

Pathology Registry of Primary Malignant Tumors of the Esophagus

Thesis

*Submitted for partial fulfillment of the master degree of In
Pathology*

By:

Shahinaz Ahmed Saad El-din

(M. B., B.Ch)

Faculty of Medicine- Ain Shams University

Supervised by

Prof Dr. Zeinab Abd El-Rahamn Kotb

Professor of Pathology

Faculty of Medicine, Ain Shams University

Prof. Dr. Gamal Mohamed Fathy

Professor of Pathology

Faculty of Medicine, Ain Shams University

Dr. Wesam Mohamed Osman

Assistant Professor of Pathology

Faculty of Medicine, Ain shams University

**Faculty of Medicine
Ain Shams University**

2015

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgement

*First of all, all gratitude is due to **God** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

*Really I can hardly find the words to express my gratitude to **Prof. Dr. Zeinab Abd El-Rahamn Kotb** Professor of Pathology, Faculty of Medicine, Ain Shams University, for her supervision, continuous help, encouragement throughout this work and tremendous effort she has done in the meticulous revision of the whole work. It is a great honor to work under her guidance and supervision.*

*I would like also to express my sincere appreciation and gratitude to **Prof. Dr. Gamal Mohamed Fathy** Professor of Pathology, Faculty of Medicine, Ain Shams University, for his continuous directions and support throughout the whole work,*

*I owe much to. **Dr. Wesam Mohamed Osman**, Assistant Professor of Pathology Faculty of Medicine, Ain Shams University for her continuous guidance, encouragement during the progress of this work and direct supervision.*

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.



Shahinaz Ahmed Saad El-din

Contents

List of Abbreviations	i
List of Tables	iii
List of Figures	v
Diagram	x
Introduction and Aim of the Work	1
Review of Literature	4
Material and Methods	59
Results	60
Discussion.....	100
Summary	107
Conclusion.....	109
Recommendations	110
References	111
Arabic Summary	--

List of Abbreviations

APC	:	Adenomatosis polyposis coli.
AJCC	:	American joint committee of cancer.
BE	:	Barrett's esophagus.
BMI	:	Body mass index.
CCL	:	Centrocyte-like.
CI	:	Confidence interval.
CRT	:	Chemoradiotherapy.
CRT-S	:	Chemorediotherapy followed by surgery.
C-S	:	Chemotherapy followed by surgery.
CT	:	Computerized tomography.
DLC 1	:	Deleted in lung esophageal cancer 1.
EAC	:	Esophageal adenocarcinoma.
EGFR	:	Epiderms growth factor receptor.
EMR	:	Endoscopic mucosal resection.
ESCC	:	Esophageal squamous cell carcinoma.
ESD	:	Endoscopic submucosal dissection.
EUS	:	Endoscopic ultrasound.
FDG-PET	:	18-fluoro-deoxyglucose positron emission tomography.
FHIT	:	Fragile histidine traid.
GERD	:	Gastroesophageal reflux disease.
GISTs	:	Gastrointestinal stromal tumors.
H2RLN	:	Serum human relaxin 2.

List of Abbreviations (Cont.)

HGD	: High grade dysplasia.
HGIN	: High grade intraepithelial neoplasia.
LES	: Lower esophageal sphincter.
LSBE	: Lower segment barrett's esophagus.
LOH	: Loss of heterozygosity.
MALT	: Mucosa associated lymphoid tissue.
MECC	: Middle east cancer consortium.
mRNA	: Messenger Ribonucleic acid.
NEPPK	: Non epidermiolytic palmoplantar keratoderma.
Ors	: Odds ratios.
PCNA	: proliferating cell nuclear antigen.
PLA2	: Phospholipase A2.
RFA	: Radiofrequency ablation.
RR	: Relative risk.
RT-PCR	: Reverse transcript polymerase chain reaction .
SCC	: Squamous Cell Carcinoma.
SEER	: Surveillance epidemiology end result.
S-CRT	: Surgery with adjuvant chemorediotherapy.
SD	: Standard deviation.
SPSS	: Statistical package for social science.
UES	: Upper esophageal sphincter.
WHO	: World health organization

