

**REVIEW OF CASES OF PLEURAL
MESOTHELIOMA PRESENTED IN GIZA
CHEST HOSPITAL IN THE PERIOD FROM
2004 TO 2007**

THESIS

*Submitted for Partial Fulfillment of Master Degree in
Chest Diseases*

By

SAMMAN ALI ZIDAN
(M.B.B.ch)

Supervised by

Prof. LAILA ASHOUR M. HELALA

Professor of Chest Diseases
Faculty of Medicine, Ain Shams University

Dr. IBRAHIM DWEDAR

Lecturer of Chest Diseases
Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University**

2010

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

 "وَقُلْ رَبِّ زِدْنِي عِلْمًا"

صدق الله العظيم

سورة طه الآية (١١٤)

Acknowledgment

In the name of Allah, most gracious and most merciful.

Before all and above all, thanks to Allah, this work has been brought to light.

I would like to express my deepest gratitude & appreciation to my Professor Laila Ashour Mohammed Helala, Professor of Chest diseases, Ain Shams University whose help, encouragements & sincere care guided me all through conducting this research.

I'm much obliged and indebted to my dear Dr. Ibrahim Dwedar, Lecturer of Chest Disease, Ain Shams University for his efficient help and great support to learn and to complete my work.

I also would like to thank the manager and staff members in Giza chest hospital for their support and encouragement throughout the work.

I also want to thank Dr. Mohammed Afifi for his support in completing this work.

At last, I would like to express my profound gratitude to my family specially my parents for their endless love & concern and my wife who gave me the full support to complete this work.

Dr.Saman Ali Zidan

CONTENTS

LIST OF ABBREVIATIONS	ii
LIST OF FIGURES	iv
LIST OF TABLES	vi
INTRODUCTION & AIM OF WORK	1
REVIEW OF LITERATURE	6
Chapter (1) Pleura	6
Chapter (2) Mesothelioma	41
SUBJECTS & METHODS	87
RESULTS	94
DISCUSSION	109
SUMMARY	120
CONCLUSION AND RECOMMENDATIONS	123
REFERENCES	126
الملخص العربي	

LIST OF ABBREVIATIONS

ADA	: Adenosine Deaminase.
B.C	: Before Christ.
B.C.G	: Bacillus – Calmette – Guerin.
CA 15-3	: Cancer Associated Antigen.
CA 19-9	: Carbohydrate Antigen.
CEA	: Carcino-embryonic Antigen.
CALGB	: Cancer and Leukemia Group B.
CK5/6	: Cytokeratine 5/6.
CD	: Cluster of lymphocyte differentiation.
CT	: Computed tomography.
DLco	: Diffusion Lung Capacity.
DMM	: Diffuse Malignant Mesothelioma.
DNA	: Deoxyribonucleic acid.
ECOG	: Eastern Cooperative Oncology Group.
EGF	: Epidermal Growth Factor.
EORTC	: European Organization for Research and Treatment of cancer
EPP	: Extrapleural Pneumectomy.
FDG	: Fluorodeoxyglucose.
FRC	: Functional Residual Capacity.
F/ml	: Fiber / milliliter.
GCV	: Ganciclovir.
G	: Gouge.
HSVtk	: Herpes Simplex Virus thymidine kinase
IGF	: Insulin Growth Factor.
IHC	: Immunohistochemistry.
IL-2	: Interleukin 2.
IL-6	: Interleukin 6.
IMIG	: International Mesothelioma Interest Group.
IMRT	: Intensity Modulated Radiation Therapy.
IFN- γ	: Interferon gamma.
IFN- α	: Interferon alpha.

