

Morphometric and DNA image analysis of endometrial hyperplasia and carcinoma

Thesis Submitted for fulfillment of M.D.degree in

Pathology

Presented by

Noha Nazeeh Mahmmoud

M.B, B.Ch, M.Sc Cairo University

Specialist of Pathology

National Research Center

Supervised by

Prof. Dr. Ahmed Mohamed Yehia El-Hennawy

Professor of Pathology

Faculty of Medicine

Cairo University

Prof. Dr. Naglaa Fathy Abbas

Professor of Pathology

National research center

Prof. Dr. Sonia Labib El- Sharkawy

Professor of Pathology

National research center

Faculty of Medicine

Cairo University

2013

*** قالوا سبحانك لا علم لنا إلا ما
علمتنا إنك أنت العليم الحكيم ***

البقرة (٣٢)

Acknowledgement

*First of all I would like to thank **Allah** who gave me the power and patience throughout my work.*

*I would like to thank **Prof. Dr. Ahmed Mohamed Yehia El-Hennawy**, Professor of Pathology, Cairo University, for his great advice and supervision in this thesis.*

*I would like to express my gratitude to **Prof. Dr. Naglaa Fathy Abbas** Professor of Pathology, National research center.*

*Many thanks to **Prof. Dr. Sonia Labib El- Sharkawy** Professor of Pathology, National research center., for the efforts she did to complete this study.*

*Special thanks to **Prof. Dr. Marcelle Nashed** Professor of Pathology, National research center. who gave me time and support to do this work.*

*I would like also to send my greetings to **Dr. Manal Badawy**, Assistant Professor of Pathology, National research center. who helped me a lot to perform this work.*

*Special thanks to **my family** whom gave me time and support to do this work.*

Index

I- Review of literature:

1. Introduction -----	1
2. Aim of the work -----	4
3. Anatomy & histology of the Uterus -----	5
4. Endometrial hyperplasia -----	12
5. Endometrial Cancer -----	18
6. Handling surgical specimens from the endometrium -----	36
7. Examination and reporting of hysterectomy specimens -----	38
8. Morphometry -----	41
9. DNA ploidy analysis -----	47

II- Material and Methods -----	52
---------------------------------------	-----------

III- Results -----	58
---------------------------	-----------

IV-Discussion -----	99
----------------------------	-----------

V- Conclusion and Recommendations-----	107
---	------------

VI- English summary -----	108
----------------------------------	------------

VII-References -----	111
-----------------------------	------------

VIII-Arabic summary -----	132
----------------------------------	------------

List of tables

Table	Title	Page
Table.1	The endometrial dating according to Noyes criteria	8
Table.2	classification of endometrial hyperplasia	13
Table.3	lists the classic features of type 1& 2 endometrial carcinoma	20
Table.4	TNM staging and FIGO staging	32
Table.5	Differential Diagnosis of Myoinvasion	35
Table.6	Items recommended in surgical pathology report	40
Table.7	Differences between Image and Flow cytometry	47
Table.8	showing difference of simple hyperplasia & carcinoma in relation to nuclear area	66
Table.9	showing difference of atypical hyperplasia & carcinoma in relation to nuclear area	66
Table.10	showing difference of simple hyperplasia & atypical hyperplasia in relation to nuclear area	66
Table.11	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to nuclear area	67
Table.12	showing difference of simple hyperplasia & atypical hyperplasia in relation to long axe(X coord)	68
Table.13	showing difference of simple hyperplasia & carcinoma in relation to long axe(X coord)	68
Table.14	showing difference of atypical hyperplasia & carcinoma in relation to long axe(X coord)	68
Table.15	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to long axe(X coord)	69
Table.16	showing difference of simple hyperplasia & atypical hyperplasia in relation to short axe (Y coord)	70
Table.17	showing difference of simple hyperplasia & carcinoma in relation to short axe(Y coord)	70
Table.18	showing difference of atypical hyperplasia & carcinoma in relation to short axe(Y coord)	70

