
بسم الله الرحمن الرحيم
وَأَنزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وَكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيمًا
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Ramadan Mustafa

Study of Iron Status as a Contributing Factor to Anemia of Cancer Patients

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The prevalence of anemia approaches 50% in patients with cancer and may increase to more than 90% in patients with certain types of cancer and in those undergoing chemotherapy or radiation therapy*;* the term functional iron deficiency (FID) has been applied to the situation characterized by iron-restricted erythropoiesis in the presence of iron stores. This is an additional cause of anemia in patients with various chronic diseases including cancer.

Aim of the study: Was to evaluate the etiology of anemia in cancer patients in relation to the iron status and the prevalence of iron restricted erythropoeisis.

Patients and methods:

All patients with childhood cancer on chemotherapy regularly following at Ain-Shams University - Pediatrics hospital- hematology-oncology unit were screened by routine blood picture for the presence of anemia. Patients with hemoglobin level ≤ 11gm/dl were subjected to history and revision of hospital records for collecting data including their age, sex, symptoms of anemia, dietary recall, bowel habits, any blood loss and/or blood transfusion, date at diagnosis of cancer, its type and chemotherapy protocol; then physical examination were done for signs of anemia and any evidence for infection. Laboratory investigations included complete blood picture, reticulocyte count, Iron profile: serum iron, serum ferritin, transferrin, total iron binding capacity, CRP, and reticulocyte hemoglobin content (RET-He). Patients admitted for infection, patients with febrile neutropenia and patients infected with hepatitis C virus were excluded from study. Cut-off level for RET-He was 29pg[1]and transferrin saturation (Tsat) 20%[2].

Patients were classified into 4 categories according the level of transferrin saturation (Tsat) and RET-He content. Category 1: with no iron deficiency (Tsat>20%)and no FID (RET-He>29pg) ; category 2 : iron deficiency (Tsat<20%) and no FID(RET-He>29pg); Category 3: replete iron (Tsat>20%) and FID (RET-He ≤29pg) and category 4 both levels below cutoff: Iron deficiency anemia.

Results:

Forty patients were included for study, 22 males (55%) and 18 females (45%). Their mean age was4.94±3.9 years (range 1.3-17). Twenty two (55%) had acute leukemia and 18 (45%) solid tumors and lymphomas their mean hemoglobin level was 9.8± 0.75gm/dl (range8.2-10.9). Mean serum ferritin was 904.1±723ng/ml, Median 757ng/ml (Range 55-2420 ng/ml). Nine (22.5%) patients had RET-He ≤29 pg/ml.

Patients with no ID and no FID: 29(72.5%), Mild ID and no FID: 1(2.5%), Replete iron stores and FID: 8 (20%), and IDA: 2(5%).

Conclusion:

Functional iron deficiency represents an appreciable etiology for anemia in childhood patients with cancer on chemotherapy. Serum ferritin level is not a reliable marker for assessment of iron status in children with cancer. Follow up of patients and treatment of each category according to their results will be implemented.

1- Thomas C, Thomas L. Biochemical markers and hematologic indices in the diagnosis of functional iron deficiency. Clin Chem. 2002 Jul;48(7):1066-76.
2- Paruthi S and Staros E: transferrin saturation: http://emedicine.medscape.com/article/2087960-overview.

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Abbreviation

ACD	Anemia of chronic disease
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
APR	Acute-phaseresponse
ASCO/ASH	AmericanSocietyof ClinicalOncologyandAmerican Society of Hematology
ATP	Adenosine tri-phosphate
bpm	beat per minute
CHr or Ret-He	Reticulocyte hemoglobin content
cm	centimeter
CNS	Central nervous system
DNA	Double stranded nucleic acid
ELISA	Enzyme-linked immuno-sorbent assay
ESAs	Erythropoiesis-stimulatingagents
FEP	Free erythrocyte protoporphyrin
FIDA	Functional iron deficiency anemia
FL	femtoliter
Ft	Serum ferritin
g	gram
g/dl	gram per deciliter
Hb	Hemoglobin
Hct	Hematocrite
HL	Hodgkin lymphoma
HYPO	Proportionofhypochromicredcells
IDA	Iron deficiency anemia
IDNA	Iron deficiency non anemia
IL	Interleukin
IQR	inter quartile range
IV	Intravenous
Kg	Kilogram
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
mg	Milligram
mg/dl	milligram per deciliter