Leu M1	: Leukocyte M1.
LDH	: Lactate Dehydrogenase.
MAb	: Monoclonal Antibody.
MM	: Malignant Mesothelioma.
MPF	: Megakaryocyte Potentiating Factor.
MPM	: Malignant Pleural Mesothelioma.
MRI	: Magnetic Resonance Imaging.
NCI	: National Cancer Institute.
NF2	: Neurofibromatosis type 2.
ODN	: Oligodeoxynucleotide.
OAS	: Overall survival.
PAO₂	: Alveolar Oxygen tension.
PAS-D	: Periodic Acid Schiff after diastase digestion.
PCO₂	: Carbon dioxide tension.
PDGF	: Platelet Derived Growth Factor.
P/D	: Pleurectomy / Decortication.
PET	: Positron Emission Tomography.
PH₂O	: Water tension.
PN₂	: Nitrogen tension.
PPDs	: Personal Protective Devices.
Rb	: Retinoblastoma.
SMRP	: Soluble Mesothelin Related Peptides.
SOB	: Shortness of breath.
SV-40	: Simian Virus 40.
T-Ag	: T- Antigen.
TGF-β	: Transforming Growth Factor β .
TNF	: Tumor Necrotic Factor.
T.T.	: Tuberculin test.
TTF-1	: Thyroid Transcription Factor 1.
VATS	: Video Assisted Thoracoscopic Surgery.
WTp53	: Wild Type of P53.
WT1	: Wilm's Tumor 1.

LIST OF FIGURES

<i>Figure</i>	<i>Subject</i>	<i>Page</i>
<i>Review of Literature</i>		
(1)	The pleural sac	6
(2)	Scanning electron micrograph showing a lymphatic stoma on the surface of the parietal pleura.	10
(3)	Malignant Pleural Mesothelioma	41
(4)	Gross Picture of mesothelioma	59
(5)	Histopathological types of MPM	60
(6)	Epithelioid mesothelioma positive for CK5/6 with perinuclear enhancement (x400)	61
(7)	Biphasic mesothelioma, both components are positive for calretinin (x100).	62
(8)	Biphasic mesothelioma with p27 positive epithelioid.	63
(9)	CXR, PA and Lat of MPM with pleural thickening.	68
(10)	CT chest of MPM with pleural thickening.	68
(11)	Typical mesothelioma in pleura 4.	69
(12)	Mesothelioma-3a plaques.	69
(13)	Typical pleural nodules in MPM.	70
(14)	MPM presenting with pleural thickening and massive pleural effusion.	70
(15)	MPM with extra pleural extension to chest wall.	71
(16)	Positron Emission tomography in MPM	71

<i>Figure</i>	<i>Subject</i>	<i>Page</i>
<i>Results</i>		
(1)	Total number of MPM cases admitted in Giza Chest Hospital every year.	95
(2)	Sex Distribution of MPM Cases.	96
(3)	Age Distribution of MPM Cases.	96
(4)	Frequency distribution of cases according to age and sex.	97
(5)	Geographical distribution of cases by city and District.	99
(6)	Distribution of cases according to governorate.	100
(7)	Variable occupation of the MPM patients.	101
(8)	The presenting symptoms of MPM patients.	102
(9)	Smoking habits among studied population	103
(10)	Radiological localization of pleural effusion in Chest radiograph (CXR).	104
(11)	C T finding among 45 patients according to the available CT reports	105
(12)	Cytological examination of pleural effusion.	106
(13)	Pathological subtypes of Mesothelioma among presented cases	108

LIST OF TABLES

<i>Table</i>	<i>Subject</i>	<i>Page</i>
<i>REVIEW</i>		
(1)	Normal composition of pleural fluid.	17
(2)	Forces governing pleural fluid production & removal.	20
(3)	Useful tests in evaluation of pleural effusion.	32
(4)	Butchart staging system.	73
(5)	The Brigham Staging System.	73
(6)	International mesothelioma interest group (IMIG) staging system.	74
<i>RESULTS</i>		
(1)	Total number of MPM cases admitted in Giza Chest Hospital every year.	95
(2)	Sex Distribution of MPM Cases.	96
(3)	Age Distribution of MPM Cases.	96
(4)	Frequency distribution of cases according to age and sex.	97
(5)	Geographical Distribution of MPM cases by city and districts.	98
(6)	Distribution of cases according to governorate.	100