Table.19	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to short axe(Y coord)	71
Table.20	showing difference of simple hyperplasia &atypical hyperplasia in relation to nuclear roundness	72
Table.21	showing difference of simple hyperplasia &carcinoma in relation to nuclear roundness	72
Table.22	showing difference of atypical hyperplasia &carcinoma in relation to nuclear roundness	72
Table.23	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to nuclear roundness	73
Table.24	showing difference of simple hyperplasia &atypical hyperplasia in relation to nuclear form ellipse	74
Table.25	showing difference of simple hyperplasia & carcinoma in relation to nuclear form ellipse	74
Table.26	showing difference of atypical hyperplasia & carcinoma in relation to nuclear form ellipse	74
Table.27	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to nuclear form ellipse	75
Table.28	showing difference of simple hyperplasia &atypical hyperplasia in relation to glandular distant	77
Table.29	showing difference of simple hyperplasia &carcinoma in relation to glandular distant	77
Table.30	showing difference of atypical hyperplasia &carcinoma in relation to glandular distant	77
Table.31	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to glandular distant	78
Table.32	showing difference of atypical hyperplasia &atypical hyperplasia in relation to glandular area	79
Table.33	showing difference of simple hyperplasia &carcinoma in relation to glandular area	79
Table.34	showing difference of atypical hyperplasia &carcinoma in relation to glandular area	79
Table.35	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to glandular area	80
Table.36	showing difference of simple hyperplasia & atypical hyperplasia in relation to glandular area fraction	81
Table.37	showing difference of simple hyperplasia &carcinoma in relation to glandular area fraction	81

Table.38	showing difference of atypical hyperplasia & carcinoma in relation to glandular area fraction	81
Table.39	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to glandular area fraction	82
Table.40	showing difference of simple hyperplasia & atypical hyperplasia in relation to volume percentage of stroma	83
Table.41	showing difference of simple hyperplasia & carcinoma in relation to volume percentage of stroma	83
Table.42	showing difference of atypical hyperplasia & carcinoma in relation to volume percentage of stroma	83
Table.43	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to volume percentage of stroma	84
Table.44	showing difference of simple hyperplasia & atypical hyperplasia in relation to D- score	85
Table.45	showing difference of simple hyperplasia & carcinoma in relation to D- score	85
Table.46	showing difference of atypical hyperplasia & carcinoma in relation to D- score	85
Table.47	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to D- score	86
Table.48	showing difference of simple hyperplasia& atypical hyperplasia in relation to DNA index	88
Table.49	showing difference of simple hyperplasia& carcinoma in relation to DNA index	88
Table.50	showing difference of atypical hyperplasia & carcinoma in relation to DNA index	88
Table.51	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA index	89
Table.52	showing difference of simple hyperplasia & atypical hyperplasia in relation to DNA content (1.5-2.5)	90
Table.53	showing difference of simple hyperplasia & carcinoma in relation to DNA content (1.5-2.5)	90
Table.54	showing difference of atypical hyperplasia & carcinoma in relation to DNA content (1.5-2.5)	90
Table.55	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA content (1.5-2.5)	91
Table.56	showing difference of simple hyperplasia & atypical hyperplasia in relation to DNA content (2.5-3.5)	92

Table.57	showing difference of simple hyperplasia & carcinoma in relation to DNA content (2.5-3.5)	92
Table.58	showing difference of atypical hyperplasia & carcinoma in relation to DNA content (2.5-3.5)	92
Table.59	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA content (2.5-3.5)	93
Table.60	showing difference of simple hyperplasia & atypical hyperplasia in relation to DNA content (>4.5)	94
Table.61	showing difference of simple hyperplasia & carcinoma in relation to DNA content (>4.5)	94
Table.62	showing difference of atypical hyperplasia & carcinoma in relation to DNA content (>4.5)	94
Table.63	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA content (>4.5)	95

