indications for Hematopoietic Stem Cell Transplants for Age ≤ 20 years, in the US, 2011

- Prognostic indicators suggest disease control is unlikely
- Need for high dose chemo and radiation (Myeloablative Conditioning)
- Client is at high risk of relapse; Disease reoccurrence after conventional chemotherapy
- Not responding to treatment; Failed remission
- SCT offers a potential cure for clients when other treatment options have been unsuccessful
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### Phases of Allogeneic Stem Cell Transplant (SCT)

<table>
<thead>
<tr>
<th>Pre-Transplant Medical Evaluation</th>
<th>Occurs outpatient; Imaging, HLA typing</th>
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</thead>
<tbody>
<tr>
<td>Conditioning Regimen/Myeloablative</td>
<td>Inpatient; Central line inserted, high dose chemo and total body irradiation (TBI)</td>
</tr>
<tr>
<td>Harvesting</td>
<td>T-Cell depletion</td>
</tr>
<tr>
<td>Transplant</td>
<td>Day 0; Donor cells transplanted via IV</td>
</tr>
<tr>
<td>Post-Transplant</td>
<td>Bone marrow and immune system recovery; Engraftment</td>
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<tr>
<td>Discharge From Hospital</td>
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### Allogeneic SCT Follow-up

- Discharge and Outpatient Follow-Up
  - Protective Isolation (Strict vs. Modified)
  - Frequent Clinic Visits
    - Frequency can vary from 1-5x/wk
  - Monitor
    - Vitals, Labs
  - Transfusions (blood products)
  - GvHD prophylaxis
  - Re-Admission
    - Fever and Neutropenia
    - Other Medical Complications

### One-year Survival by Year of Transplant, Donor and Age, Worldwide

![Graph showing one-year survival rates by year, donor type, and age](chart)

- Acute Leukemia, CML, or MDS early disease status.

### Short and Long-Term Complications of SCT

- **Short-term Complications**
  - Infections
    - Viral
      - Herpes Simplex Virus (HSV)
      - Cytomegalovirus (CMV)
      - Varicella zoster
      - Epstein-Barr Virus (EBV)
    - Bacterial
      - Staphylococcus epidermidis
      - Klebsiella
      - Streptococcus pneumoniae
    - Fungal
      - Candida
      - Aspergillus
      - Pneumocystis jiroveci (carinii)

- **Long-term Complications**
  - Acute Effects of Myeloablative Conditioning
    - High-Dose Chemo
      - Nausea and vomiting
      - Appetite Loss
      - Fatigue
    - Peripheral Neuropathy
      - Mucositis/Mouth Sores
      - Reduced Blood Counts
      - Hair Loss
    - Total Body Irradiation (TBI)
      - Fatigue
      - Skin Reactions/burns
      - Fibrosis
      - Hair Loss
      - Xerostomia

(Chen, Abu-Elheiga, & Jodele, 2013)
Graft versus Host Disease (GvHD)

- Increasing Incidence
  - Occurs in approximately 20-50% of pediatric patients following SCT (Jesudas, Malesky, Chu, Fischer, & Kamat, 2013)
- Unique to allogeneic transplants
- Extremely immunosuppressive
- Affects skin, liver and GI system; causes organ toxicity
- Grading system I-IV
- Acute vs. Chronic

Acute GvHD (aGvHD)

- First 100 days following SCT
- Skin rash or itchy, dry skin
- Diarrhea, abdominal pain
- Liver enzyme and/or bilirubin abnormalities
- Nausea
- Anorexia
- Malabsorption of nutrients from the intestinal tract
- Dry eye syndrome; Irritation of the conjunctivae or cornea of the eyes

Chronic GvHD (cGvHD)

- Develops after 100 days & up to several years following SCT
- Skin fibrosis, pigment changes and/or hardening or tightening of the skin
- Fasciitis; Joint contractures
- Dry eye syndrome
- Cataracts
- Dry mouth, changes in the mucosa of the mouth, sores in the mouth
- Diarrhea
- Lung problems (wheezing, abnormal pulmonary function tests)

Organ Toxicity

- Cardiovascular
  - Pericardial Effusion
  - Cardiomyopathy
  - Hypertension
  - Valvular anomaly
  - Conduction anomaly
- Pulmonary - Pneumonitis
  - Idiopathic Pneumonia Syndrome (IPS)
  - Infection Induced Pneumonia

Organ Toxicity (continued)