(7)	Variable occupation of the MPM patients	101
(8)	Presenting symptoms of MPM patients.	102
(9)	Smoking habits among the studied population.	103
(10)	The physical signs recorded in the files of 115 patients.	104
(11)	Radiological localization of pleural effusion in Chest radiograph (CXR).	104
(12)	C T finding among 45 patients (out of 115 patients) according to the available CT reports.	105
(13)	Cytological examination of pleural effusion	106
(14)	The different types of performed pleural biopsy	106
(15)	Diagnostic yields of different types of pleural biopsy and thoracocentesis	107
(16)	Pathological subtypes of Mesothelioma among 115 cases	107
(17)	The iatrogenic complications of pleural biopsy and thoracocentesis.	108

INTRODUCTION

The pleural space is enclosed by the visceral pleura, which covers the lungs, and by the parietal pleura, which lines the chest wall, diaphragm, and mediastinum. mesothelial cells form a continuous layer over the whole of the visceral and parietal pleural surfaces. Mesothelioma is a form of cancer that is almost always caused by previous exposure to asbestos. In this disease, malignant cells develop in the mesothelium (*Wang et al, 1985*).

Most people who develop mesothelioma have worked on jobs where they inhaled asbestos particles, or have been exposed to asbestos dust and fiber in other ways, such as by washing the clothes of a family member who worked with asbestos, or by home renovation using asbestos cement products. Unlike lung cancer, there is no association between mesothelioma and smoking (*Muscat and Wyender, 1991*).

Although reported incidence rates have increased in the past 20 years, mesothelioma is still a relatively rare cancer. The incidence is approximately one per 1,000,000. For comparison, populations with high levels of smoking can have a lung cancer incidence of over 1,000 per 1,000,000. Incidence of malignant mesothelioma currently

ranges from about 7 to 40 per 1,000,000 in industrialized western nations, depending on the amount of asbestos exposure of the populations during the past several decades (*Bruce and Richard, 2005*)

Malignant pleural mesothelioma most commonly presents in the fifth to seventh decades of life. the most frequent presenting symptoms are pleuritic chest pain, dyspnea, and cough. Some patients are asymptomatic at diagnosis. Video-assisted thoracoscopy or open thoracotomy is often necessary to make the diagnosis (*Fishman et al, 2002*)

Mesothelioma is more responsive to radiation than non-small cell carcinoma, yet better used for preventing chest wall recurrences after thoracoscopy/thoracotomy and in improving local control after pleurectomy or extra-pleural pneumonectomy. Surgical intervention has been useful in palliating the major symptoms of the disease (*Fishman et al, 2002*).

Surgery in this disease is controversial. Seeding is frequent, and tumor may actually grow out of the thoracotomy incision used to treat the tumor. Some say surgery should be limited to achieving a diagnosis. Others advocate thoracotomy with pleurectomy whereas others

perform a radical extrapleural pneumonectomy to remove all the pleura and lung on the affected side. Although 2 year survival after the procedure is improved with up to one-third surviving, 5 year survival is dismal

(Baumgartner F.J, 2003)

For patients with localized disease and who can tolerate radical surgery, radiation is often given post-operatively as consolidative treatment. The entire hemithorax is treated with radiation therapy, and often given simultaneously with chemotherapy **(Sugarbaker, et al 1999)**

Asbestos has been recognized in Egypt since a long time as ancient Egyptians were using it in mummification. Mesothelioma in Egypt is mainly attributed to environmental origin with a high incidence of women and young adults affected. The incidence of mesothelioma is rising in Egypt. Epidemiological data for 635 malignant mesothelioma (MM) patients last 4 years in the third millennium were collected from the National Cancer Institute (NCI), Cairo University and Abbassia Chest hospital. This number is more than four times the number diagnosed in the previous 11 years at NCI. A clinico pathological study was done for 100 malignant pleural

mesothelioma (MPM) patients and showed that asbestos exposure and simian virus-40 (SV40) positivity were evident in 67% and 60% of cases, respectively. The median survival was 14.3 months and the 1 and 2 year survival rates were 60% and 27%, respectively. Asbestos in Cairo is a silent killer and measures toward eliminating it entirely or at least strictly controlling human contact with this dangerous carcinogen have to be taken in order to combat the coming epidemic of mesothelioma in Egypt. (*Gaafar and Aly Eldin 2005*).

AIM OF THE WORK

The aim of this study is to review the cases of malignant mesothelioma admitted to Giza Chest Hospital in the period between 2004 and 2007.