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STUDY OF SERUM SOLUBLE CD44 LEVELS IN LEUKEMIC PATIENTS

Submitted in partial fulfillment of the requirements of the MD degree in

"Internal Medicine"

By

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بسم الله الرحمن الرحيم

سنريهم آياتنا في الآفاق
وفي أنفسهم حتى يتبين
لهم أنه الحق ، أولم يكف
بربك أنه على كل شيء
شهيد

(سورة فصلت ، الآية ٥٣)

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CONTENTS

Abbreviations

***CD:** cluster of differentiation

***AML:** acute myeloblastic leukemia

***ALL:** acute lymphoblastic leukemia

***CML:** chronic myeloid leukemia

***CLL:** chronic lymphocytic leukemia

***HTL-V:** human T lymphocytic leukemia virus

***EBV:** Epstein Barr virus.

***HLA:** human Leucocytic antigen.

***PAS:** periodic acid –chiff stain .

***SBB:** Sudan black B stain .

***GVL:** graft versus leukemia effect.

***GVHD:** graft versus host disease .

***IL2:** interluken 2 .

***LAK cells:** lymphokine – activated killer cells.

***ISG:** interferon stimulated genes.

***DFS:** disease free survival.

***CAMs:** cell adhesion molecules.

***VLA:** very late antigen.

***VCAM:**vascular cell adhesion molecule.

***ECM:** extra cellular matrix.

***TMB:** tetra methyle benzene.

INTRODUCTION

Introduction

CD44 is an adhesion molecule of the proteoglycan family that is expressed on the surface of virtually all hematopietic cells. [1] Several functions of the CD44 molecule are reported including cell to extra cellular matrix adhesion, lymphocyte homing, lymphohematopoiesis, T cell activation and tumor metastasis. [2]

These functions depend on the ability of CD44 to recognize the extracellular matrix component; hyaluronic acid [3,4]. CD44 is also expressed on epithelial cells, fibroblasts, muscle cells and a wide varicty of tumors. [5]

The standard CD44 isoform is expressed on all types of mature blood cells,[5,6] on the majority of mononuclear bone marrow precursors and on all CD34+HPC ,the level of its expression varies according to hematopietic cell lineage and stage of differentiation. [7,8]

Soluble CD44 has been suggested to be shed at least partially from tumor cells, shedding is most likely a consequence of the activity of endogenous proteolytic mechanisms, although s-CD44lakes the cytoplasmic tail, it seems to be biologically active according to several functional studies. [9]

CD44 has been suggested to be involved in the metastatic process of both human malignancies and experimental animal tumors. CD44-ve lymphomas appear to be more often local and have a better prognosis than lymphomas that express CD44. [10]

This work will carried out to study s-CD44 in serum of leukemic patients to assess its value in monitoring the disease activity, extent and response to treatment.

LEUKEMIA

Introduction:

Leukemias are clonal neoplastic proliferations of immature cells of the hematopoietic system, which are characterized by aberrant or arrested differentiation., Leukemia cells rapidly accumulate in the bone marrow cavity, ultimately replacing most of the normal hematopoietic cells, thus resulting in the signs and symptoms of the disease. These include most prominently; bone marrow failure and its consequences of anemia, hemorrhage, and infection. Leukemia cells circulate into the blood and then into other tissues throughout the body with patterns characteristic of the particular type of leukemia. [11]

Acute leukemias, which can be broadly grouped as either lymphoblastic or myeloblastic, can be identified phenotypically and genetically and are characterized by a rapid clinical course usually necessitating immediate treatment. [12] Acute leukemias are derived from and biologically resemble, primitive hematopoietic progenitor cells; in contrast chronic leukemias have the phenotype and biologic character of more mature cells. [11]

Chronic myeloid leukemia, however, over time may transform to an acute blastic phase and will thereafter more closely resemble an acute leukemia in its biology, clinical course, and need for therapy. [12]

Incidence:

The acute leukemias are rare diseases but have a disproportionately large impact on cancer survival statistics among children and young adults. Although the acute leukemias account for less than 3% of all cancers. These diseases are the leading cause of death due to cancers, in the United States in persons under 35 years of age. [13]

REVIEW OF LITERATURE

The incidence rate of acute myelogenous leukemia (AML) in the united states is about 2.5 per 100,000 persons, for ALL, the rate is about 1.3 per 100,000 persons. AML has a slight male predominance (1.5:1) and accounts for 25% of both acute and chronic leukemias. AML affects about 9000 people a year in the united states, While ALL affects about 4000 people, with a similar predominance of males. The incidence of acute leukemias in the united states has not changed substantially over the last 20 years, although there is a slight trend upward among those diagnosed with ALL and slight fall in the number of diagnosis of AML in this time period. In ALL, the incidence in African-Americans is about half that seen in whites; in AML, rates are similar between these two groups. [13]

Interestingly, age specific incidences differ dramatically between ALL, which has a median age at diagnosis of 10 years and AML, which has a median age of 65 years. AML is rare below the age of 40, but incidence rises progressively with age from about 1 per 100,000 at age 40 to more than 15 per 100,000 at age 75 or older. In contrast, ALL has its peak incidence at less than 10 years and has a second smaller rise in persons older than 70. [14]

Cancer data from national cancer institute, Cairo University in EGYPT; during a period of time between 1970 and 1985, showed that about 4% of attendant patients were leukemic from total number of patient of 32305 patients, this figure now greatly increased [15].

The most common cancer among children in Egypt is leukemia, followed by lymphoma, brain tumors, bony, kidney and suprarenal tumors. [16]

In National Cancer Institute, Cairo University, ALL patients represents 23.3% of all pediatric malignancies and 75% of pediatric leukemia. [17]

Risk factors for leukemia:

The clear relationship between the atomic bomb radiation, [18] Or use of carcinogenic therapies and the development of secondary leukemias has led to