A STUDY OF LUPUS ANTICOAGULANT IN ACUTE LEUKEMIA

THESIS
Submitted for partial fulfillment of
M.Sc. Degree In
Internal Medicine

By

Mohammed Abd El-Samie El-Hadary
M.B., B.Ch.

Supervisors

Prof. Dr. MO'TASSAM S. AMER
Professor of Internal Medicine

Dr. EMAD E. BARKAT
Assist. Prof. of Internal Medicine

Dr. NEVINE NABIL KASSEM
Lecturer in Clinical Pathology

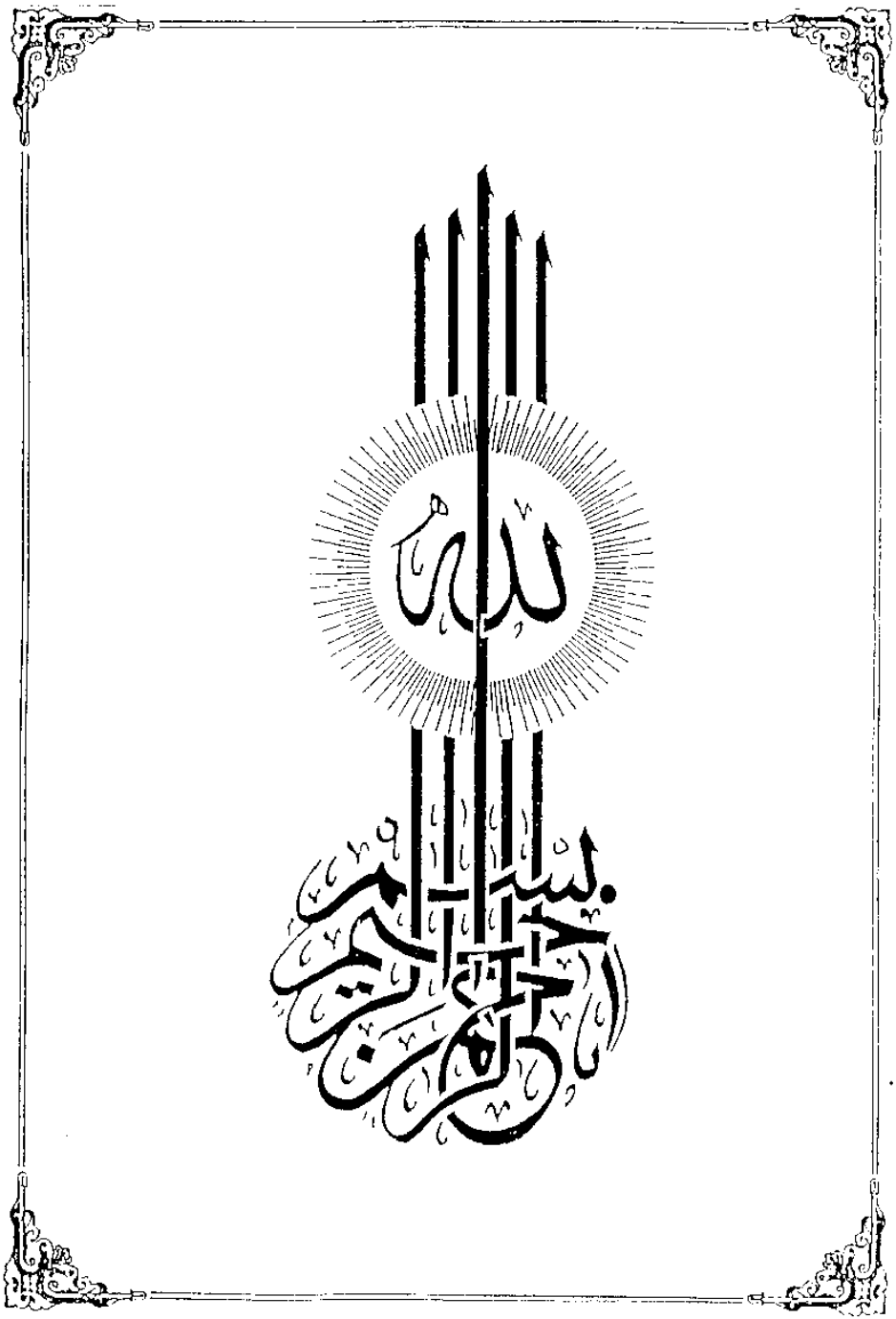
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY
1993