List of figures

<i>Figure</i>	<i>Title</i>	<i>Page</i>
<i>fig.1</i>	Histogenetic concept of type 1 endometrial carcinoma	24
<i>fig.2</i>	Histogenetic concept of type 2 endometrial carcinoma	25
<i>fig.3(1-5)</i>	endometrioid adenocarcinoma	33
<i>fig.4</i>	Schematic presentation for obtaining tissue for histologic examination	37
<i>fig5</i>	The cell growth cycle	49
<i>fig.6</i>	Endometrial simple hyperplasia (H&E X10)	59
<i>fig.7</i>	Endometrial simple hyperplasia (H&E X20)	59
<i>fig.8</i>	Endometrial atypical hyperplasia (H&E X10)	60
<i>fig.9</i>	Endometrial atypical hyperplasia (H&E X20)	60
<i>fig.10</i>	Endometrial carcinoma infiltrating the muscles (H&E X10)	61
<i>fig.11</i>	Endometrial carcinoma infiltrating the muscles (H&E X20)	61
<i>fig.12</i>	Endometrial simple hyperplasia showing dilated glands lined by tall columnar , single layered within abundant cellular stroma (H&E X20)	62
<i>fig.13</i>	Endometrial atypical hyperplasia showing irregular with intraglandular tufts lined by stratified epithelium lost their polarity within scant stroma (H&E X20)	62
<i>fig.14</i>	Endometrial carcinoma showing irregular with intraglandular bridging lined by stratified epithelium lost their polarity within scant stroma (H&E X20)	62

fig.15	Endometrial simple hyperplasia showing smooth , oval uniform sized nuclei with numerous mitosis in the stroma and the glands (H&E X 40)	63
fig.16	Endometrial atypical hyperplasia showing large ,irregular variable sized nuclei with numerous mitosis (H&E X 40)	63
fig.17	Endometrial carcinoma showing large ,irregular variable sized nuclei with variable nucleolei (H&E X 40)	63
fig.18	Morphometrical nuclear measurement for endometrial hyperplasia	64
fig.19	Morphometrical nuclear measurement for atypical endometrial hyperplasia	64
fig.20	Morphometrical nuclear measurement for endometrial carcinoma	65
fig.21	showing difference of simple hyperplasia & carcinoma in relation to nuclear area	66
fig.22	showing difference of atypical hyperplasia & carcinoma in relation to nuclear area	66
fig.23	showing difference of simple hyperplasia & atypical hyperplasia in relation to nuclear area	66
fig.24	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to nuclear area	67
fig.25	showing difference of simple hyperplasia & atypical hyperplasia in relation to long axe(X coord)	68
fig.26	showing difference of simple hyperplasia & carcinoma in relation to long axe(X coord)	68
fig.27	showing difference of atypical hyperplasia & carcinoma in relation to long axe(X coord)	68
fig.28	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to long axe(X coord)	69
fig.29	showing difference of simple hyperplasia & atypical hyperplasia in relation to short axe (Y coord)	70

fig.30	showing difference of simple hyperplasia & carcinoma in relation to short axe(Y coord)	70
fig.31	showing difference of atypical hyperplasia & carcinoma in relation to short axe(Y coord)	70
fig.32	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to short axe(Y coord)	71
fig.33	showing difference of simple hyperplasia & atypical hyperplasia in relation to nuclear roundness	72
fig.34	showing difference of simple hyperplasia & carcinoma in relation to nuclear roundness	72
fig.35	showing difference of atypical hyperplasia & carcinoma in relation to nuclear roundness	72
fig.36	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in relation to nuclear roundness	73
fig.37	showing difference of simple hyperplasia & atypical hyperplasia in relation to nuclear form ellipse	74
fig.38	showing difference of simple hyperplasia & carcinoma in relation to nuclear form ellipse	74
fig.39	showing difference of atypical hyperplasia & carcinoma in relation to nuclear form ellipse	74
fig.40	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to nuclear form ellipse	75
fig.41	Morphometrical glandular measurement for simple hyperplasia	76
fig.42	Morphometrical glandular measurement for atypical hyperplasia	76
fig.43	Morphometrical glandular measurement for endometrial carcinoma	76
fig.44	showing difference of simple hyperplasia & atypical hyperplasia in relation to glandular distant	77
fig.45	showing difference of simple hyperplasia & carcinoma in relation to glandular distant	77

