

Paget's Disease of the Breast and Our Clinical Experience at Ain Shams University Hospitals

Thesis

*Submitted for Partial Fulfillment of Master Degree in
General Surgery*

By

Paula Samir Nazim Sadary

M.B.B.Ch., Faculty of Medicine – Ain Shams University (2015)

Under Supervision of

Prof. Dr. Ashraf abd el Moghny Mostafa

Professor of Breast Surgeries

Faculty of Medicine - Ain Shams University

Dr. Karim Fahmy abd el Moaty

Lecturer of General Surgery

Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University

2019

Acknowledgment

*First and foremost, I feel always indebted to God,
the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and
profound gratitude to Prof. Dr. Ashraf abd
el Moghny Mostafa, Professor of Breast
Surgeries, Faculty of Medicine - Ain Shams
University for his keen guidance, kind
supervision, valuable advice and continuous
encouragement, which made possible the
completion of this work.*

*I am also delighted to express my deepest
gratitude and thanks to Dr. Karim Fahmy
abd el Moaty, Lecturer of General Surgery,
Faculty of Medicine - Ain Shams University, for
his kind care, continuous supervision, valuable
instructions, constant help and great assistance
throughout this work.*

*I would like to express my hearty thanks to
all my family for their support till this work
was completed.*

*Last but not least my sincere thanks and
appreciation to all patients participated in this
study.*

Paula Samir

List of Contents

Title	Page No.
List of Tables	i
List of Figures	ii
List of Abbreviations	vii
Introduction	1
Aim of the Study	10
Review of Literature	
☞ Anatomy of Breast	11
☞ Types of Breast Cancer	16
☞ Risk Factors of Breast Cancer	22
☞ TNM Staging of Breast Cancer	24
☞ Paget's Disease of Breast	26
Materials and Methods	79
Results	81
Discussion	100
Summary	104
References	105
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	TNM staging.....	24
Table (2):	Shows symptomatology, radiological finding and lymph node results.....	81
Table (3):	Shows biopsy, staging, receptors, surgical and hormonal treatment.....	85
Table (4):	Shows radio and chemotherapy, recurrence and survival of patients	91
Table (5):	Shows relation between positive lymph node by pathology and other risk factors.....	93
Table (6):	Shows relation between positive lymph node by pathology and mass radiologically and its size	96
Table (7):	Shows relation between positive lymph node by pathology and biopsy and staging.....	98

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Alveoli and ducts of breast.....	12
Figure (2):	Arterial supply of breast.....	14
Figure (3):	Lymphatic drainage of breast	14
Figure (4):	Division of breast lobes.....	16
Figure (5):	Normal duct and invasive ductal carcinoma.	17
Figure (6):	Paget disease of the nipple.....	28
Figure (7):	Clinical features of Paget disease in a 36-year-old woman with a 2-year history of pruritic erythema of the left nipple.....	31
Figure (8):	Paget disease in a 55-year-old woman with a 1-year history of pruritic erythematous change of the left nipple	33
Figure (9):	Drawings show categories of Paget disease of the breast	35
Figure (10):	Paget disease without DCIS in a 68-year-old woman with eczema and skin pigmentation of the left nipple	36
Figure (11):	Associated DCIS in a 35-year-old woman with Paget disease of the right nipple.....	37
Figure (12):	Paget disease with associated invasive breast cancer in a 57-year-old woman with a 1-year history of eczema of the right nipple-areolar complex.....	38
Figure (13):	Paget disease with associated DCIS in a 61-year old woman with a 1-year history of a pruritic erythematous scaly patch of the left nipple areolar complex.....	41