List of Tables

<i>Table</i>	<i>Title</i>	<i>Page</i>
1	WHO histological classification of oesophageal tumours	7
2	Genetic alterations in squamous cell carcinoma of the oesophagus	39
3	Genes and proteins involved in carcinogenesis in Barrett oesophagus	41
4	TNM system, specifically referring to depth of invasion in T staging	45
5	Aspect of staging is essential in determining stage-specific protocols for treatment	45
6	Age distribution among the studied cases	61
7	Sex distribution among the studied cases	62
8	Clinical presentation of the studied cases	63
9	Specimens types of the studied cases	64
10	Lesions site from the studied cases	65
11	Histopathological diagnosis of the studied cases	66
12	Age distribution among the SCC cases	67
13	Sex distribution among the SCC cases	68
14	Clinical presentation of SCC cases	69
15	Specimens types from the SCC cases	70
16	Specimens sites from the SCC cases	70
17	Differentiation grades of the studied SCC specimens	71
18	Stages of SCC in the radical specimens	73
19	Age distribution among the studied adenocarcinoma cases	75
20	Sex distribution among the studied adenocarcinoma cases	76
21	Clinical presentation of adenocarcinoma cases	77

List of Tables (Cont.)

<i>Table</i>	<i>Title</i>	<i>Page</i>
22	Specimens types of the studied adenocarcinoma cases	78
23	Specimens sites from the studied adenocarcinoma cases	79
24	Differentiation grades of the studied adenocarcinoma specimens	80
25	Stages of adenocarcinoma in radical specimens	81
26	Distribution among the studied Barrett's cases	83
27	Sex distribution among the studied Barret's cases	84
28	Clinical presentation of Barret's cases	85
29	Percentage site of the lesion Specimens sites from the studied Barret's cases	86
30	Differentiation percentages of the associated Reflux and dysplasia in studied Barrett's in cases	87

List of Figures

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
1	H&E stain of a biopsy of the normal esophageal wall, showing the stratified squamous cell epithelium of the esophageal wall	5
2	Histological section of the gastro-esophageal junction, with a black arrow indicating the junction	6
3	Low-grade intraepithelial neoplasia with an increase in basal cells, loss of polarity in the deep epithelium and slight cytological atypia	10
4	High grade intraepithelial neoplasia of oesophageal squamous epithelium	11
5	Squamous cell papilloma of distal oesophagus	13
6	Endoscopic view of a superficial squamous cell carcinoma presenting as a large nodule (CA) in a zone of erosion	17
7	After spraying of 2% iodine solution, the superficial extent of the tumour becomes visible as unstained light yellow area (CA, arrows)	17
8	Verrucous carcinoma	19
9	Spindle cell carcinoma	21
10	Basaloid squamous cell carcinoma	22
11	Highly infiltrative adenocarcinoma in Barrett oesophagus (pT3), with extension into the cardia	24
12	Barrett oesophagus	25
13	Adenocarcinoma, tubular type	26
14	Barrett oesophagus with low-grade intraepithelial neoplasia on the left and high-grade on the right	30

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
15	High-grade intraepithelial neoplasia in Barrett oesophagus	31
16	Granular cell tumour of oesophagus	35
17	Stromal tumour of the oesophagus, involving the oesophageal muscle layer beneath a normal mucosa	36
18	Location of the tylosis esophageal cancer gene on chromosome 17q	38
19	Spectrum of TP53 mutations in squamous cell carcinoma (SCC) and adenocarcinoma (ADC) of the oesophagus	39
20	Endoscopy in patients who have esophageal cancer	43
21	EUS-guided fine-needle aspiration biopsy (arrow) of celiac axis lymph node	48
22	T, N, and M classifications for esophageal carcinoma	50
23	Age distribution among the studied cases	61
24	Clinical presentation of the studied cases	63
25	Age distribution among the SCC cases	67
26	Clinical presentation of SCC cases	69
27	Age distribution among the adenocarcinoma cases	75
28	Clinical presentation of adenocarcinoma cases	77
29	Age distribution among the studied Barret's cases	83
30	Clinical presentation of Barret's cases	85
31	Well differentiated squamous cell carcinoma with prominent keratin pearls Hx&E, x100	88

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
32	Moderately differentiated squamous cell carcinoma, Hx&E, x100	88
33	Moderately differentiated squamous cell carcinoma, (higher magnification of previous image) Hx&E, x200	89
34	Moderately differentiated squamous cell carcinoma showed no muscle infiltration (stage T1) Hx&E, x40	89
35	Basaloid squamous cell carcinoma, Hx&E, x40	90
36	Basaloid squamous cell carcinoma, Hx&E, (higher view of previous image) x400	90
37	Well differentiated adenocarcinoma Hx&E, x100	91
38	well differentiated adenocarcinoma (higher magnification of the previous image), H x & E, x400	91
39	Moderately differentiated adenocarcinoma infiltrating the muscle (higher magnification of previous image) Hx&E, x100	92
40	Malignant glands infiltrating the muscle layer (higher magnification of previous image) Hx&E x200	92
41	Poorly differentiated adenocarcinoma showing sheets of malignant cells with occasional glands formation Hx&E, x100	93
42	Poorly differentiated adenocarcinoma with sheeting pattern of growth showed foci of signet ring cells, Hx&E, x400	93