- Liver
  - Veno-Occlusive Disease (VOD)
- Hemosiderosis
- Renal
  - Acute Kidney Injury (AKI)
  - Chronic Kidney Disease (CKD)
- Endocrine System
  - Hypothyroidism
- Growth Hormone Deficiency

Musculoskeletal Issues

- Osteopenia/Osteoporosis
- Osteonecrosis/Avascular Necrosis (AVN)
- Myopathy
- Compression Fractures
- Muscle Contractures
- Postural Instability
- Intrinsic Muscle Weakness
- Stunted Growth/Short Stature
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### Neurological Complications
- May occur in up to 15% of children undergoing SCT (Chima et al., 2013)
- Seizures (Cordelli et al., 2013)
- Acute Encephalopathy
- Intracranial Hemorrhage
- Posterior Reversible Encephalopathy Syndrome (PRES)

### Sensory System Impairments
- Ocular
- Cataracts
- Dry Eye Syndrome/Sicca Syndrome
- Retinitis
- Auditory
  - Hearing Loss (Gurney, Ness, Rosenthal, Forman, Bhatia, & Baker 2006)
  - Persistent Dizziness
- Sensory Regulation

### Additional Complications
- Psychiatric
- Graft Failure/Rejection
- Disease Relapse
- Secondary Malignancies
  - Risk is 2-3 times higher in children following SCT (Jesudas et al., 2013)
  - Myelodysplastic Syndrome (MDS)/AML

### Long-Term Impact of SCT Complications
- 93% of SCT survivors have at least 1 adverse effect after 7 years of follow-up (Jesudas et al., 2013)
- Strongest association between reduced QOL and impaired functional status is the presence of GvHD (Baker & Fraser, 2008)
- Focus of care moves beyond cure of the original disease to late effects and quality of life
- Pediatric SCT patients are at greater risk for decreased social skills, impaired physical independence and restricted participation in routine ADLs and mature relationships (Ness et al., 2005)

### Functional Implications of SCT

### Late Effect Impairments of SCT

(Ness et al., 2009)
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**Impaired Development and Motor Skill Acquisition**

- Young children are more sensitive than older to the adverse late effects of SCT secondary to the sensitivity of growing muscle and nervous tissue to irradiation
- Strong association between cGvHD and muscle weakness, resulting in impaired motor performance
- Dynamic muscular endurance impaired in abdominals and back

(Hovi, Kurimo, Taskinen, Vettenranta, Vettenranta, & Saarinen-Pihkala, 2010)

**Psychosocial and Behavioral Issues**

- Changes in mood and affect
- Increased fear, frustration and anxiety
- Decreased peer interaction & social outcomes
- Decreased self esteem
- Increased dependence on family care
  - “Learned helplessness”
- Decreased motivation

(Stowell, 1987)

**Impaired ADL Performance**

- Fatigue, pain, neurologic deficits, decreased strength, balance and conditioning all interfere with physical performance and participation in ADLs
- Physical performance limitations were most common in young adult SCT survivors with cGvHD (Ness et al., 2005)
- 10% of long-term SCT survivors who underwent childhood transplantation report physical participation restriction that limits independence in personal care or routine activities (Ness et al., 2005)

**Impaired Cognition**

- Decreased Concentration/Shortened Attention Span
- Impaired Short Term Memory
- Decreased IQ (Titman et al., 2008)
- Learning Deficits
  - Child survivors of SCT were 3x more likely than same aged peers to participate in special education (Ness et al., 2005)
- Younger children shown to be more sensitive than older ones to adverse late effects of SCT in regard to neurocognitive function (Hovi et al., 2010)

**Decreased Play, Leisure and School Based Skills**

- Prolonged absence from school secondary to hospitalization and a compromised immune system
- Physical limitations impede participation in leisure activities (sports, climbing, outdoor play)
- Protective isolation limits peer interactions and play

(Kruz, Adams, Zahr, Killen, Cameron, & Wasson, 1996)

**Role of Occupational Therapy**
Rehabilitation Protocols and Parameters

- **Guidelines for safe intervention**
  - Developed in collaboration with medical team:
  - Protective isolation precautions
  - Lab Values: Hemoglobin > 7; Platelets > 10; ANC > 1
  - Cardiac Parameters (Okada, Meeske, Menteer, & Freyer, 2012)
  - Weight Bearing Precautions and Activity Status
  - Activity during chemotherapy infusions, blood product transfusions
  - MediPort restrictions

