CD 47 Assessment In Immune Thrombocytopenic Purpura

Thesis

Submitted for partial fulfillment of M.D. degree ***in Internal Medicine***

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2014

بسم الله الرحمن الرحيم

سورة البقرة الآية: ٣٢

Acknowledgement

of all, all gratitude is due to **God** *almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

Really I can hardly find the words to express my gratitude to **Prof. Dr. Abdel Rahman Abdel Hamid Soliman,** *Professor of Internal medicine and Haematology, faculty of medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.*

I would like also to express my sincere appreciation and gratitude to **Prof. Dr. Hanaa Mohmed Afifi,** *Professor of Clinical Pathology, faculty of medicine, Ain Shams University, for her continuous directions and support throughout the whole work.*

I would like to express my deepest gratitude and sincere thanks to **Assistant Prof. Dr. Gihan Mohamed Kamal Shams El-Din,** *Assistant professor of Internal Medicine and Hematology faculty of medicine, Ain Shams University, for suggesting and planning this work, her instructive supervision, continuous guidance, unlimited help and unfailing support, valuable instructions throughout the work and final revision of the manuscript.*

I owe much to. **Dr. Mohamed Hamdy Attya,** *Lecturer of Internal medicine and Haematology Faculty of Medicine - Ain Shams University.*

I am obliged to **Dr. Walaa Ali Elsalakawy,** *Lecturer of Internal medicine and Haematology Faculty of Medicine – Ain Shams University, who offered her great help and her professional experience for completion of this work.*

Nour Elhuda Hussien Abdalla

Contents

List of Abbreviations

ADCC	:	Antibody-dependent cellular cytotoxicity
ADCP	:	Antibody-dependent cellular phagocytosis
AEA	:	Anti-erythrocyte autoantibodies
AIF	:	Apoptosis-inducing factor
AIHA	:	Autoimmune hemolytic anemia
ALL	:	Acute lymphoblastic leukemia
ALPS	:	Autoimmune lymphoproliferative syndrome
AML	:	Acute myeloid leukemia
AN	:	Absolute number
ANA	:	Antinuclear antibody
Anti-D	:	anti-D immunoglobulin
Anti-LKM	:	Anti –liver- kidney-microsomal anti body
APL	:	Acute promyelocytic leukemia
ASH	:	American Society of Hematology
B-CLL	:	B-cell chronic lymphocytic leukemia
Beta-TG	:	beta-thromboglobulin
BUN	:	Blood urea nitrogen
C AMP	:	Cyclic adenosine monophosphate
Cag A	:	Cytotoxin associated gene A
CBC	:	Complete blood cell count
CBD	:	C- terminal cell binding
CD	:	Cluster of differentionation
CLL	:	Chronic lymphocytic leukemia
CMV	:	Cytomegaloviurs
CNS	:	Central nervous system
CPB	:	Cardiopulmonary by pass
CR	:	Complete remission
Cr	:	Creatinine
CRs	:	Complement receptors
CT	:	Computed tomography
CVID	:	Common variable immunodeficiency
DCs	:	Denderitic cells
DDAbs	:	Drug dependant platelet antibodies

List of Abbreviations (Cont.)

DDAVP	:	Desmopressin acetate
DIC	:	Disseminatd intravascular coagulopathy
DITP	:	Drugs induced thrombocytopenia
DLBCL	:	Diffuse large B cell lymphoma
DNA	:	Deoxy ribonuclic acid
EBV	:	Epstien Barr viurs
ECG	:	Electrocardiogram
ESR	:	Erythrocyte sedmintation rate
FAK	:	Focal adhesion kinase
FDA	:	Food and Drug Administration
FL	:	Follicular lymphoma
G6PD	:	Glucose 6 phosphate dehydrogenase
GIT	:	Gastrointestinal tract
GPIb-IX-V	:	Glycoprotein Ib-IX-V complex
GPVI	:	Glycoprotein VI
Hb	:	Haemoglobin
HCV	:	Hepatitis C viurs
HIT	:	Heparin-induced thrombocytopenia
HITT	:	Heparin-induced thrombocytopenia and thrombosis
HIV	:	Human immune deficiency viurs
H-Pylori	:	Helicobacter pylori
HRQoL	:	Health-related quality of life
I DCs	:	Immature human monocyte derived dendertic cell
IAP	:	Integrin-associated protein
ICH	:	Intracrainal hemorrage
IFN-α	:	Interferon alfa
IgA	:	Immunoglobulin A
IgG	:	Immunoglobulin G
IgM	:	Immunoglobulin M
IL	:	Interlukin

List of Abbreviations (Cont.)

