

Pathological Review of Malignant Uterine Body Tumors At Ain Shams University Hospitals 2001-2005

Thesis

Submitted for the partial fulfillment of the
M.Sc. Degree in pathology
Presented by

Mohammed Abd-Elrazek Nassef

M.B, B.Ch.,

Demonstrator of pathology

Pathology Department, Faculty of medicine
Misr University for Science and Technology

Under Supervision of

Prof. Bothina Mahmoud Said

Professor of pathology

Faculty of medicine-Ain Shams University

Prof. Ragaa Amin Fawzy

Professor of pathology

Faculty of medicine-Ain Shams University

Prof. Ahmed Mohy-Eldin Zaki

Professor of pathology

Faculty of medicine-Ain Shams University

Faculty of medicine - Ain Shams University

2009

قال تعالى: (إِنَّ اللَّهَ بِعِدَّةِ عِلْمِ السَّاعَةِ وَبَدْرِ الْقُرْآنِ
وَبِعِلْمِ مَا فِي الْأَرْحَامِ وَمَا تَدْرِي نَفْسٌ قَالًا تَكْسِبُ عَدَا
وَمَا تَدْرِي نَفْسٌ بِأَيِّ أَرْضٍ تَقُومُ إِنَّ اللَّهَ عَلِيمٌ خَبِيرٌ)

صدق الله العظيم | سورة البقرة - الآية: 34

Acknowledgment

First and forever, thanks for ALLAH helping me to begin and complete this work.

I would like to express my sincere gratitude and thanks to Prof. Bothina Mahmoud Said, Professor of pathology for her kind support and guidance to complete this work.

I am also, very grateful to Prof. Ragaa Amin Fawzy Professor of pathology for her kind supervision, scientific support and patience reviewing this work.

Very special thanks to Prof. Ahmed Mohy-Elden Zaki, Professor of pathology for his kind supervision, scientific support and patience reviewing this work.

I also like to express my warmest thanks to all staff members of early cancer detection unit of maternity hospital specially Prof. Mahmoud Yosef head of the department and Prof. Sahar Ezz-ElArab for supplying us with the needed information for this work.

Very special thanks to Prof. Nadia Mokhtar, Professor of pathology for supplying us with information needed to complete this work.

I also like to thank all staff members of pathology department of Ain-Shams University specially Prof. Shadia Mabrouk head of the department for supporting this work.

I also like to express my warmest thanks to all staff members and colleagues in pathology department of Misr University for Science and Technology specially Dr. Mahmoud Tag Elsabah for helping and giving advice through out this work.

Finally, I should express my thanks to my family for their kind support and advice through out this work.

Contents

	Page
List of tables	I
List of graphs	IV
List of figures	VI
List of abbreviations	VII
Introduction	1
Aim of work	4
Review of literature	6
Histology of the uterine body.	7
Epidemiology and etiology of uterine body malignant tumors	8
Risk factors of uterine body malignant tumors	11
Classification of uterine body malignant tumors	22
Epithelial tumors (Endometrial carcinoma)	26
Types and pathological features of Endometrial Carcinoma	30
Malignant mesenchymal tumors	42
Types and pathological features of malignant mesenchymal tumors	43
Mixed Epithelial uterine tumors	49
Miscellaneous tumors	53
Lymphoid and haematopoietic tumors	54
Secondary carcinoma	55
Grading and staging of body corpus malignant tumors	56
Cytology, histochemical and immunohistochemical features	63
Molecular genetic features	65
Spread and metastases of uterine body malignant tumors	66
Prognosis of uterine body malignant tumors	67

Materials and methods	76
Results	79
Discussion	127
Conclusion and recommendations	139
Summary	164
References	142
Records	164
Protocol	236
Arabic summary	246

