Significance Of CD27 Expression In B Cell Precursor ALL Patients

Thesis

Submitted For Partial Fulfillment of Master Degree
Of Clinical and Chemical Pathology

By
Suzi Zakaria Adib
M.B., B.Ch., Ain Shams University

Supervised By

Professor/ Hanaa Mohammed El Sayed Afifi
Professor of Clinical & Chemical Pathology
Faculty of Medicine - Ain Shams University

Professor/ Mona Ahmed Ismail
Professor of Clinical & Chemical Pathology
Faculty of Medicine- Ain Shams University

Faculty of Medicine
Ain Shams University
2014

First thanks to **ALLAH** *to whom I relate any success in achieving any work in my life.*

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Hanaa Mohammed El Sayed Afifi,** *Professor of Clinical and Chemical Pathology for her meticulous supervision, kind guidance, valuable instructions and generous help.*

Special thanks are due to **Prof. Mona Ahmed Ismail,** *Assistant Professor of Clinical and Chemical Pathology for her sincere efforts, outstanding support, active participation and guidance.*

Suzi Zakaria

Contents

Page No.

List of Figures

Figure No. ***Page No.***

List of Tables

Table No. ***Page No.***

List of Abbreviations

ABL.....Ableson proto-oncogene; gene on chromosome 9

AIDS.....Acquired immunodeficiency syndrome

ALL.....Acute lymphoblastic leukemia

AML.....Acute myeloid leukemia

AUL.....Acute undifferentiated leukemia

BCP-ALL.....B cell precursor-Acute lymphoblastic leukemia

BCR.....Breakpoint cluster region; gene on chromosome 22

BM.....Bone marrow

Bso.....Basophilic

C CD3 .....Cytoplasmic CD3

C Ig.....Cytoplasmic immunoglobulin

CALLA .....common acute lymphoblastic leukemia antigen

CBC.....Complete blood count

CBF .....Core binding factor

CD .....Cluster of Differentiation

CD27 L.....CD27 ligand

CNS .....Central nervous system

CR .....Complete remission

CSF.....Cerebrospinal fluid

DCs.....Dendritic cells

DL ..... Dichroic lenses

DS..... Down syndrome

EBV..... Epstein-Barr virus

EDTA..... Ethylene diamine tetra-acetic acid

EM..... Electron Microscope

EMO..... Extramedullary involvement

EO ..... Eosinophilic

FAB ..... French–American–British

FAB ..... French-American-British.

FCM ..... Flowcytometry

FITC..... Flourescein isothiocyanate

FS ..... Forward scatter

GPA..... Glycophorin A

Hb..... Hemoglobin

HIV ..... Human immunodeficiency virus

HLA ..... Human leukocyte antigen

HOX genes....HOX: Homeobox genes, master transcriptional regulators of early development

HSCS..... Histiocytes

IAP ..... Inhibitor of apoptosis proteins

Ig ..... Immunoglobulins

IL..... Interleukin

IPT ..... Immunophenotyping

JAK.....Janus Kinase

kDa.....kilodalton

LDH .....Lactate dehydrogenase

LNs.....Lymph nodes

MIC-M.....Morphologic Immunophenotyping Cytogenetic and Molecular genetic

MLL.....Mixed-lineage leukemia

MLL-AF4.....Mixed-lineage leukemia- ALL1 fused gene from chromosome 4

MoAb .....Monoclonal antibody

MPAL .....Mixed phenotype acute leukemia

MPO.....Myeloperoxidase

MRD.....Minimal residual disease

MS.....Multiple Sclerosis

NGF.....Nerve growth factor

NK.....Natural Killer

NOS.....Non other specific

PAS.....Periodic-acid-schiff

PB.....Peripheral blood

PBS.....Phosphate buffered saline

PBX1 .....Pre-B-cell transforming gene on chromosome 1

PCR.....Polymerase chain reaction

PE.....Phycoerythrin

PLT ..... Platelets

PMTs..... Photomultiplier tubes

RB ..... Retinoblastoma protein/gene

RBCS ..... Red blood cells

S Ig ..... Surface immunoglobulin

SBB ..... Sudan black

SCC ..... Side light scatter

SD..... Standard deviation

SS..... Side scatter

T effs ..... Effector T cells

TCR.....T-cell receptor

TdT ..... Terminal deoxynucleotidyl transferase

TEL ..... Translocation ETS leukemia (ETS is a family of transcriptional factors)

TEL-AML1... Translocation ETS leukemia-acute myeloid leukemia-1

Th .....T helper cells

TLC..... Total leukocytic count

TNF ..... Tumor necrosis factor

Tregs ..... Regulator T cells

WBC..... White blood cell count

WHO..... World Health Organization

INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) is characterized by the malignant proliferation and accumulation of early lymphoid precursor cells in the bone marrow, blood and lymphoid organs. This disease is the most frequent form of leukemia in children & comprising almost one-third of all pediatric cancers ***(Trehan et al., 2009).***

Combination chemotherapy together with central nervous system prophylaxis has improved the treatment of ALL, and overall cure rates now approach 80%. Despite this improvement, about 20-25% of the patients still relapse ***(Lee-Sherick et al., 2010).***

A number of clinical and biological factors at the time of presentation are relevant to the prognosis and affect the response to treatment ***(Amirghofran et al., 2011).*** These prognostic factors include age, gender, number of blasts, white blood cells (WBC) and platelet number, cytogenetic abnormalities, extramedullary involvement (EMI) and immune phenotype ***(Fathi et al., 2012).***

CD27 is a member of the tumor necrosis factor family. It is expressed on T cells, Nk cells and memory B cells. The interaction betweenCD27 and its ligand CD70 plays an

important role in the maturation and activation of these cells ***(Croft et al., 2009).***

It plays an important role in lymphoid differentiation and apoptosis. Induced on normal B lymphocytes after antigenic challenge it is a marker of memory B cells. Increased expression of the membrane form of CD27 on ALL blasts has been reported and ligation of CD27 has been shown to induce apoptosis ***(Nilsson et al., 2005).***

Interestingly, the CD27 antigen can be detected both as transmembrane protein and as soluble protein in serum, as a shorter metalloprotease cleavage product (sCD27). Increased levels of sCD27 have been associated with immune activation in diseases such as AIDS, multiple sclerosis and systemic lupus erythromatosus. However, its role in B cell ALL is still not clear ***(De Miltio et al., 2002).***