MYCOBACTERIAL PULMONARY INFECTION IN CHILDHOOD LEUKEMIA & LYMPHOMA

Thesis submitted for the partial fulfillment of Master Degree in Pediatrics

By

Dr. Hesham Mahmoud Ahmed Abou Allwaffa

M.B. B.Ch. 1989 Under Supervision of

Dr. Mona Hussein El-Samahy

Assistant Professor of Pediatrics Ain Shams University Faculty of Medicine

EIE. 155 H. M Dr. Azza Abdel Gawad Tantawi

> Lecturer of Pediatrics Ain Shams University

> > Faculty of Medicine

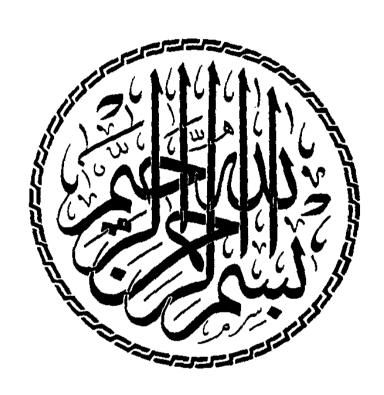
Dr. Aisha Mamdoh Hafez

Lecturer of Microbiology & Immunology Ain Shams University

Faculty of Medicine

Ain Shams University Faculty of Medicine 1993

~7037





ACKNOWŁEDIMENI

- I wish to express may deep appreciation and gratitude to Ass. Prof. Dr. Mona K.M. Samahy Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for giving me the privilege of working under her instructive supervision and helpful guidance.
- I wish to express my deep gratitude to Prof. Ahmed Samy Nhalifa Professor of Pediatrics, Ain Shams University for giving me the chance to work under his supervision In the Hematology—Oncology Clinic, Children's Hospital, Ain Shams University.
- I also express may deep thanks and gratitude to Dr. Appa Abdol Lawad Lecturer of Pediatrics, Ain Shams University, Faculty of Medicine for her great support, encouragment and help throughout the whole work.
- I also express special gratitude to **Dr. Aisha Mamdoh** Lecturer of Microbiology and Immunology, Faculty of Medicine, Ain Shams University for her honest supervision, helpful suggestion, sincere effort and outstanding assistance through every step of this work.
- I also express special thanks for Dr. All Jaki Lecturer of Microbiology and Immunology Faculty of Medicine, Ain Shams University for his kind help.
- To my friends, my family, all patients and their families and to everyone who participated in some way or other to let this work come to such a final picture I owe my thanks and gratitude.

CONTENTS

	Page
Introduction.	
Aim of the work.	
Review of literature	
*Childhood acute leukemia.	3
*Non -Hodgkin's lymphoma.	12
*Hodgkin`s lymphoma.	16
*Mycobacteria.	20
*Tuberculous mycobacteria.	20
*Non tuberculous mycobacteria.	33
*Infection in leukemia and lymphoma.	40
*Mycobacterial infections with malignancy.	44
Subjects and methods.	
Results.	
Discussion.	
Conclusion and recommendations	
Summary.	85
References.	
Arabic summary.	

List of Tables

		Page
Table (1)	FAB classification of ALL.	7
Table (2)	FAB classification of AML.	7
Table (3)	Cytochemical classification of acute leukemia.	8
Table (4)	Markers of acute lymphocytic leukemia.	9
Table (5)	General strategy of treatment of acute leukemia.	10
Table (6)	NCI work formulation & it's relation to the Rappoport	14
	Classification of NHL.	
Table (7)	Regimens used in treatment of NHL.	15
Table (8)	Staging Classification of HD.	17
Table (9)	Rye's Classification of Hodgkin's disease.	18
Table (10)	Clinical spectrum of tuberculosis.	25
Table (11)	Score chart to diagnose tuberculosis.	26
Table (12)	The preferred therapy of tuberculosis in children.	31
Table (13)	Runyon Classification for Mycobacteria.	33
Table (14)	Most common sites of infection for NTM.	35
Table (15)	Commonly used drugs for Non-tuberculous mycobacteria.	39
Table (16)	The immune defects associated with hematological	43
	and lymphoid malignancies and the most common	
	infecting organism.	
Table (17)	Clinical and Laboratory data of group I (cancer patients).	55
Table (18)	Clinical and Laboratory data of group II patients	56
	with chronic chest infection	

Table (19)	Clinical and Laboratory data of group III(control group)	57
Table (20)	Comparison of hemogram and ESR in the 3groups	59
Table (21)	Comparison of the 3 groups as regards the weight	60
	and height percentile.	
Table(22)	Comparison of the BCG scar and tuberculin	63
	skin testing using 5IU in the 3 groups.	
Table (23)	Comparison between the 3 groups as regards the	64
	clinical picture suggestive of tuberculosis, suggestive	
	chest x-ray and bacteriological diagnosis.	
Table (24)	Shows the clinical picture, laboratory data, chest	67
	x-ray findings and bacteriological examination of the	
	3 patients with bacteriological proved tuberculosis.	