List of tables

	Page
Table 1: Architectural grading of endometrial carcinoma by "FIGO" 3-grade system.	62
Table 2: Nuclear Grading of endometrial carcinoma in modified "FIGO" 3-grade system.	62
Table 3: Grading of endometrial carcinoma by "FIGO" 2-grade system.	63
Table 4: Grading of endometrial stromal sarcoma	63
Table 5: TNM and FIGO staging of non-trophoblastic tumors of Uterine Corpus	
Table 6: Relative frequency of malignant tumors in Early Cancer Detection Unit	81
Table 7: Rates of gynecologic tumors and uterine tumors per year and uterine tumors out of all gynecologic tumors	82
Table 8: Relative frequency of uterine body malignant tumors	85
Table 9: Descriptive Statistics	86
Table 10: Distribution of age groups	87
Table 11: Age adjusted rate of cases of uterine body tumors	88
Table 12: Primary origin of uterine tumors	89

Table 13: Histopathological diagnosis of uterine body tumors	89
Table 14: Histopathological diagnosis of uterine tumors	90
Table 15: Histopathological diagnosis of uterine tumors and primary origin	91
Table 16: Histopathological diagnosis of uterine tumors subjected to endometrial biopsy before hysterectomy	92
Table 17: Comparison between Histopathological diagnosis of uterine tumors according to age	93
Table 18: Comparison between endometrioid adenocarcinoma of uterine tumors according to age	94
Table 19: Comparison between Typical endometrioid adenocarcinoma according to age	95
Table 20: Comparison between Variants of endometrial carcinoma according to age	96
Table 21: Comparison between diagnosis according to Parity	97
Table 22: Comparison between endometrioid adenocarcinoma according to Parity	98
Table 23: Comparison between Variants of endometrial carcinoma according to Parity	98
Table 24: Comparison between Uterine mesenchymal tumors according to Parity	98

Table 25: Comparison between Histopathological diagnosis of uterine tumors according to duration of marriage	99
Table 26: Hyperplasia in D & C specimens	100
Table 27: Hyperplasia in hysterectomy specimens	101
Table 28: Grading of endometrioid carcinoma of uterine corpus by "FIGO" 3-grade system	102
Table 29: Grading of endometrioid carcinoma of uterine corpus by "FIGO" 2-grade system	103
Table 30: Grading of sarcoma of uterine corpus	104
Table 31: Comparison between endometrioid adenocarcinoma according to invasion	105
Table 32: Comparison between Variants of endometrial carcinoma according to invasion	106
Table 33: Comparison between Uterine mesenchymal tumors according to invasion	107
Table 34: Comparison between Mixed uterine tumors according to invasion.	107
Table 35: Staging of carcinoma of uterine corpus	108

List of graphs

	Page
• Female malignant tumors	80
• Female gynecologic malignant tumors	83
• Rate of gynecologic malignant tumors per year.	83
• Uterine malignant tumors	84
• Rate of uterine malignant tumors per year	84
• Uterine body malignant tumors	85
• Endometrial biopsy and hysterectomy specimens	85
• Age and uterine body malignant tumors	87
• Age adjusted rate of cases of uterine body malignant tumors	88
• Histopathological diagnosis of uterine body tumors	89
• Comparison between Histopathological diagnosis of uterine tumors according to age	93
• Comparison between endometrioid adenocarcinoma of uterine tumors according to age	94
• Comparison between endometrioid adenocarcinoma of uterine tumors according to age	95
• Comparison between Variants of endometrial carcinoma according to age	96
• Comparison between diagnosis according to Parity	97

• Comparison between Histopathological diagnosis of uterine tumors according to duration of marriage	99
• Grading of endometrioid carcinoma of uterine corpus by "FIGO" 3-grade system	102
• Grading of endometrioid carcinoma of uterine corpus by "FIGO" 2-grade system	103
• Grading of sarcoma of uterine corpus	104
• Comparison between endometrioid adenocarcinoma according to invasion	105
• Comparison between Variants of endometrial carcinoma according to invasion	106
• Comparison between Uterine mesenchymal tumors according to invasion	107
• Staging of carcinoma of uterine corpus	109

