Coping with Pediatric Post-transplant Issues

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Risk Factors for Late Complications

Pre-HCT exposures and comorbidities

Primary therapy

Conditioning regimen

GVHD

Other exposures (infections, drugs)

Pre-HCT

HCT

Post-HCT

Genetic predisposition

Age and gender

Lifestyle factors

Long-Term Effects BMT Survivors

### Growth and development
- Linear growth
- Skeletal maturation
- Intellectual function
- Emotional/social maturation

### Fertility and Reproduction
- Fertility
- Health of Offspring

### Vital Organ Function
- Cardiac
- Pulmonary
- Renal
- Endocrine
- Vision/Hearing

### Second Neoplasms
- Benign
- Malignant

### Health-Related Quality of Life

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# Long-Term Effects BMT Survivors

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Cardiovascular

Chemotherapy
– Cardiomyopathy (muscle damage)
  • Anthracyclines – Daunorubicin, Doxorubicin
  • Alkylators – Cyclophosphamide

Radiation (structures damaged)
– Coronary arteries
– Heart valves
– Pericardium (lining around heart)
Metabolic Syndrome and CV Risk

- Hyperlipidemia
- Hypertension
- Abdominal obesity
- Glucose intolerance/hyperglycemia: diabetes

Survivors after HCT have a higher risk of:

This may increase the risk for cardiovascular related events (heart attack, stroke) at relatively young age
Cardiovascular

Screening (annual)
- History
- Weight, Blood Pressure
- Lipid profile, blood sugar level
- [Echocardiogram, ECG]

Risk modification
- Avoid smoking
- Limit alcohol
- Diet – low fat, low cholesterol
- Exercise
Endocrine Issues

Chemotherapy
  – Infertility
    • Alkylators – Cyclophosphamide

Radiation
  – Infertility
  – Growth hormone deficiency
  – Thyroid – low, high, nodules, cancer
Endocrine-Fertility

Screening
- History and physical exam
- Laboratory screening: LH, FSH, estradiol, testosterone

Risk modification (at diagnosis)
- Sperm/(egg) banking
- Evaluation by reproductive endocrinologist
- Fertility counseling
Inherited Genetic Risks to Offspring

• Study of 2198 offspring of cancer survivors found **NO** increased risk of congenital abnormalities
• Large study 4214 children born to cancer survivors found **NO** increase of genetic disease
• Multiple studies have looked at cancer risk in offspring of childhood cancer survivors and none have detected any increased risk of cancer in offspring
• After BMT: more miscarriages
Endocrine Late Effects

Problem: Testicular or Ovarian Dysfunction

**Evaluation-Males**
- puberty onset and development
- Testosterone, FSH, LH
- Testicular volume, semen analysis

**Evaluation-Females**
- Puberty onset, menstrual history
- FSH, LH, estrogen

Close (annual or more) follow-up of growth and pubertal development required for all pediatric survivors through adolescence
Endocrine Dysfunction-Growth

- Growth Hormone Deficiency (GH)
  - many receiving TBI will have GH deficiency
  - CNS radiation +/- TBI majority develop GH deficiency
  - catch up growth not usually seen, but further negative deviation away from normal does not occur
Endocrine Late Effects

Problem: Thyroid Dysfunction

Evaluation

• History and physical exam
  – signs/symptoms of hypothyroidism
    • fatigue, cold intolerance, weight gain, headache, trouble concentrating, constipation, dry skin.
  – frequently asymptomatic
  – consistency/size of thyroid

• Follow thyroid function every year following transplant
  – may be abnormal early (6mo.) or many years later
Osteopenia/Osteoporosis

- Risks
  - Steroids
  - Methotrexate
  - Radiation therapy
  - Hypogonadism
  - Early menopause
  - Growth hormone deficiency
  - Hyperthyroidism
Osteopenia/Osteoporosis

Screening
– DXA Scan (Dual energy X-ray absorptiometry)

Risk modification
– Hormone replacement therapy
– Vitamin D
– Calcium
– Bisphosphonates
Airway and Pulmonary Disorders

- 10-15% pts after BMT will have delayed or chronic pulmonary complications
- Late onset lung complications
  - strongly assoc. with cGVHD
  - response to lung injury
- Risk Factors
  - GVHD
  - radiation therapy to chest
  - Certain chemotherapy drugs that have pulmonary toxicity
Pulmonary

