Late Effects after a Pediatric Transplant, Transitioning to Adult Care

Celebrating a Second Chance at Life Survivorship Symposium

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Robert Krance MD
Texas Children's Hospital

Continuous Care for Pediatric Patients After Transplantation

Robert Krance, MD
Baylor College of Medicine
Center for Cell and Gene Therapy

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Goals for Pediatric Transplant Patients in the Long-Term Survivorship Clinic

- Prevent complications
- Provide effective treatment for complications that cannot be prevented
- Promote lifelong healthy habits
- Support measures that improve quality of life
  - School
  - Occupation/vocation
  - Interpersonal/social
  - Emotional

Recognize Your Specific Circumstance

- Illness which necessitated transplant
  - Diagnosis impacts long term concerns
- Side effects of pre-transplant treatment
- Specifics of transplant therapy
  - Conditioning
  - GVHD preventive therapy
  - Complications
Long Term Survivorship Recommendations

- Be the Match (National Marrow Donor Program)
  - bethematch.org/patients-and-families/life-after-transplant/
- International Late Effects of Childhood Cancer Guideline Harmonization Group
  - ighg.org/guidelines
- Children’s Oncology Group
  - survivorshipguidelines.org

Re-Immunization

- Begin by 12 months:
  - DTaP, Pneumococcus, Hemophilus, Meningococcus, Hepatitis A/B, Polio
  - Inactivated virus vaccine
- No sooner than 24 months and no GVHD or immunosuppression:
  - Measles, Mumps, Rubella, HPV
  - *if no antibody, Varicella vaccine (not Shingles vaccine)
- SARS CoV2 and Influenza
Genetic Conditions and Late Effects

- Non-bone marrow manifestations of genetic diseases
  - Fanconi Aplastic Anemia
  - Dyskeratosis Congenita
  - Blackfan-Diamond
  - Schwachman-Diamond
  - Sickle Cell Anemia and Thalassemia
  - Immunodeficiency Disorders
  - Genetic disorders of metabolism

Oral Care

- Up to half of children undergoing transplantation will develop oral complications
- Conditioning therapy and age at diagnosis
  - Cavities (caries)
  - Dry mouth
  - Tooth development
- Orthodontia and routine dental care
Heart Health – Potential Problems

• Over a lifetime patients are at risk of cardiac complications
  • Cardiomyopathy with/without heart failure
  • Pericarditis
  • Valvular heart disease
  • Coronary heart disease
  • Cardiac arrhythmia

Heart Health – Risk Factors

• Anthracyclines total dose
  • Doxorubicin equivalent dose:
    • daunomycin, doxorubicin, idarubicin, epirubicin, amsacrine
• Irradiation dose
  • TBI
  • Chest radiation
• Combined or separate administration
• Other factors contribute to risk
  • Smoking, obesity, diabetes, dyslipemia, sedentary lifestyle, etc.
Heart Care Screening Recommendations*

- Risk-based: dose radiotherapy and/or anthracyclines
  - High risk, lifetime risk for cardiac disease 36%
    - Echocardiogram every 2 years
- Intermediate risk
  - Echocardiogram every 5 years
- Low risk
  - Echocardiogram not necessary

*International Late Effects of Childhood Cancer Guideline Harmonization Group

Bone Health

- Osteochondroma (exostosis)
  - TBI
  - Benign tumor at metaphyseal sites (growth plates)
- Avascular necrosis
  - Hip most frequent
  - MRI preferred imaging technique
Bone Health

- Osteoporosis
  - TBI, cranial or craniospinal radiotherapy, steroid
  - Hypogonadism and growth hormone deficiency
  - Bone fragility can lead to non-traumatic fractures
- DXA scan
- Calcium and vitamin D
  - No smoking, moderate alcohol, and physical activity
  - Bisphosphonate

Kidney Health – Risk Factors

- Kidney function often diminished without signs or symptoms
  - Chemotherapy:
    - ifosfamide, cisplatinum, methotrexate
  - Radiotherapy (RT)
  - Other drugs:
    - tacrolimus, cyclosporin, vancomycin, foscarnet, etc.
Kidney Health – Monitoring, Prevention

• Monitor Kidney Function
  • Urinalysis
  • Creatinine Clearance or Glomerular Filtration Rate
• Hypertension
• Avoid NSAIDs: Ibuprofen, naprosyn, etc.
• Nephrologist for hypertension or proteinuria

Lung Health

• Lung disease associated with GVHD or early post transplant lung injury
  • Bronchiolitis obliterans (BOS)
  • Cryptogenic organizing pneumonia (BOOP)
• Lung injury
  • Drugs: bleomycin, busulfan, nitrosureas
  • Radiotherapy (RT): TBI, chest RT
Lung Health – Monitoring, Prevention

- Pulmonary function test
  - Pretransplant
    - Diffusion capacity
    - 6 years
    - Repeat during first 12 months post-transplant
- NO SMOKING EVER
  - Second-hand smoking

Skin Health

- Chronic GVHD
  - Loss of pigmentation, ulcers, thickened skin, eczema-like rash
- Malignancy
  - Radiation therapy and cGVHD
  - Sun exposure
  - Melanoma, squamous cell carcinoma, and basal cell carcinoma
    - Mole check
Pituitary Gland Health

- Pituitary Gland
  - Growth hormone deficiency
  - Gonadotrophic hormone deficiency
    - FSH
    - LH
  - Adrenocorticotrophic hormone deficiency (ACTH)
  - Thyroid stimulating hormone deficiency (TSH)
- Radiation (TBI)
- Disease: leukemia, brain tumor, other

