A pilot study of some endocrine sequelae in survivors of childhood cancers

Protocol Thesis
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دراسة استكشافية لبعض مضاعفات الغدد الصماء في المتعافين من أمراض السرطان في الأطفال

رسالة مقدمة

توطئة للحصول علي درجة الدكتوراة في طب الاطفال

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Introduction:

The type of cancer observed during childhood and adolescence vary greatly and differ by age group, sex, and race ***(Ries et al., 1999).***

Survival rates for certain childhood malignancies have increased dramatically over the last 20 years, with 5-year survival rates in many common childhood malignancies in excess of 70% (Murray et al., 2002). As a consequence of the complex treatment regimens employed to achieve such remarkable cure rates, significant detrimental effects on the endocrine system, growth, and fertility are well recognized. Additionally, survivors of childhood cancer are at risk of subsequent malignant neoplasms and show increased mortality from non malignant disease ***(Oeffinger et al., 2000).***

Endocrine sequelae of cancer therapy include thyroid carcinoma, hyperparathyroidism and hypopituitarism. Growth hormone secretion is recognized to be the most vulnerable of the hypothalamo-pituitary axes to radiation induced damage ***(Murray et al., 1999).***

The influence of chemotherapy, when used as the only form of treatment for cancer, on growth is poorly understood and has been studied in patients with hematologic neoplasms. In most of these studies, an influence on growth parameters (height/growth rate) was observed, whether as a reduction in growth rate during chemotherapy followed by catch up growth or in chronic form with absent or reduced subsequent recovery ***(Roman et al., 1997).***

Growth hormone deficiency that originate during childhood will cause suboptimal linear growth and a reduced final height, while young adults may experience the varied metabolic derangements and psychological abnormalities recognized as the "adult growth hormone deficiency syndrome*" (Sklar, 2000).*

Aim of the study:

The aim of this study is to evaluate the effect of chemotherapy and radiotherapy on growth and growth hormone secretion (at various levels of the hypothalamo-pituitary axis) in survivors of childhood cancer.

Patients and methods:

The study will be conducted on 50 of survivors of childhood cancer diagnosed and treated according to the protocols of hematology and oncology clinic _ Children's Hospital _Ain Shams University.

Survivors are defined as patients who are relapse free twelve months after completion of therapy. They will be divided into 2 groups:

1.Group I:

A- Survivors of acute lymphoblastic leukemia who received chemotherapy only.
B- Survivors of acute lymphoblastic leukemia who received chemotherapy and radiotherapy.

2.GroupII:

Survivors of solid tumors received chemotherapy and radiotherapy excluding brain tumors.

The studied groups will be subjected to the following:

1. History taking laying stress on:

a) Type of the disease.
b) Sex of the patient and age of start of therapy.
c) Duration and type of treatment.
d) Type and cumulative dose of every single chemotherapeutic drug used in treatment.
e) Irradiation site and dose of radiotherapy and fractionation schedule.
f) The available anthropometric data will be collected from the files before the start of treatment.

2. Thorough clinical examination including:

a) Anthropometric measurements using the Egyptian growth charts
-Weight of the patients wearing minimal clothing will be measured with an electric scale, height using stadiometer.
- Body mass index calculated as weight divided by height² (Kg/height² "m").
- Measuring skin fold thickness using the method of Tanner.

3. Laboratory studies including:

a) Hematological examination: CBC and bone marrow examination.
b) Liver and kidney functions.
c) Growth hormone assessment:
Basal level.
After provocation using clonidine (which stimulates growth hormone secretion by acting at the hypothalamic level) and growth hormone releasing hormone (which stimulates growth hormone secretion by acting at the pituitary level).

d) Serum IGF-1 level.
c) T4 and TSH assessment to exclude hypothyroidism.

4. Plain x-ray of the left hand to assess bone age.

5. Other needed investigations to ensure maintained remission.

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List of Abbreviations

AIDS	: Acquired immune deficiency syndrome
ALL	: Acute lymphoblastic leukemia
AML	: Acute myeloid leukemia
ANOVA	: Analysis of variance
APCs	: Antigen presenting cells
BCG	: Bacillus calmate and guanine
BM	: Bone marrow
BMI %	: Body mass index percentile
BMI SDS	: Body mass index standard deviation score
BMI	: Body mass index
BMT	: Bone marrow transplantation
BRMs	: Biologic response modifiers
CAI	: Central adiposity index
CMV	: Cytomegalovirus
CNS	: Control nervous system
CT	: Computed tomography
CTV	: Clinical target volume
CTX	: Cytoxan
DNA	: Deoxy ribonucleic acid
EBV	: Epstein Barr virus
EBVCA	: Epstein-Barr viral capsid antigen
G-CSF	: Granulocyte colony stimulating factors
GH	: Growth hormone
GHRH	: Growth hormone releasing hormone
GTV	: Gross tumor volume
GVHD	: Graft versus hast disease

Gy : Gray
HDL-C : High density lipoprotein-cholesterol
HHV 8 : Human herpes virus 8
HIV : Human immunodeficiency virus
HLA : Human leucocyte antigen
HSCs : Hematopoietic stem cells
HSCT : Hematopoietic stem cell transplantation
Ht % : Height percentile
Ht SDS : Height standard deviation score
HTLV-I : Human T cell leukemia virus type-I
HTLV-II : Human T cell leukemia virus type-II
HTLV-III : Human T cell leukemia virus type-III
IG : Immunoglobulin
IGF_1 : Insulin like growth factor-1
IGF_2 : Insulin like growth factor-2
IgG : Immunoglobulin G
IL-2 : Interleukin-2
JAR : Janus kinase
LAK : Lymphokine activated killer
LDL-C : Low density lipoprotein-cholesterol
MEN_2 : Multiple endocrine neoplasia type 2
MHC : Major histocompatability complex
MIBG : m-iodobenzylguanidine
6-MP : 6-mercaptopurine
MTX : Methotrexate
NHL : Non Hodgkin's lymphoma
PB : Peripheral blood
PBSC : Peripheral blood stem cells

PTV : Planning target volume
SI units : International system units
SISFT : Suprailiac skin fold thickness
SSSFT : Subscapular skin fold thickness
STAT : Signal transduction and transcription
TBI : Total body irradiation
TCR : T cell receptor
TG : Triglycerides
TIL : Tumor-infiltrating lymphocytes
TRH : Thyroxine releasing hormone
TSH : Thyroid stimulating hormone
UCB : Umbilical cord blood
W.C. : Waist circumference
VCR : Vincristine
VP-16 : Vepside
W/H : Waist / Hip ratio

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