

PROGNOSTIC SIGNIFICANCE OF CD56 EXPRESSION IN ACUTE LEUKEMIAS

Thesis

Submitted for Partial Fulfillment of Master
Degree in
Clinical and Chemical Pathology

By

Sally Hafez Mohamed Mohamed Hafez
(M.B.B.CH)

Faculty of medicine, Ain Shams University

Supervised by

Professor/ Basima Mahmoud Ahmed

Professor of Clinical and Chemical Pathology
Faculty of Medicine-Ain Shams University

Professor/ Nagwa Abdelaziz Kantoush

Professor of Clinical and Chemical Pathology
National Research Center

Doctor/ Mona Ahmed Ismail

Assistant Professor of Clinical and Chemical Pathology
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University

ظهور سي دي 56 (إن-كام) كعامل لأستقراء مآل ابيضاض الدم الحاد

رساله

توطئه للحصول على درجة الماجستير
في الباثولوجيا الاكلينيكيه و الكيمائيه

مقدمه من

طبيبه / سالي حافظ محمد محمد حافظ

بكالوريوس الطب و الجراحه العامه
كلية الطب - جامعة عين شمس

تحت اشراف

الأستاذ الدكتور / بسيمه محمود احمد

أستاذ الباثولوجيا الاكلينيكيه و الكيمائيه
كلية الطب - جامعة عين شمس

الأستاذ الدكتور / نجوى عبد العزيز

قنطوش

أستاذ الباثولوجيا الاكلينيكيه و الكيمائيه
المركز القومي للبحوث

الدكتور / منى أحمد إسماعيل

أستاذ مساعد الباثولوجيا الاكلينيكيه و الكيمائيه
كلية الطب - جامعة عين شمس

كلية الطب - جامعة عين شمس

2011

SUMMARY

CD56 (NCAM) antigen is a member of immunoglobulin super family. It is commonly expressed in natural killer cytotoxic lymphocytes (NK cells), CD56 mediates adhesion between cells through homophilic bonds, it has been implicated as having a role in neurite outgrowth, synaptic plasticity, learning and memory.

The acute leukemia has the lowest survival rates in all cancers. So, the assessment of the prognostic factors in acute leukemia is very important. CD56 expression was described to have a prognostic impact in acute leukemias.

Detection of CD56 expression at diagnosis is of high clinical relevance, because its expression has a direct consequence for treatment stratification, being associated with poor prognosis.

The aim of the present study was to determine the expression of CD56 antigen on the surface of myeloid and lymphoid blasts, from patients with acute leukemia, in a trial to correlate the expression of this molecule to various clinical and laboratory data, and determining its diagnostic value for acute leukemia immunophenotyping, as well as its relation to treatment response.

2011

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(قَالُوا سُبْحَانَكَ لَا عِلْمَ
لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ)

صدق الله العظيم
سورة البقرة آية (30)

Dedicated To.....

My Father & Mother

My Husband "Col.Eng. Abdelkhalek"

My Child "Yahya"

Sally





Acknowledgments

*First and last, I thank "**Almighty Allah**" as I deeply owe **HIM** mercy, support and guidance in my whole life.*

*I would like to express my endless gratitude and appreciation to **Prof. Dr. Basima Mahmoud Ahmed**, Professor of Clinical and Chemical pathology, Faculty of Medicine, Ain Shams University, for giving me the honor of working under her supervision and providing me a lot of encouragement throughout this work,*

*My grateful thanks to **Prof. Dr. Nagwa Abdelaziz Kantoush**, Professor of Clinical and Chemical pathology, National Research Center, for here constant guidance, keen supervision and valuable help.*

*I would like to acknowledge my profound gratitude to **Dr. Mona Ahmed Ismail**, Assistant Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for here active supervision, valuable advice, precious comments and kind help throughout this study.*

