Endocrine Late Effects in Survivors of Pediatric SCT

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Figure 3.1: Survival of childhood cancer patients diagnosed 1966-2000, by period of diagnosis

% still alive

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

0 5 10 15 20 25 30 35 40

Years since diagnosis

Five-year survival rates for two time periods for pediatric cancer diagnosed from birth to 19 years old.
Cure Had Not Come Without a Price

- Increasing population of SCT survivors

- Survivors are at risk for chronic or late-occurring health problems caused by their cancer or its treatment

- Thirty years after diagnosis 75% of all survivors will experience at least one late treatment effect
Endocrine Complications

- Most common late effect in survivors of childhood cancer & SCT
- Observed in 20%-50% of survivors
- Followed into adulthood
Risk Factors for Endocrine Dysfunction

- Primary diagnosis & its treatment
- Age at transplant
- Conditioning regimen
- Gender of patient
- Post Transplant exposure; GvHD, Steroids
- Tyrosine kinase inhibitors (TKI)
Endocrine Complications

- Growth impairment
- Thyroid dysfunction
- Puberty
- Gonadal failure
- Metabolic Syndrome
Growth Impairment - Etiology

- Exposure to spinal radiation, TBI
- Chemotherapy treatments
- Age at SCT
- Production of sex hormones
- Hypothyroidism
- Growth hormone (GH) deficiency
- Suboptimal nutrition
• Hypothalamus/pituitary radiotherapy & TBI
• Radiotherapy- dose and time dependent effect
• Imatinib- tyrosine kinase inhibitor

• Should be investigated when linear growth velocity decelerates over a 6-month period
Evaluation

• Accurate measurement of height
• Measurement of bone age
• Two measurements of GH secretion

• Treatment with rGH replacement therapy is not initiated until 12 months after completing cancer treatment
• Safety of treatment?
Thyroid Dysfunction

- Hypothyroidism is the most common thyroid abnormality
- Radiation to neck, cranio-spinal & TBI
- Busulfan-based regimens
- TKI- Sorafenib, Sunitinib, Imatinib
Cumulative incidence of developing thyroid dysfunction after HCT in childhood

A

B
• Surveillance for thyroid dysfunction is crucial
• Hypothyroidism may occur decades later

• TSH, fT4
• Replacement therapy
Puberty

• Substantial changes in gonadal and GH activity
• Development of secondary sexual characteristics
• Increased growth velocity

• Initiation & completion of puberty requires an intact hypothalamic–pituitary–gonadal axis

Puberty is when parents get difficult.
• Pubertal delay or failure occurs in girls & boys
• Depends on conditioning regimen

• Pubertal development should be carefully monitored after SCT
• Supplemental hormone therapy
Central Precocious Puberty

- Early activation of the hypothalamic–pituitary–gonadal axis
- Onset of puberty prior to the ages of 8-9 years
- Pre-mature closure of growth plates
- Treatment with GnRH agonist
Ovarian Failure

- The ovary is sensitive to the adverse effects of cancer treatments
- Treatments cause a reduction in the ovarian follicle reserve
- Gonadal failure is associated with exposure to CY, BU, and TBI
- Elevated FSH reduced levels of anti-Müllerian hormone (AMH)
Ovarian insufficiency and pubertal development after hematopoietic stem cell transplantation in childhood

[Graph and table data]

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Males

• Germ cells in the testes normally continue to produce sperm during adulthood

• Risk of gonadal failure depends on type of therapy and doses administered

• CY, TBI destroy germ cells within the testes
• Impairment of spermatogenesis may be permanent or temporary

• Recovery is related to agent and dose received

• Many (48%-85%) males who undergo SCT will experience testicular failure with azoospermia
Preserving children’s fertility: children’s right to an open future

Males
- Sperm banking
- Testicular tissue cryopreservation so far, this has not led to live births
Females

- Embryo or oocyte cryopreservation
- Ovarian tissue cryopreservation

The only option for pre-pubertal and young females
NCI, NHLBI/PBMTC First International Conference on Late Effects after Pediatric Hematopoietic Cell Transplantation: Endocrine Challenges—Thyroid Dysfunction, Growth Impairment, Bone Health & Reproductive Risks

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The endocrine system is highly susceptible to damage by high-dose chemotherapy and/or irradiation during hematopoietic cell transplantation (HCT) during childhood. The specific endocrine organs most commonly affected by HCT include the thyroid gland, the pituitary, and the gonads. In addition, hormones controlling the development and stability of the skeletal system are also affected. Insufficiency of thyroid hormone results in the most common late sequelae of HCT, and occurs more often in young children. Despite advances in treatment, hypothyroidism continues to affect children cured of leukemia. Hypothyroidism is also found in the pituitary, the production of growth hormone is a problem of unique concern to the pediatric endocrinologist. Children with leukemia have a decreased bone mineral density at baseline, which is a risk factor for both girls and boys. Both girls and boys have a decreased bone mineral density at baseline, which is a risk factor for both girls and boys. Bone mineral density is decreased in both girls and boys at baseline. Bone mineral density is decreased in both girls and boys at baseline.
Nurses Role in Long-Term follow-up

- Multidisciplinary team
- Coordinate care
- Age specific
- Education on disease, late effects, health behavior
- Counseling
Conclusions

• Need for information on disease & side effects
• Importance of life-long follow-up care
• Need for international guidelines

• Transition to adult care
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