fig.46	showing difference of atypical hyperplasia & carcinoma in relation to glandular distant	77
fig.47	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to glandular distant	78
fig.48	showing difference of atypical hyperplasia & atypical hyperplasia in relation to glandular area	79
fig.49	showing difference of simple hyperplasia & carcinoma in relation to glandular area	79
fig.50	showing difference of atypical hyperplasia & carcinoma in relation to glandular area	79
fig.51	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to glandular area	80
fig.52	showing difference of simple hyperplasia & atypical hyperplasia in relation to glandular area fraction	81
Fig.53	showing difference of simple hyperplasia & carcinoma in relation to glandular area fraction	81
fig.54	showing difference of atypical hyperplasia & carcinoma in relation to glandular area fraction	81
fig.55	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to glandular area fraction	82
fig.56	showing difference of simple hyperplasia & atypical hyperplasia in relation to volume percentage of stroma	83
fig.57	showing difference of simple hyperplasia & carcinoma in relation to volume percentage of stroma	83
fig.58	showing difference of atypical hyperplasia & carcinoma in relation to volume percentage of stroma	83
fig.59	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to volume percentage of stroma	84
fig.60	showing difference of simple hyperplasia & atypical hyperplasia in relation to D- score	85
fig.61	showing difference of simple hyperplasia & carcinoma in relation to D- score	85

fig.62	showing difference of atypical hyperplasia & carcinoma in relation to D- score	85
fig.63	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to D- score	86
fig.64	Histogram for DNA content of the control case	87
fig.65	showing difference of simple hyperplasia& atypical hyperplasia in relation to DNA index	88
fig.66	showing difference of simple hyperplasia& carcinoma in relation to DNA index	88
fig.67	showing difference of atypical hyperplasia & carcinoma in relation to DNA index	88
fig.68	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA index	89
fig.69	showing difference of simple hyperplasia & atypical hyperplasia in relation to DNA content (1.5-2.5)	90
fig.70	showing difference of simple hyperplasia & carcinoma in relation to DNA content (1.5-2.5)	90
fig.71	showing difference of atypical hyperplasia & carcinoma in relation to DNA content (1.5-2.5)	90
fig.72	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA content (1.5-2.5)	91
fig.73	showing difference of simple hyperplasia & atypical hyperplasia in relation to DNA content (2.5-3.5)	92
fig.74	showing difference of simple hyperplasia & carcinoma in relation to DNA content (2.5-3.5)	92
fig.75	showing difference of atypical hyperplasia & carcinoma in relation to DNA content (2.5-3.5)	92
fig.76	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA content (2.5-3.5)	93
fig.77	showing difference of simple hyperplasia & atypical hyperplasia in relation to DNA content (>4.5)	94

<i>fig.78</i>	showing difference of simple hyperplasia & carcinoma in relation to DNA content (>4.5)	94
<i>fig.79</i>	showing difference of atypical hyperplasia & carcinoma in relation to DNA content (>4.5)	94
<i>fig.80</i>	showing difference of simple hyperplasia , atypical hyperplasia & carcinoma in to DNA content (>4.5)	95
<i>fig.81</i>	Histogram comparing DNA content in the control case (blue colored) and in simple hyperplasia (green colored)	96
<i>fig.82</i>	Histogram comparing DNA content in the control case (blue colored) and in simple hyperplasia (green colored)	96
<i>fig.83</i>	Histogram comparing DNA content in the control case (blue colored) and in atypical hyperplasia (green colored)	97
<i>fig.84</i>	Histograms comparing DNA content in the control case (blue colored) and in three carcinoma cases(green colored)	98

Abbreviations

- * ACEH : Atypical complex endometrial hyperplasia
- * AH : Atypical hyperplasia
- * AJCC : American Joint Committee of Cancer
- * BrdU : bromodeoxyuridine
- * CD10 : Cluster differentiation 10
- * CD34 : Cluster differentiation 34
- * CT : Computerized tomography
- * D&C : Dilatation and curratage
- * DNA : Deoxyribonucleic acid
- * DUB : Dysfunctional uterine bleeding
- * EMA : Epithelial memberan antigen
- * EC : Endometrial carcinoma
- * EIC : Endometrial intraepithelial carcinoma
- * EIN : Endometrial intraepithelial neoplasia
- * EM : Endomerium
- * FCM : Flow cytometry
- * FIA : Fluorescence image analysis
- * FIGO : Federation International of Gynecology and Obstetrics
- * IA : Image analzer system = ICM : Image cytometry
- * IOD : Integrated Optical density
- * IHC : Immunohistochemical
- * LVSI : Lymphovascular space invasion
- * MAH : Marked atypical hyperplasia
- * ME : Menstrual endomerium