Holistic Multi-Disciplinary Approach

- **Physical Therapy**
- **Primary Medical Team, RN and PCT**
- **Volunteers/Sitters**
- **School Teachers**
- **Social Work**
- **Psychiatry**
- **Prosthetist/Orthotist**

Holistic Multi-Disciplinary Approach

- **Child Life Therapists**
  - Schedules
  - Behavior Charts
  - Games, Arts & Crafts targeting client specified interests or area of need
  - Wii, Video Games
  - Reserving Playroom

- **Integrative Medicine**
  - Music Therapy
  - Massage
  - Martial Arts
  - Yoga
  - Dance Therapy

Preventative Programming

- Automatic OT and PT referral
  - Initial evaluation completed prior to transplant
  - Frequency of follow up set at minimum of 1 x/week

- Standardized Assessments
  - PedsQL (Caocci et al, 2011)
  - MOCA
  - COPM
  - BOT-2
  - PDMS
  - VMI
  - DAY-C

Interventions and Treatment Strategies

- **Psychosocial Considerations**
  - Building rapport with caregiver and client
  - Create safe and supportive environment
  - Encouraging independence from caregivers
  - Increasing self-esteem and frustration tolerance with “just right challenges”
  - Modeling limit setting and boundaries
  - Setting standard for age appropriate behaviors

(Stowell, 1987)
Intervention and Treatment Strategies

- **ADL Training and Modifications**
  - Encourage sleep/wake cycles
  - Encourage regular active participation in OOB ADLs
  - **Toilet training**
  - Assess need for adaptive equipment/DME
  - Energy conservation/work simplification
  - Clothing fasteners
  - Shoe tying

- **Play and Leisure**
  - Educate family and caregivers re: safe handling and safe line management
  - Encourage client engagement in age appropriate and meaningful activity and play
  - Providing floor mats and size appropriate furniture
  - Make most out of isolation room and available windows
  - Incorporating technology (iPad, video games)

- **Therapeutic Exercise**
  - Conditioning: OOB activity, stationary, bike, upper body ergometer (UBE)
  - UE ROM program
  - Resistive Therapeutic Exercise: therapy band, hand weights, rock wall climbing
  - Gross and Bilateral Coordination
  - Fine motor coordination
  - In-hand manipulation, therapy putty, games/crafts with small manipulatives

- **Cognitive Training**
  - Executive functioning
  - Calendar activities
  - Encourage communication and **language** development
  - Mayer-Johnson
  - Dynavox
  - Simple sign language

- **Sensory Play and Exploration**
  - Snoezelen Cart/Room
  - Sensory Integration
  - Sensory Diet
  - Alert Program

- **Manual Therapy**
  - Soft tissue mobilization
  - Myofascial release (MFR)
  - Massage
  - PROM/Stretching

*(Inoue et al., 2010)*

*(Careddo et al., 2007)*
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Intervention and Treatment Strategies

- Neuromuscular Re-education
- Scapular mobility
- Postural training
- Neuro-Developmental Treatment (NDT)
- Proprioceptive Neuromuscular Facilitation (PNF)

Interventions and Treatment Strategies

- School Based Activities
- Performing adult directed activities
- Turn taking
- Color, letter and number recognition
- Handwriting
- Keyboarding
- Scissor Skills

Intervention and Treatment Strategies

- Orthotics and Splint Fabrication
- Prosthetic & Orthotic clinic
  - LE orthotics: AFO, shoe inserts, UCBL, SMO
  - UE splints: resting hand, wrist cock-up, night splints
  - Dynasplint/Ultraflex (LE and UE)

  Lymphedema Therapy Consultation

Discharge from Inpatient and Follow-up

- Acute Inpatient Rehab
- Home Services (VNS, Early Intervention)
- Outpatient OT Referrals
- School Based Services
- Vision Services

Conclusion

- Advances in SCT techniques are improving survivorship rates
- These pediatric clients may be encountered by occupational therapy practitioners in a variety of settings
- Short and long term complications following SCT can have a profound effect on pediatric clients and negatively impact overall QOL well beyond the initial hospitalization
- Children and parents need support and education before, during, and after the SCT process
- Occupational therapists can provide skilled intervention and education to maximize pediatric client function and QOL throughout the SCT process and beyond
- Further research is required on the SCT population and OT interventions during and after transplant

Questions?
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References


References (cont.)


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