

CD 47 Assessment In Immune Thrombocytopenic Purpura

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العليم

صدق الله العظيم

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Contents

List of Abbreviations	i
List of Tables	v
List of Figures	vii
Introduction and Aim of the Work	1
Review of Literature	4
Chapter 1	
* Immune Thrombocytopenic Purpura	4
Chapter 2	
* CD47 in Health and Disease	83
Patients and Methods	134
Results	143
Discussion	162
Summary	171
Recommendations	173
References	174
Arabic Summary	--

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 differentiation
CLL	: Chronic lymphocytic leukemia
CMV	: Cytomegalovirus
CNS	: Central nervous system
CPB	: Cardiopulmonary by pass
CR	: Complete remission
Cr	: Creatinine
CRs	: Complement receptors
CT	: Computed tomography
CVID	: Common variable immunodeficiency
DCs	: Dendritic cells
DDAbs	: Drug dependant platelet antibodies

List of Abbreviations (Cont.)

DDAVP	: Desmopressin acetate
DIC	: Disseminated intravascular coagulopathy
DITP	: Drugs induced thrombocytopenia
DLBCL	: Diffuse large B cell lymphoma
DNA	: Deoxy ribonucleic acid
EBV	: Epstein Barr virus
ECG	: Electrocardiogram
ESR	: Erythrocyte sedimentation 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 virus
HIT	: Heparin-induced thrombocytopenia
HITT	: Heparin-induced thrombocytopenia and thrombosis
HIV	: Human immune deficiency virus
H-Pylori	: Helicobacter pylori
HRQoL	: Health-related quality of life
IDCs	: Immature human monocyte derived dendritic cell
IAP	: Integrin-associated protein
ICH	: Intracranial hemorrhage
IFN- α	: Interferon alpha
IgA	: Immunoglobulin A
IgG	: Immunoglobulin G
IgM	: Immunoglobulin M
IL	: Interleukin

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 ribonucleic 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
SIRP α	:	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
TNF α	:	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

List of tables

<i>Table</i>	<i>Title</i>	<i>Page</i>
1	Mechanism of development of drug dependent platelet antibodies	48
2	Difference between classic DITP and HIT	52
3	Foods, beverages and natural products associated with definite evidence for the development of drug-induced immune thrombocytopenia	53
4	First-line agents for the management of primary ITP	68
5	American Society of Hematology (ASH) recommendations for use of second line therapy in children and adults with ITP	74
6	Demographic data of the studied groups and controls as regard age and lab. Data	143
7	Comparison between the studied groups as regard gender	144
8	Comparison between the studied groups as regard age	145
9	Comparison between the studied groups as regard c/o	146
10	Comparison between cases and controls as regard all laboratory data	147
11	Comparison between the studied groups and controls as regard (CD47)	149
12	Comparison between the studied groups and controls as regard platelet count	151
13	Comparison between patients of group III as regard response to treatment	152
14	Comparison between platelets before treatment and after 3 months of treatment within patients of group III	153

List of tables (Cont.)

<i>Table</i>	<i>Title</i>	<i>Page</i>
15	Comparison between patients of group III and controls as regard CD47 and platelets	154
16	Comparison between the studied groups as regard condition and number of relapses	155
17	Correlation between CD47 versus variables of group I	156
18	Correlation between CD47 versus variables of group II	157
19	Correlation between CD47 versus variables of group III	158
20	Correlation between CD47 versus the condition in the total cases	159
21	Correlation between CD47 versus the gender	160
22	Validity of CD47 in prediction of outcome	161

List of Figures

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
1	Image from blood smear Gimes stained showing platelets surrounded by red blood cells	4
2	Platelets derive from blood stem cells	6
3	3D Rendering of Platelets	7
4	Scanning electron micrograph of blood cells.	8
5	Platelet clumps in a blood smear	10
6	Diagram of the structure of a platelet .	11
7	New definitions for the phases of the disease	19
8	Schematic representation of pathophysiology of cITP.	20
9	Demonstration of three major recognition sites (A, B and C) of PA anti-GPIIb/IIIa autoantibodies.	22
10	pproach to the diagnosis and manament if a pateient with new-onset thrombocytopenia in whom drug-induced immune thrombocytopenia is suspected.	56
11	Emergency therapy and initial treatment in ITP	73
12	Structure of CD47.	74
13	Interactions of CD47.	86
14	Ligation of SIRP α will result in phosphorylation of the two ITIMS.	88
15	Association of CD47 with the Rh and band 3 complexes in the erythrocyte membrane	93

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
16	CD47 regulates phagocytosis of host cells by interacting with SIRP- α (a) CD47 on viable normal host cells.	100
17	Apoptotic cells and CD47.	104
18	Cancer cells and expression of CD47	107
19	Prophagocytic signaling or inhibitory signaling.	113
20	Fc γ R and CR-mediated erythrophagocytosis can be down-regulated by CD47/SIRP α interaction	116
21	CD47 is more prominently expressed by disseminated lymphoma cells and that targeting CD47.	124
22	Combination strategies targeting CD47 in cancer	126
23	Assessment of CD47 by flow cytometry in new diagnosed ITP pateint.	139
24	Assessment of CD47 by flow cytometry in non-responder ITP pateint.	140
25	Assessment of CD47 by flow cytometry in responder ITP pateint.	140
26	Assessment of CD47 by flow cytometry in control.	141
27	Comparison between the studied groups as regard gender.	144
28	Comparison between the studied groups as regard age.	145
29	Comparison between the studied groups and controls as regard (CD47)	150
30	Comparison between the studied groups as regard platelet count (pre treatment and post treatment	151

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
31	Comparison between patients of group III as regard response to treatment.	152
32	Comparison between platelets before treatment and after 3 months of treatment within patients of group III.	153
33	Comparison between the studied groups as regard condition and number of relapses	155
34	Correlation between CD47 versus number of relapses of group I	156
35	Correlation between CD47 versus hemoglobin of group II	157
36	Correlation between CD47 versus platelet of group III	158
37	Correlation between CD47 versus the condition in the total cases	159
38	ROC curve showing CD47 validity as a prognostic marker in ITP cases	161

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 Fc γ 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). **(Oldenburg 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 (SIRP α) is an immunoglobulin (Ig) superfamily member with 1 or 3 extracellular Ig domains (alternative splicing) and an intracellular tail with 2 immunoreceptor. **(Oldenburg , 2013).**

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

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