MIDA	Moderate iron deficiency anemia
n	number
NHL	Non-Hodgkin lymphoma
PCV	Peaked cell volume
pg/dl	pictogram per deciliter
pg	pictogram
RBCs	Red blood cells
RDW	Red cell distribution of width
RMS	Rhabdomyosarcoma
SEER	Surveillance Epidemiology and End Results
SI	Serum iron
SIDA	Severe iron deficiency anemia
SPSS	Statistical Program for Social Science
sTfR	Serumsolubletransferrinreceptor
Tf	Transferrin
Tsat	Transferrinsaturation
TIBC	Total iron binding capacity
US	United States
WBC	white blood cell
Yrs	Years
µg/dl	microgram per deciliter
µg/l	microgram per liter

Introduction

Anemia is a common complication of cancer and its treatment. The prevalence of anemia (hemoglobin level (Hb) < 12 g/dL) approaches 50% in patients with cancer and may increase to more than 90% in patients with certain types of cancer and in those undergoing chemotherapy or radiation therapy ***(Henry, 1998; Ludwig et al., 2004).***

Cancer-related anemia may be characterized as anemia of chronic disease, mediated by inflammatory cytokines that have a direct inhibitory effect on erythropoiesis and may inhibit the production of erythropoietin. Other causes of anemia in patients with cancer include chemotherapy, radiation therapy, nutritional factors, and bleeding associated with gastrointestinal or genitourinary malignancies ***(Weiss et al., 1993).***

It has long been known that chronic inflammation affects iron turnover by restricting the release of iron from the macrophages in the reticuloendothelial system ***(Konijn andHershko, 1997).***

More recently these effects have been further elucidated and the term functional iron deficiency (FID) has been applied to the situation characterized by iron-restricted erythropoiesis in the presence of iron stores. This is an additional cause of anemia in patients with various chronic diseases including cancer***(Viatte et al., 2006; Weiss and Goodnough, 2005).***

Thus FID may be described as a situation in which the individual has adequate iron stores but insufficient available iron at the site of erythroblast production ***(Weiss and Goodnough , 2005).***

Aim of the work

To evaluate the etiology of anemia in cancer patients in relation to the iron status and the prevalence of iron restricted erythropoiesis.

To evaluate the role of reticulocyte hemoglobin content in assessment of iron status in anemia of cancer patients.

Childhood cancer

Introduction:

Childhood cancer is not a single disease, but includes a variety of malignancies in which abnormal cells divide in an uncontrolled manner. These cancer cells can invade nearby tissues and can migrate by way of the blood or lymph systems to other parts of the body ***(National Cancer Institute; Dictionary of Cancer Terms, 2009)***.

Cancer in childhood is quite rare compared with cancer in adults, but it still causes more deaths than any factor, other than injuries, among children from infancy to age 15 years ***(National Cancer Institute; A Snapshot of Pediatric Cancer, 2009).***

The annual incidence of childhood cancer has increased slightly over the last 30 years; however, mortality has declined significantly for many cancers due largely to improvements in treatments ***(National Cancer Institute; A Snapshot of Pediatric Cancer, 2009).***

The causes of the increased incidence are not fully understood, but the changes have been too rapid to be explained by genetics and too steady to be explained by the introduction of better diagnostic techniques, which would be expected to cause a one-time spike in rates. The proportion of this increase caused by environmental factors has yet to be determined ***(Reis et al., 1999).***

The most common types of childhood cancers:

The types of cancers that occur most often in children are different from those seen in adults. The most common cancers of children are:

- Leukemia