Pituitary Gland Health - Interventions

- Growth hormone deficiency
  - Insulin Growth Factor (IGF) and IGF Binding Protein
  - Growth in height over time
  - Bone age
- Thyroid and gonad function can impact growth
- Growth hormone therapy before puberty
  - Precocious puberty
Thyroid Gland Health – Potential Problems

• Thyroid
  • Hypothyroidism
    • TBI or RT to neck: mantle irradiation, mediastinum
    • TSH and FT4
  • Hyperthyroidism
  • Thyroid cancer
    • Neck exam and palpation
    • Ultrasound

Male Health – Puberty, Fertility

• Testes
  • TBI or Radiation Therapy
  • Alkylating agents or platinum-based
  • Pituitary
• Before or after puberty
  • Delayed or arrested puberty
  • Post pubertal gonadal deficiency
• Infertility
Male Health – Potential Interventions

• Testis
  • Germ cells (Sperm cells)
    • FSH (follicle stimulating hormone)
  • Pubertal development and masculinity (Leydig cells)
    • LH (luteinizing hormone)
    • Testosterone
  • Before puberty (12 years)
    • Morning testosterone, LH and FSH
  • Sperm cryopreservation

Female Health – Puberty, Fertility

• Ovary
  • Estrogen and germ cell development
    • FSH and LH complementary
  • Germ cells are fixed at birth
    • Puberty and fertility dependent upon total germ cell number
    • Failure to feminize
    • Infertility
Female Health – Ovarian Failure

• Primary or Secondary Ovarian Failure
  • Before puberty
    • Failure to initiate or complete puberty
  • Post puberty
    • Failure to resume menses
    • Premature menopause
  • Menopausal

Reproductive Health

• Infertility rate 75%
  • Age at treatment
    • Prepubertal male
    • Postpubertal female
  • TBI
  • Busulfan
• Pregnancy outcome
  • Miscarriage and other complications, BUT
  • Healthy babies
Eye and Ear Health

- Neurocognitive Development
  - Speech
  - Behavior
  - Schooling
- Hearing loss and tinnitus
  - Cisplatinum (platinum-derivatives)
  - Brain radiotherapy (RT)
  - Ventricular shunt
  - Genetic disorders
- Cataract formation; corneal opacification
  - RT
  - Genetic disorders
  - CMV retinitis

Hepatic (Liver) Health

- Liver injury
  - Drugs, Radiation Therapy, veno-occlusive disease, viral infection
  - Transfusion iron overload
    - 10 red blood cell transfusions
- Liver enzymes, ferritin, MRI
- Focal nodular hyperplasia (FNH)
- Nonalcoholic fatty liver disease
  - Nonalcoholic steatohepatitis (NASH)
Metabolic Syndrome

- Constellation
  - Hypertension
  - Abdominal Obesity (waist circumference)
  - Hyperlipidemia
  - Abnormal glucose metabolism
- Cardiac disease
- Diabetes

Metabolic Syndrome – Cause, Prevention

- Causes
  - Uncertain but radiation therapy and drugs must be suspect
  - Growth hormone insufficiency
  - Steroids – dose and duration
- Obesity
  - Inflammatory state
- Diet, weight control, and physical activity
Malignancy (cancer)

- Incidence remains uncertain
  - Overall, twice general population
  - Risk increases over time
  - Both autologous and allogeneic stem cell transplant
    - MDS/AML
    - Lymphoproliferative disease
    - Breast cancer

Malignancy – Causes after Transplant

- Multiple variables
  - Patient specific
    - genetic factors
    - age at transplant
  - Diagnosis
  - Conditioning therapy
    - Radiation therapy
  - GVHD
Malignancy – Screening, Prevention

• Breast cancer
  • Hodgkin lymphoma
  • Thyroid cancer
  • Annual MRI and breast US or mammogram begin 25 years or 8 years post treatment
• Skin squamous cell carcinoma
  • Chronic GVHD
• CNS tumor
  • CNS leukemia and cranial RT

Neurocognitive Development

• Neurocognition:
  • brain function that generate complex behaviors of day-to-day life
• Many variables can impact neurocognition
  • TBI and cranial irradiation
  • Transplant at young age
• Most patients test within the average population range
Neurocognitive Development

- Neurocognitive testing by first anniversary
  - Ideal, test before conditioning
  - Repeat testing as needed but at a minimum at new stage of education: preschool, first grade, 6th grade, etc.
- Memory, concentration, organization
- Timely and appropriate intervention

Fatigue

- “the persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion that is not proportional to recent activity and interferes with usual functioning”
- Daytime sleepiness
- Poor social, behavioral, adaptive functioning
- Active interventions have shown benefit
Exercise Tolerance

- Integration: cardiac, pulmonary, muscular systems
- Exercise intolerance
  - Global longitudinal strain vs. ejection fraction
  - Oxygen uptake
  - Heart rate response

Final Thoughts

- Create a mindset, lifelong!
- Establish post transplant follow up
  - Transplant center programs
  - Knowledgeable providers
- Life-style health habits
  - Diet
  - Exercise
  - Address unhealthy behavior: obesity, smoking, drugs, alcohol, anxiety, depression
- Healthy habits are essential to promote healthy adults
Questions?

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bmtinfonet.org  ♦  help@bmtinfonet.org  ♦  847-433-3313

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Robert Krance MD