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (14):	Paget disease with associated invasive breast cancer in a 54-year-old woman with a palpable mass in the right breast and eczematous change of the right nipple-areolar complex	42
Figure (15):	Paget disease with associated DCIS in a 60-year-old woman with itching of the left nipple and bloody discharge from the left nipple	43
Figure (16):	Paget disease of the left nipple in a 63-year-old woman	45
Figure (17):	Paget disease with associated DCIS in a 67-year-old woman with a palpable mass associated with retraction of the left nipple	46
Figure (18):	Normal nipple enhancement patterns at MR imaging.....	48
Figure (19):	Paget disease with associated DCIS and invasive breast cancer in a 35-year-old woman with a palpable mass in the right breast	50
Figure (20):	Paget disease with associated invasive breast cancer in a 56-year-old woman with a palpable mass in the left breast.....	52
Figure (21):	Surgical treatment of paget's disease of the breast.	58
Figure (22):	Modified radical mastectomy.	59
Figure (23):	Steps of modified radical mastectomy.....	64
Figure (24):	Continue of steps of modified radical mastectomy.....	68
Figure (25):	Sentinel lymph node biopsy.....	74

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (26):	Steps of sentinel lymph node biopsy.....	77
Figure (27):	Showing age category of paget's disease of the breast.	82
Figure (28):	Showing skin affection of paget's disease of the breast.	83
Figure (29):	Showing lymph node by pathology of paget's disease of the breast.	84
Figure (30):	Showing classification of paget's disease of the breast.	86
Figure (31):	Showing receptors of paget's disease of the breast.	87
Figure (32):	Showing surgical treatment of paget's disease of the breast.....	88
Figure (33):	Showing hormonal treatment of paget's disease of the breast.	89
Figure (34):	Showing staging of paget's disease of the breast.	90
Figure (35):	Showing chemotherapy of paget's disease of the breast.	91
Figure (36):	shows that patients having radiotherapy were 15 patients (75%).....	92
Figure (37):	Showing relation between age and lymph node by pathology.	94
Figure (38):	Showing percent of lymph node by pathology in relation to age.....	94

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (39):	Showing relation of lymph node by pathology to symptomatology of paget's disease of the breast.	95
Figure (40):	Showing relation of lymph node by pathology to presence of mass radiologically.	96
Figure (41):	Showing relation of lymph node by pathology to size of mass radiologically.	97
Figure (42):	Showing relation of lymph node by pathology to biopsy.	98
Figure (43):	Showing relation of lymph node by pathology to staging of breast cancer.	99

ABSTRACT

Background: Worldwide, breast cancer comprises 10.4% of all cancer incidences among women, making it the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer death. In 2004, breast cancer caused 519,000 deaths worldwide (7% of cancer deaths; almost 1% of all deaths). Breast cancer is about 100 times more common in women than in men, although males tend to have poorer outcomes due to delays in diagnosis.

Aim of the Work: To clarify clinical, pathological features and outcomes of the treatment modalities for Paget's disease of the breast at Ain Shams University Hospitals.

Materials and Methods: Our study was held as a retrospective cohort study to clarify clinical, pathological features and outcomes of the treatment modalities for Paget's disease of the breast at Ain Shams University Hospitals.

Results: At Ain Shams university hospitals patients having pagetoid cells by biopsy and no mass radiologically will undergo simple mastectomy and if pathology proved any malignancy in breast tissue axillary clearance will be done and may be followed by radiotherapy.

Conclusion: Patients having pagetoid cells by biopsy and a mass radiologically which is invasive or insitu with microinvasion will undergo modified radical mastectomy and may be followed by radiotherapy. But if pagetoid cells and mass radiologically which is in situ simple mastectomy will be done.

Keywords: *Breast - Paget's Disease - Cancer*

List of Abbreviations

<i>Abb.</i>	<i>Full term</i>
<i>ALND</i>	<i>Axillary Lymph Node Dissection</i>
<i>DCIS</i>	<i>Ductal Carcinoma in Situ</i>
<i>ER</i>	<i>Estrogen Receptor</i>
<i>H&E</i>	<i>Hematoxylin and Eosin</i>
<i>IDC</i>	<i>Infiltrating Ductal Carcinoma</i>
<i>ILC</i>	<i>Infiltrating Lobular Carcinoma</i>
<i>LCIS</i>	<i>Lobular Carcinoma in Situ</i>
<i>MPD</i>	<i>Mammary Paget's disease</i>
<i>MR</i>	<i>Magnetic Resonance</i>
<i>NCI</i>	<i>National cancer institute</i>
<i>NOS</i>	<i>Not otherwise specified</i>
<i>PR</i>	<i>Progesterone receptor</i>
<i>SNLD</i>	<i>Sentinel Lymph Node Dissection</i>