*Thanks are due to **Dr. Dalia Adel Abdelhaleem**, Researcher of Clinical and Chemical pathology, National Research Center, for her valuable suggestion and considerable effort throughout this work,*

*My greatest thanks and gratitude to **my husband** for his actual help and support.*

Last but not least, I would like to record my greatest thanks and gratitude to my family for their actual help and support, and to everyone who helped and encouraged me in the production of this work,

LIST OF CONTENTS

Title	Page No.
<i>Introduction.....</i>	<i>1</i>
<i>Aim of the work</i>	<i>3</i>
<i>Review of literature</i>	
▪ <i>Acute leukemia.....</i>	<i>4</i>
▪ <i>CD 56.....</i>	<i>61</i>
<i>Subjects and methods.....</i>	<i>67</i>
<i>Results.....</i>	<i>75</i>
<i>Discussion.....</i>	<i>111</i>
<i>Summary</i>	<i>119</i>
<i>Conclusion</i>	<i>121</i>
<i>Recommendations</i>	<i>122</i>
<i>References.....</i>	<i>123</i>
<i>Arabic summary</i>	

LIST OF FIGURES

Fig. No.	Title	Page No.
Figure (1):	Schematic illustration of a flow cytometer.....	37
Figure (2):	Analysis of human peripheral blood cells by flow cytometry (<i>Paraskevas et al., 2004</i>).....	39
Figure (3):	(A) Schematic of NCAM showing five Ig domains, two fibronectin type III repeats, the membrane anchor, and the predicted hinge at the Ig5-Fn III junction. (B and C) Model showing the isologous Ig3 contacts (B) and the proposed adhesion between antiparallel Ig12 domains (C)	63
Figure (4):	Flowcytometric analysis of AML case, left histogram; shows gated blasts, right histogram; shows positive CD56 (NCAM) expression (86.1%).	102
Figure (5):	Flowcytometric analysis of ALL case, left histogram; shows gated blasts, right histogram; shows positive CD56 (NCAM) expression (33.9).....	102
Figure (6):	Flowcytometric analysis of AML case, left histogram; shows gated blasts, right histogram; shows negative CD56 (NCAM) expression (4.63%).....	103
Figure (7):	Flowcytometric analysis of ALL case, left histogram; shows gated blasts, right histogram; shows negative CD56 (NCAM) expression (13.8%).....	103
Figure (8):	Correlation between CD56 and CD34 in AML patients	104

LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
Figure (9):	Correlation between CD56 and CD34 in ALL patients.	105
Figure (10):	Association between cytogenetics and CD56 expression in AML patients.	106
Figure (11):	Association between cytogenetics and CD56 expression in ALL patients.....	107
Figure (12):	Association between outcome and CD56; expression in AML patients.....	108
Figure (13):	Association between fate and CD56 expression in AML patients.....	108
Figure (14):	Association between fate and CD56 expression in ALL patients.....	109
Figure (15):	Association between outcome and CD56 expression in ALL patients.....	109

LIST OF TABLES

Table No.	Title	Page No.
Table (1):	Morphological and cytochemical (FAB) classification of AML (2008).....	7
Table (2):	MIC classification of acute leukemia	15
Table (3):	WHO classification system of acute myeloid leukemia (2008):	17
Table (4):	Cytogenetic Abnormalities Sufficient to Diagnose AML with MD-related Changes*	23
Table (5):	Acute Myeloid Leukemia, Not Otherwise Specified (NOS)	25
Table (6):	WHO classification of ALL (2008)	31
Table (7):	Score for biphenotypic acute leukemia.	34
Table (8):	Panel of monoclonal antibodies for the diagnosis of Acute Leukemias:	43
Table (9):	Prognostic factors in acute myeloid leukemia	53
Table (10):	Prognostic factors in childhood ALL.....	60
Table (11):	Prognostic factors in adults ALL.....	60
Table (12):	Demographic and clinical data of studied AML patients.....	84
Table (13):	Demographic and clinical data of studied ALL patients.....	85
Table (14):	Haemtological data of studied AML patients	86
Table (15):	Haemtological data of studied ALL patients	87
Table (16):	Cell surface markers of studied AML patients.	88
Table (17):	Cell surface markers of studied ALL patients	89

LIST OF TABLES (Cont...)