ITAM	:	Immunoreceptor tyrosine-based activation motif
ITP	:	Immune thrombocytopenic purpura.
IVH	:	Intravascular hemolysis
IVIG	:	Intravenous immunoglobulin.
IWG	:	International Working Group
Lab.	:	Laboratory
LDH	:	Lactate dehydrogenase
MCL	:	Mantel cell lymphoma
MDS	:	Myelodysplastic syndrome
MHC	:	Major histocompatibility complex
MMF	:	Mycophenolate mofetil
MR	:	Mannose receptor
MRD	:	Minimal residual disease
MRI	:	Magnetic resonance imaging
mRNA	:	Messenger ribonuclic acid
NAD	:	NO abnormality detected
NHL	:	Non-Hodgkin lymphoma
NMMIIA	:	Non muscle myosin type II A
NO	:	Nitric oxide
P I 3	:	Phosphoinositide 3 kinase
PAMPs	:	Pathogen-associated molecular patterns
PARC-ITP	:	Pediatric and Adult Registry of Chronic ITP
PBMCs	:	Peripheral blood mononuclear cells
PKA	:	Protein kinase A
PKC	:	protein kinase C
PLT	:	platelets
PRRs	:	Pattern recognition receptors
PT	:	Prothrombin time
PTT	:	Partial thromboplastin time
RBCs	:	Red blood cells
RF	:	Rheumatoid factor
RGD	:	Arginine glycine aspartic acid

List of Abbreviations (Cont.)

RhAG	:	Rh associated glycoprotein
ROS	:	Reactive oxygen species
RP%	:	Percentage number
SIRP	:	Signal regulatory protein
SIRPα	:	Signal-regulatory protein α
SLE	:	Systemic lupus erythematosus
T Reg	:	Regulatory T- cells
TAMs	:	Tumour-associated macrophages
Th	:	T-helper cells
TLC	:	Total leucocyte count
TNFα	:	Tumor-necrosis-factor-α
TPO	:	Thrombopoietin
TPO-R	:	Thrombopoietin Receptor agonist
TSP	:	Thrombospondin
TSP-1	:	Thrombospondin-1
UFH	:	Unfractionated heparin
vWF	:	von Willebrand factor
WAS	:	Wiskott-Aldrich syndrome
WAS P	:	Wiskott-Aldrich syndrome protien
WBCs	:	White blood cells

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Introduction

Immune thrombocytopenic purpura (ITP) is an autoimmune disease characterized by low platelet counts as a result of antibody-mediated destruction of platelets. ***(Cines and Blanchette ,2002).***

Platelet autoantibodies are of the immunoglobulin G (IgG) type and are most commonly directed to the glycoprotein IIb/IIIa complex. However, most patients have antibodies directed to several different platelet surface proteins**.** ***(McMillan et al.,2008).***

Extensive research has shown that production of antiplatelet antibodies in ITP is strongly related to the presence of autoreactive T cells and an altered cytokine environment**.** ***(Cooper et al., 2007).***

Platelets coated with IgG autoantibodies undergo accelerated clearance through Fcγ receptor–mediated phagocytosis by macrophages, usually in the spleen and liver. ***(Cines and Blanchette ,2002).***

ITP can be treated with corticosteroids or intravenous gamma globulin (IVIG). ***(Oldenborg et al., 2000).***

In more severe cases of ITP, and in cases of tolerance to corticosteroids, splenectomy may be required to reduce platelet destruction**.** ***(Cines and Blanchette ,2002).***

Signal regulatory protein α (SIRPα) is an immunoglobulin (Ig) superfamily member with 1 or 3 extracellular Ig domains (alternative splicing) and an intracellular tail with 2 immunoreceptor. ***(Oldenborg , 2013).***

SIRPα is expressed preferentially by neurons and myeloid cells such as neutrophils, monocytes, and monocyte-derived cells**. *(Oldenborg et al., 2000)***.

The ligand for (SIRPα) is the cell-surface glycoprotein CD47 (integrin-associated protein, IAP), which is expressed by virtually all cells in the host. ***(Oldenborg et al., 2002).***

Interaction between target cell CD47 and (SIRPα) counteracts macrophage phagocytosis of CD47-expressing host cells.Platelets also express CD47, so inhibitory CD47/SIRPα signaling regulates normal platelet turnover and clearance of platelets in (ITP). So targeting SIRPα may be a new means of reducing platelet clearance in ITP ***(Mattias et al., 2005).***