List of figures

	Page
Figure 1: Endometrial hyperplasia	110
Figure 2: Endometrial hyperplasia with no atypia	110
Figure 3: Endometrial hyperplasia with atypia	110
Figure 4: Endometrial hyperplasia with mild atypia	111
Figure 5: Endometrial hyperplasia with sever atypia	111
Figure 6-7: Complex hyperplasia	111
Figure 8-15: Endometrioid adenocarcinoma (Grade I)	112
Figure 16-20: Endometrioid adenocarcinoma (Grade II)	114
Figure 21-22: Endometrioid adenocarcinoma (Grade III)	115
Figure 23-24: Villoglandular adenocarcinoma	116
Figure 25-29: Adenocarcinoma with squamous differentiation	116
Figure 30-32: Secretory adenocarcinoma of endometrium	117
Figure 33-34: Mucinous adenocarcinoma of endometrium	118
Figure 35-36: Papillary serous adenocarcinoma of endometrium	119
Figure 37: Squamous cell carcinoma of endometrium	119
Figure 38-41: Clear cell adenocarcinoma of endometrium	120
Figure 42-48: Endometrial stromal sarcoma	121
Figure 49-53: Malignant mixed mullerian tumor	122
Figure 54-60: Leiomyosarcoma	124
Figure 61: Lymphoma	126
Figure 62: Metastatic carcinoma	126
Figure 63-64: Myometrial invasion	126

List of abbreviations

CCA = Clear cell adenocarcinoma

CTCN = Coagulative tumor cell necrosis

D & C = Dilatation and curettage

EIC = Endometrial intra-epithelial carcinoma

ESS = Endometrial stromal sarcoma

FIGO = The International Federation of Gynecology and Obstetrics

HNPCC = Hereditary nonpolyposis colorectal cancer

HPF = High power fields

LMP = Low malignant potential

LVSI = Lymphovascular space invasion

MMMTs = Malignant mixed mullerian tumors

MMR = Mismatch repair genes

NOS = Not otherwise specified tumors

PAS = The periodic acid-Schiff

PNET = Primitive neuroectodermal tumors of uterus

SD = Standard deviation

SHBG = Sex hormone binding globulin

TNM = Tumor, Node and Metastasis system

UPSC = Uterine papillary serous carcinoma

USMN = Uterine smooth muscle neoplasms

WHO = World Health Organization

Introduction

Introduction

Uterine cancer is the fourth most common malignancy in women, following breast cancer, lung and colorectal cancer. However, as it is usually detected in early stages, it is not a common cause of cancer deaths. (Schulden, et al.2004)

Endometrial carcinoma is the most common malignant tumor of the female genital system in developed countries. Where estrogen-dependent neoplasms account for 80-85% of cases and the non-estrogen dependant tumors makes up the remaining 10-15 %.(Hinkula, et al.2002).

Risk factors of uterine cancer includes obesity, nulliparity, late menopause occurring in women older than 52 years, exogenous unopposed estrogen, tamoxifen, diabetes, hypertension, high dietary fat consumption, radiation therapy. (Clement, et al.2002).

The cardinal symptom of endometrial carcinoma is abnormal uterine bleeding, which occurs in 90 percent of cases. Even one drop of blood in a postmenopausal woman not on hormone replacement constitutes a symptom and is an indication for diagnostic testing to exclude endometrial cancer. Overall, 5 to 20 percent of postmenopausal women with uterine bleeding will have endometrial cancer. (Akslen 2005)

Endometrioid adenocarcinoma is the most common endometrial malignancy, accounting for more than 75% of all endometrial cancers, and is relatively rare in pre-menopausal women. (Alkushi, et al. 2003)

The typical early clinical presentation, most cases of endometrial cancer are endometrioid adenocarcinoma that is well-differentiated and stage I disease. Overall 5-year survival rates for all grades and histological subtypes are 87%, 72%, 51%, and 9% for stage I, II, III, and IV disease, respectively. The nuclear grade is an important determinant of prognosis. For stage I disease, 5-year survival rates for Grade I, Grade II, and Grade III endometrial carcinoma is 92%, 87%, and 74%, respectively. (Ben-Shachar, et al. 2005)

Tumor type, grade of differentiation, depth of myometrial invasion, lymphovascular space invasion (LVSI), coexistence of endometrial hyperplasia, stage, and lymph node metastasis are used to predict the clinical outcome for patients with endometrial carcinoma. (Ferrandina, et al.2002).

Uterine sarcomas have a poor prognosis, and survival is much worse than that reported for endometrial adenocarcinoma, with an overall survival of less than 50% at 2 years, even when presenting at an early stage. (Rovirosa, et al.2002).