List of Figures

		Page
Figure (1)	Histogram comparing between the presence	62
	of BCG scar and the results of tuberculin	
	intradermal test	
Figure (2)	Histogram comparing the prevalence of bacter-	65
	iological pulmonary tuberculosis in cancer	
	patients& immunocompetent patients.	
Figure (3)	Chest x-ray picture of patient no (7).	68
Figure (4)	Chest x-ray picture of patient no (8).	69
Figure (5)	Chest x-ray picture of patient no (20).	70
Figure (6)	Chest x-ray picture of patient no (35).	71
Figure (7)	Chest x-ray picture of patient no (23).	72
Figure (8)	Slope of L.J. with growth.	73
Figure (9)	Picture of acid fast bacilli in sputum stained	74
	with Zeilh-Neelsen.	
Figure (10)	Picture of acid fast bacilli from growth on L.J.	75
	stained with Zeilh-Neelsen.	

List of Abbreviations

AIDS Acquired immundeficiency syndrome.

ALL Acute lymphatic leukemia.

AML Acute myeloid leukemia

BCG Bacillus Calmette and Guerine.

CD4 T. helper lymphocyte.

ELISA Enzyme linked immunosorbent assay.

FAB French-American classification of acute leukemia.

G.C.S.F. Granulocyte -colony stimulating factor.

GM.C.S.F. Granulocyte-Macrophage colony stimulating factor.

HTLV.1 Human-T-lymphocyte virus 1.

IL1 Interleukin 1.

LFS Leukemia Free Survival.

MAC Mycobacteria avium intracellular complex.

McAb Monoclonal antibody.

NHL Non-Hodgkin lymphoma.

MOTT Mycobacteria other than tuberculosis.

NTM Non-tuberculous mycobacteria.

PCR Polymerase chain reaction. PPD Purified protein derivatives.

RFS Relapse free survival.
ZN Zeilh- Neelsen stain.

INTRODUCTION AIM OF THE WORK

INTRODUCTION

With advances in the effective treatment of childhood leukemia and lymphoma using combination chemotherapy and radiotherapy, infectious complications became a major cause of morbidity and mortality during therapy of malignancies (Albano and Pizzo, 1988).

Pulmonary infections in patients with malignancies are caused by a wide variety of microorganisms involving mycobacteria. The association of mycobacteriosis with malignant diseases has been recognised for several years. In the last years ,infections caused by atypical mycobacteria have been described with increasing incidence in malignant patients (Rolston et al,1985).

Recently Stark (1992) reported a higher incidence of nontuberculous mycobacteria in patients with leukemia and lymphoma, the infection confined to the lung in 75-88% of cases.

AIM OF THE WORK

The aim of the present work is to assess the role of mycobacteria whether tuberculous or nontuberculous as etiologic agents of pulmonary infection in children with leukemia and lymphoma suffering from chronic chest infection.

REVIEW OF LITERATURE

Childhood Acute Leukemia

Acute leukemia accounts for approximately 30% of childhood cancer in the United States (Pratt,1985). Among childhood acute leukemia patients, 82% have acute lymphocytic leukemia (ALL), while approximately 18% have acute myelocytic leukemia (Poplack,1985). In Egypt Khalifa et al (1993) reported a prevalence of leukemia of 56.3% among pediatric malignant diseases. ALL accounts for 77% of childhood acute leukemia while acute myelocytic leukemia (AML) accounts for the remaining 23% (Khalifa et al,1982).

Age and sex distribution:

Acute leukemia is a disease of both children and adults. Childhood ALL has a peak incidence between the age of 3 and 5 years (Fernbach, 1984). This peak does not occur uniformly throughout the World, being absent in Africa and many developing nations, which has prompted speculation that this peak may reflect environmental exposure associated with modernization. However, there is no specific age distribution in AML (Ramot & Magrath, 1982; Poplack 1985).

Childhood acute leukemias occur more often in males than females. The male to female ratio among Egyptian childhood acute leukemias is 2.6:1 and 2.7:1 in ALL and AML respectively (Fayez, 1987).

Seasonal Variations:

Seasonal variations in the incidence of childhood leukemia have been reported in some studies, however, it has not been observed among Egyptian patients (Greenberg & Shuster1985; Fayez, 1987).

Geographical distribution:

International data show a marked disparity in the incidence of childhood acute leukemia which is worldwide with a lower disease incidence in Africa and Middle East and higher rate in China, Japan, United States, England and Europe (Greenberg and Shuster,1985). The occurrence of acute leukemia was demonstrated to be increased in immigrate populations, supporting the possible role of environmental factors in determining the potential expression of malignancy (Ramot & Magrath,1982).

Etiology Of Acute Leukemia:

The exact etiology of acute leukemia is unknown, however, certain risk factors are recognized (Mc Credit, 1983).

It has been suggested that ALL is predominantly a disease of middle and upper socioeconomic classes. However, the socioeconomic status may reflect many exposures and other influences, including maternal age, parent education and occupational exposures and therefore it is difficult to be considered directly as single risk factor. (Mc Whuter, 1982).

The race has also a contributing role, as occurrence of ALL in the white race is about 20-30 percent greater than in the black race. However, this may reflect social class difference rather than the race itself (Neglia and Robison, 1988).

The role of *environmental agents* have been widely studied. The detection of the critical time of exposure is of a great value. The preconception and the prenatal periods may be of particular interest because of the natural differentiation of primitive cells (Neglia and Robison, 1988).

Prenatal exposure to diagnostic ionizing radiation was shown to be associated with childhood ALL. The risk is estimated to be 1.5 to 2 times that of non-exposed population (Stewart and Kneale, 1970). Adult AML has a relation with exposure to ionizing radiation, paint solvent, petroleum products and cancer chemotherapeutic agents. Studies show a positive correlation between the nature of the agent of exposure and the frequency of specific