INTRODUCTION

Worldwide, breast cancer comprises 10.4% of all cancer incidences among women, making it the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer death. In 2004, breast cancer caused 519,000 deaths worldwide (7% of cancer deaths; almost 1% of all deaths). Breast cancer is about 100 times more common in women than in men, although males tend to have poorer outcomes due to delays in diagnosis (*American Cancer Society, 2017*).

Cancer cells are very similar to cells of the organism from which they originated and have similar (but not identical) DNA and RNA. This is the reason why they are not very often detected by the immune system, in particular, if it is weakened (*American Cancer Society, 2017*).

Paget's disease of the breast, a disorder of the nipple–areola complex, first described by Sir James Paget in 1874 (*Alvero, 2017*).

It is an uncommon disease, accounting for 1–4.3% of all the breast carcinomas (*Alvero, 2017*).

It is often associated with underlying ductal carcinoma *in situ* and/or invasive ductal cancer (*Alvero, 2017*).

Paget's disease is much more frequent in women because of the predominance of breast cancer in females. It occurs most commonly in post-menapausal women, often during the sixth decade of life (mean age 57 years), but it has been observed in adolescents and in elderly patients also (*Mkhinini et al., 2016*).

Therefore, Paget disease of the nipple is nearly always a sign of underlying breast malignancy. Underlying cancer is common even in women with a benign-appearing mammogram and no palpable mass. Patients with a palpable mass or suspicious mammographic findings have a high likelihood of invasive cancer, and these factors were significantly associated with a worse outcome (*Mkhinini et al., 2016*).

Incidence of breast cancer different types in Egypt was that Infiltrating duct carcinoma was the most predominant histological type constituting 76.4% of cases, followed by mixed infiltrating duct and lobular carcinoma (5.7%), lobular carcinoma (2.9%) and carcinoma NOS (2.3%). Proportion of 1.7% was observed for mucinousadenocarcinoma, comedo-carcinoma, medullary-carcinoma and mixed infiltrating duct carcinoma. Paget's disease represented 1.1 % of all pathological diagnoses (*Ibrahim et al., 2008*).

AIM OF THE STUDY

In this study we aim to clarify clinical, pathological features and outcomes of the treatment modalities for Paget's disease of the breast at Ain Shams University Hospitals.

Chapter 1

ANATOMY OF BREAST

Breast is present in both females and males and bounded by 2nd rib superiorly, 6th rib inferiorly, sternum medially and axilla laterally. It is supported by pectoral muscles, serratus anterior muscles and Cooper's ligaments (*Zucca-Matthes et al., 2016*).

It is predominantly circular, except minor oblong part, which extends further into axillary region ("axillary tail"). And Divided into 4 quadrants.

Areola:

It is Darkened area around nipples containing *Glands of Montgomery* which are small sebaceous glands. It Enlarges during pregnancy and provide lubrication and protection to nipple (*Zucca-Matthes et al., 2016*).

Nipple:

It is Porous which contains terminal ends of milk ducts and deliver milk to baby. Both areola & nipple have erectile smooth muscles (also prevents leaking) (*Moore et al., 2009; Auerbach & Riordan, 2004*).

Parenchyma (functional):

It is Glandular with ducts makes up 2/3 of the tissue under areola & nipple.

Glandular tissue consists of 15-20 lobes each containing lobules which contains alveoli which contains lactocytes (*Zucca-Matthes et al., 2016*).

Alveoli drain to small ducts draining to larger ducts draining to milk ducts then to nipple (*Zucca-Matthes et al., 2016*).



Figure (1): Alveoli and ducts of breast (*Auerbach & Riordan, 2004*).

Stroma (supporting) containing Adipose interspersed throughout breast, Cooper's ligaments, Blood vessels, Lymphatics and Nerves (*Zucca-Matthes et al., 2016*).