Table No.	Title	Page No.
Table (18):	CD56, FAB, cytogenetics data, prognosis and mortality of studied AML patients	90
Table (19):	CD56, FAB, cytogenetics data, prognosis and mortality of studied ALL patients	91
Table (20):	Comparison between patients with positive expression of CD56 versus patients with negative expression of CD56 as regards demographic, clinical and hematological qualitative parameters in AML patients.....	92
Table (21):	Comparison between patients with positive expression of CD56 versus patients with negative expression of CD56 as regards demographic, clinical, hematological and immuno-phenotyping quantitative parameters in AML patients	93
Table (22):	Comparison between patients with positive expression of CD56 versus patients with negative expression of CD56 as regards demographic, clinical and hematological qualitative parameters in ALL patients	94
Table (23):	Comparison between patients with positive expression of CD56 versus patients with negative expression of CD56 as regards demographic, clinical, hematological and immunophenotyping quantitative parameters in ALL patients	95
Table (24):	Association between outcome and CD56 expression in different AML FAB subtypes.....	96
Table (25):	Association between fate and CD56 expression in different AML FAB subtypes.....	97

LIST OF TABLES (Cont...)

Table No.	Title	Page No.
Table (26):	Association between cytogenetics as a prognostic parameter and CD56 expression in AML patients.....	98
Table (27):	Association between cytogenetics as a prognostic parameter and CD56 expression in ALL patients.....	99
Table (28):	Association between treatment outcome, fate and CD56 expression in AML patients	100
Table (29):	Association between treatment outcome, fate and CD56 expression in ALL patients	101

LIST OF ABBREVIATIONS

Abbrev.	Full Term
ABL	Acute basophilic leukemia
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
AML-MRC	AML with myelodysplasia-related changes
AML-NOS	Acute myeloid leukemia not otherwise categorized
ANLL	Acute non lymphoblastic leukemia
APL	Acute promyelocytic leukemia
APMF	Acute panmyelosis with myelofibrosis
BAL	Biphenotypic acute leukemia
bcl-2	B-cell lymphoma 2
BCRP	Breast cancer resistance protein
BM	Bone marrow
BPDC	Blastic plasmacytoid dendritic neoplasm
CBC	Complete blood count
CBF β	Core-binding factor β
CBFA2	Core-binding factor 2
CCG	Children's Cancer Group
CD	Cluster of differentiation
CEBPA	CCAAT/enhancer binding protein alpha
CEC	Circulating endothelial cells
CFU-GM	Colony forming factor-grnulocyte, momcyte
CNS	Central nervous system
CR	Complete remission
CSF	Cerebrospinal fluid
CX CR4	CX chemokine receptor 4

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full Term
cyt	Cytoplasmic
DEK-NUP214	Sidekick homolog 1-nucleoproyien 214
Del	Deletion
DL	Dichronic lenses
DNA	Deoxyribonucleic acid
DS	Down syndrome
EDTA	Ethylene diamine tetra-acetic acid
EGIL	European group for the immunological characterization of leukemias
Eo	Eosinophilic
ETO	Eight twenty one
ETV6	Ets variant 6
FAB	French-American-British
FACS	Fluorescence-activated cell sorting
FCM	Flow cytometry
FITC	Fluorescein isothiocyanate
FITC	Fluorescein isothiocyanate
FLT-3	Fms-like tyrosine kinase-3
FN III	Fibronectin III
FS	Forward angle scatter
GATA1	globin transcription factor 1
G-CSF	Granulocyte colony stimulating factor
Hb	Hemoglobin
HLA-DR	Human leukocytic antigen
HS	High signeficance