بسم الله الرحمن الرحيم

"وقل رب زدني علما"

صدق الله العظيم

سورة طه / ١١٤



ACKNOWLEDGEMENT

I would like to express my deep thanks and sincere gratitude to my Professor Dr. Mo'Tassam Salah Amer, professor of internal medicine,Faculty of Medicine, Ain Shams University, for givin me the privilage to work under his supervision.

My true feeling of Sincere gratitude to Professor Dr. Emad Barakat, assistant professor of internal medicine, Ain Shams University, for his useful advice, great help and constant guidance.

I am also so greatful for Dr. Nevine Nabil Kassem, lecturer of clinical pathology, Ain Shams University whom I owe many valuable remarks and a lot of precious time and effort.

Finally, I would like to express my thanks to all those who shared in bringing out this presentation to the light.

CONTENTS

LIST OF ABBREVIATIONS

A.C.A.	= Anticardiolipin Antibodies.
A.C.L.	= Anti cardiolipin syndrome.
A.L.L.	= Acute Lymphoid Leukemia.
A.M.L.	= Acute myeloid leukemia.
A.P.L.A.	= Anti phospholipid antibodies.
A.P.A.	= Anti phospholipid.
A.P.T.T.	= Activated Partial Thrombo-plastin time.
A.T.L.	= Adult. T. Cell Leukemia.
B.M.	= Bone marrow.
C.M.L.	= Chronic myeloid leukemia.
C.T.	= Computarized Axial Tomography.
D.R.V.V.T.	= Dilute Russel Viper Venons time.
D.I.C.	= Dissemenated Intravascular coagulation.
E.B.	= Epstein Barr.
E.L.I.S.A.	= Enzyme Linked Immuno absorbant Assay.
F.	= Female.
F.A.B.	= Frensh - American - Britich.
H.T.L.V-I	= Human T-cell Lymphotropic virus type I.
H.T.L.V-II	= Human T-cell Lymphotropic virus type II.
Ig G	= Immunoglobulin G.
Ig M	= Immunoglobulin M.
K.C.T.	= Kaolin Clotting time.
K.C.T.T.	= Kaolin-Cephalin Clotting time.
L.A.C.	= Lupus Anticoagulant.
L.D.H.	= Lactate Dehydrogenase.
M.	= Male.
PAPs	= Primary Antiphospholipid syndrome.
PNP	= Platelet neutralizing procedure.
P.T.T.	= Partial thromboplastin time.
RBCs	= Red Blood Corpuscles.
PAS	= Periodic Acid Schiff
S.L.E.	= Systemic Lupus Erythmatosus.
T.d.T.	= Deoxynucleotidyl transferase.
T.T.P.	= Thrombotic thrombocytopenic purpura.
Va	= Proaccelerin or labile factor.
VDRL	= Venereal Disease Research Laboratory.

LIST OF TABLES

INTRODUCTION

INTRODUCTION

The lupus Anticoagulant (LAC) has certainly received its fair share of attention in recent years. It is inappropriately named, neither being restricted to patients with systemic lupus erythematosus, nor having any anticoagulant properities except in some in vitro tests *(Harris 1990).*

It appears frequently to result from an autoimmune phenomena, sometimes in association with drug ingestion, viral illnesses or lymphoproliferative disease. Whereby certain individuals develops antibodies which are either directed against, or cross-react with, negatively charged phospholipids. The latter contain phosphodiesterase groups which appear to be the antigenic stimulus, since they also occur in substances which sometimes cross react with the antibodies, such as the mitochoridrial lipid, cardiolipin and degraded single-stranded DNA.