Screening

• Physical Exam
• CXR and/or CT of lungs
• Pulmonary function tests

Risk Factor Modification

• Counseling against smoking
• Close follow-up if PFT or symptom changes
Ophthalmologic Problems

• Cataracts secondary to TBI
  – single dose TBI: incidence at 5 yr 80%
  – fractionated TBI:
    • 50% incidence at dose > 1200 cGy
    • 30-35% at < 1200 cGy
  – chemo only regimen: 20% incidence

• Infections
  – primarily related to cGVHD
  – Viral (CMV, Varicella, herpes)
Dental Problems

• Oral mucosa is major target of cGVHD
  – Dry mouth
• Periodontal disease, cavities
  – most prevalent after radiation
• Abnormal dentition and facial bone development in children
  – particularly if <7 yrs at time of treatment
  – hypoplastic upper/lower jaw

Survivors/parents need to be aware of dental health risks and maintain close dental follow-up after HCT
Neuropsychologic Risk Factors

• CNS Radiation
  – brain tumors, leukemia (CNS prophylaxis or treatment)
  – effects slow to appear and may be progressive
  – age of child very important (< 6 yrs)
  – Range of deficits quite variable
Neuropsychologic Evaluation

- Careful history
  - cognitive development, memory, school performance, behavior changes, motor dysfunction, seizures

- Vision and hearing screening

- Neuropsychological testing (TBI @ grade school ages or younger, or if radiation in addition to TBI)

- EEG, MRI if indicated
New Malignancies in Cancer Survivors

- **Solid Tumors**
- **Hematologic malignancies**
  - Therapy related leukemia
- Estimates put the risk of a new/second cancer at between 3-5% by 20-25 years from original diagnosis
  - 3 to 6-fold increase risk compared to general population
What does this mean for survivors?

• Be aware of risks of second and subsequent cancers
• Know if they require special screening that others their age do not typically need
• Lead a healthy lifestyle and avoid things known to increase risk of cancer
  – Excess sun exposure
  – Tobacco
  – Excess alcohol
  – Obesity
Chronic GVHD Can Affect Any Organ

- Skin and connective tissue — thickening, stiffness, pigment changes, nail abnormalities, rash
- GI tract — malabsorption syndrome, esophageal stricture
- Liver — Liver function abnormalities
- Ocular — dry eyes
- Oral — dry mouth, oral ulcerations
- Muscles — stiffness, weakness
- Lungs — scarring, poor function
- Other — blood count problems, kidney problems, neuropathy (nerve pain)
Care for survivors = Care for the Whole Person

- Neurocognitive deficits
- Anxiety
- Depression
- Social Withdrawal
- Loss
- School/work re-entry
- Insurance
Patient Toolkit

- Patient-friendly version of the long-term screening recommendations
- 6, 12, 24+ month guides
- Each includes tests, evaluations and glossary
- Checklist to prepare for checkup
- Space for notes
- Includes Mobile App information

bethematch.org/For-Patients-and-Families/Support-and-resources/Educational-resources/Survive-resources/
Internet Resources

• Fred Hutch
  – Long Term Follow-up Program
    • www.fredhutch.org/en/treatment/long-term-follow-up/information-for-patients.html
  – Survivorship Program
    • www.fredhutch.org/en/treatment/survivorship.html
    • Phone: (206) 667-2814
    • survivor@fhcrc.org

• National Marrow Donor Program: Be The Match
  – bethematch.org/For-Patients-and-Families/Children-and-transplant/Follow-up-care/
Survivorship Care Plan (1)

- **Diagnosis:** Cancer type, stage, histology, date and age at diagnosis

- **Care Providers:** Treatment facility and oncology health care providers and PCP with contact information

- **Treatment details:** Chemotherapy, with selected cumulative doses, radiotherapy doses and fields, surgical procedures, blood product exposures
Survivorship Care Plan (2)

- **Complications** on/off treatment with long-term implications

- Associated *potential risks* of treatment including second malignancy or specific organ toxicity with screening and follow-up recommendations

- Sent to survivor and healthcare providers
Pediatric Cancer Survivors Have Unique Challenges

Long-term follow-up is considerably more complex in survivors of pediatric cancer than of cancer later in life.

A lifetime of follow-up needed with the need for ongoing assessment of adverse effects on growth, development, education and employment.
Long Term Survivors

**Future Directions**

- Find ways to identify which patients are at highest risk for late effects secondary to therapy
- Determine what parts of the treatment are causing the most significant long term problems and find ways to modify the treatment or prevent late effects
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