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
43	Adenocarcinoma with perineural invasion Hx&E, x100	94
44	Adenocarcinoma with perineural invasion higher magnification of previous image, Hx&E, x400	94
45	Adenocarcinoma infiltrating the lymph node with extranodal extension Hx&E, x200	95
46	Focus of reflux nearby Barrett's esophagus showed basal cell hyperplasia and elongated papillae containing prominent congested capillaries and inflammatory cells Hx&E, x200	95
47	Higher view of the reflux showed basal cell hyperplasia, congested capillaries and eosinophils in the epithelium H x & E, x400	96
48	Columnar metaplasia with goblet cells with no dysplasia (intestinal metaplasia) (Barrett's esophagus) Hx&E x100	96
49	Higher view of the intestinal metaplasia with no dysplasia (Barrett's esophagus) Hx&E, x200	97
50	Barrett's esophagus with villous architecture and atypia indefinite for dysplasia Hx&E, x200	97
51	Barrett's esophagus with villous architecture and atypia indefinite for dysplasia, higher magnification of the previous image, Hx&E, x 400	98
52	Barrett's esophagus with villoglandular polyp showed variable degree of dysplasia Hx&E, x200	98

List of Figures (Cont.)

<i>Fig.</i>	<i>Title</i>	<i>Page</i>
53	Barrett's esophagus with villoglandular architecture and high grade dysplasia higher magnification of previous image Hx&E, x400	99

List of Diagram

<i>Diagram</i>	<i>Title</i>	<i>Page</i>
1	Sex distribution among the studied cases	62
2	Specimens types of the studied cases	64
3	Specimens site from the studied cases	65
4	Pathological diagnosis of the studied cases	66
5	Sex distribution among the SCC cases	68
6	Specimens sites from the SCC cases	70
7	Differentiation grades of the studied SCC specimens	72
8	T-grade of the segmental esophagectomy SCC specimens	74
9	N-grade of the segmental esophagectomy SCC specimens	74
10	Sex distribution among the adenocarcinoma cases	76
11	Specimens sites from the adenocarcinoma cases	79
12	Differentiation grades of the studied SCC specimens	80
13	T-grade of the segmental esophagectomy adenocarcinoma specimens	81
14	N-grade of the segmental esophagectomy adenocarcinoma specimens	82
15	Sex distribution among the studied Barret's cases	84
16	Differentiation grades of the studied Barret's specimens	87

Introduction

Esophageal cancer is diagnosed in about 400,000 patients per year, which makes it the ninth most common malignancy worldwide and sixth on the list of cancer mortality causes (*Peter and Siersema 2008*).

According to the National Cancer Institute, in the United States there were approximately 17990 new cases and 15210 deaths in 2013. Despite many advances in diagnosis and treatment, the 5-year survival rate for all patients diagnosed with esophageal cancer ranges from 15% to 20% (*Pennathur A et al., 2013*).

The epidemiology of esophageal cancer in developed nations has dramatically changed over the past forty years. Forty years ago squamous cell carcinoma (SCC) was responsible for greater than 90% of the cases of esophageal carcinoma in the United States. Adenocarcinoma has now become the leading cause of esophageal cancer in the United States, representing 80% of cases. In 1975 esophageal adenocarcinoma (EAC) affected four people per million, in 2001 the rate had increased to twenty-three people per million. Making it the fastest-growing cancer in United States, according to the National Cancer Institute (*Kyle J Napier et al., 2014*).

Esophageal squamous cell carcinoma (ESCC) is defined as a tumor in the squamous epithelium that lines the normal esophagus. Adenocarcinomas are tumors that are located at the interface of the distal esophagus and proximal stomach. The prognosis of esophageal cancer has slightly improved over the last few years in patients eligible to undergo a surgical resection; however, the 5-year survival rate in the resected group is still not higher than 30% to 35% (*Omluo JM et al, 2007, Chang AC et al., 2008*).