Recently, However, it has been demonstrted that the LAC can be neutralized by phospholipids which assume a hexagonal configuration at 37°C *(Rauch et al, 1989).*

These modifications are sometimes the result of cell membrane damage. Consequently, the immunological disorder which produces the clinical sequelae of LAC is often referred to as the antiphospholipid syndrome. Paradoxically, the LAC is associated not with a bleeding diathesis but with an increased incidence of thromboembolism and obstetrical complications particularly spontaneous abortion. The clinical sequelae of LAC have recently been reviewed by lechner (1987) and Triplett (1990).

The screening and confirmatory laboratory tests used to detect and classify LAC are designed to be highly lipid sensitive, and a list of some of those which are widely applied to patients with unexplained thrombosis or recurrent abortions is given in Table (1), Procedural details of tests for the laboratory identification of LAC are beyond the scope of this review, but are provided elsewhere *(Exner et al., 1990).*

Table (1): Methods of detection of LAC

Test	Reference to Method	Diagnostic Kit
APTT with 50:50 N/P mix	Machin et al (1991)	-----
Kaolin clotting time	Exner et al (1978)	------
Dilute Russell's Viper venom time	Machin et al (1991)	------
Platelet Correction test	Thiagarajan et al (1986)	American Diagnostics
Dilute thromboplastin time (Thromboplastin inhibition test)	Machin et al (1991)	
Anticardiolipin titre	Triplett et al (1983)	LEP
Antiphospholipid antibodies	Machin et al (1991)	
	Schleideret al (1976)	-----
	Liu et al (1989)	-----
	Harris et al (1983)	LEP
	Triplett et al (1988)	Stago

REVIEW OF LITERATURE

THE ACUTE LEUKEMIA

DEFINITION:

Acute leukemia is the result of a malignant event or events occuring in early hematopoietic precursor, the affected cell gives rise to progency that fail to differentiate and instead continue to proliferate in an uncontrolled fashion. As a result immature myeloid cells, lymphoid cells, or blast cells rapidly accumulate and progressively replace the bone marrow. (Cheson BD, et al, 1990)

ETIOLOGY:

Fredrich R. Appelboum 1992 found that many possible events can cause acute leukemia which are:

1) Radiation:

Ionizing radiation is leukemogenic. ALL, AML and CML are all increased in incidence in patients given radiation therapy for ankylosing spondylitis and in survivors of the atomic bomb basts of Hiroshima and Nagasaki.

2) Oncogenic viruses:

The search for viral cause of leukemia found that two rare types of leukemia associated with retroviruses. Human T cell lymphotropic virus type I (HTLV-1) is considered the causative agent of adult T cell leukemia (ATL). A second human retrovirus termed (HTLV II) has been isolated from several patients with a syndrome resembling Hairy cell leukemia.

3) Genetics and congenital factors:

Several autosomal recessive disorders associated with chormosomal instability are prone to terminate in acute leukemia, including bloom syndrome, fanconi anaemia and ataxic telangiectasia. Other congenital disorder associated with an increased incidance of leukemia are Down'syndrome and infantile X linked agammagolobulinemia.

4) Chemicals:

Prior exposure to alkylating agents such as chlorambucil, melphalan and nitrogen mustard is associated with an increased risk of AML.

INCIDENCE:

ALL is the most common cancer and the second leading cause of death in children under 15 year of age. All has a maximal incidence between 2 and 10 years of age. The incidence of AML gradually increase with age without an early peak. Approximately half of AML cases occur in patients under age 50.

PATHOPHYSIOLOGY:

The mechanism of normal marrow suppression in leukemia is complex in many patients with hypercellular marrow, pancytopenia is probably the result at least in part of physical replacement of normal marrow precursors by leukemic cells. Some patients develop pancytopenia with a hypocellular marrow. However marrow failure is not simply due to physical replacement of the marrow space but also may be due to substances released by the malignant cells.

CLASSIFICATION:

Bennett JM, Caovsky D, Daniel MT, et al (1985) classify acute leukemia in a variety of ways including morphalogy,