CARCINOID TUMOURS AND CARCINOID SYNDROME

ESSAY

SUBMITTED FOR PARTIAL FULFILMENT

OF MASTER DEGREE IN GENERAL SURGERY

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FACULTY OF MEDICINE

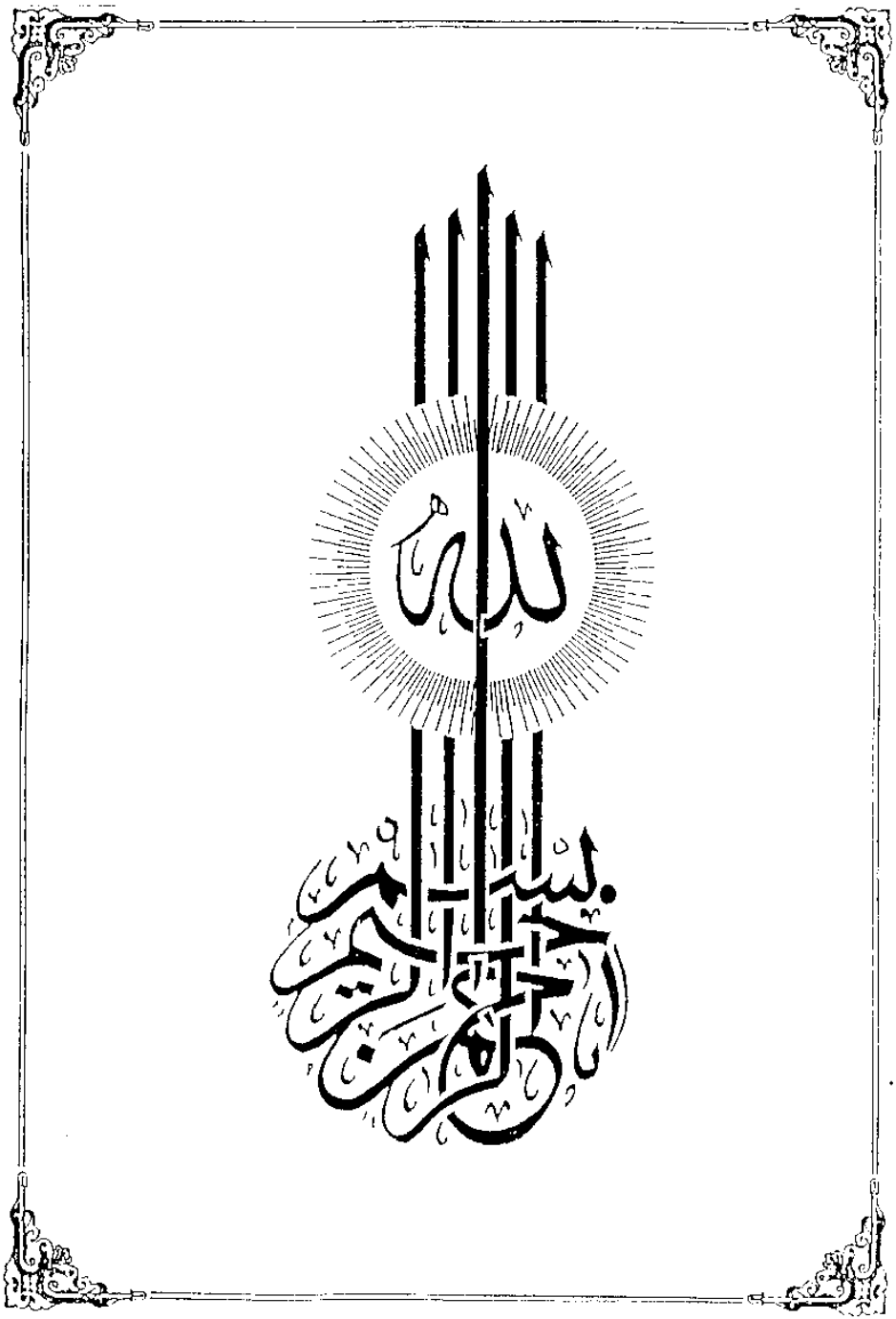
AIN SHAMS UNIVERSITY

1990

بسم الله الرحمن الرحيم

وقل اعملوا فسيرى الله عملكم ورسوله والمؤمنون

صدق الله العظيم



ACKNOWLEDGEMENT

I would like to express my sincer gratitude to **PROF DR. SAYED ABD EL MOETY EL MAHARAKAWY**, Assistant Prof. of General Surgery Ain Shams University, for his generous guidance in accomplishing this work. His great effort and desine of Perfection will always be my best example.

I wish also to express how deeply grateful I am to **DR. ALI MOUSA** , Lecturer of General Surgery Ain Shams University , he did not sprae any effort in guiding me towards the best and his valuable advise has honored this work.

REDA AWAD

TO MY MOTHER

AND

"TO THE MEMORY OF MY FATHER"

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INTRODUCTION

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Carcinoid tumors are neoplasm arising fromthe enterochromaffin [argentaffin] cells and produce peptide or catecholamine hormones. They are considered as neuro endocrine or amine precursor uptake and decarboxylation [APUD] tumors.

Carcinoid tumors were described by ***Oberndorfer in 1907*** as a *morphologically distinct subset of small intestinal* neoplasms with less aggressive behavior than that of the intestinal adenocarcinoma ***[Maruyama et al., 1988]***.

Carcinoid tumors are uncommon malignant neoplasms which collectively account for less than one percent of all cancers of small intestine ***[Greenberg et al., 1987]***.

From their structure, carcinoids were of at first thought to be carcinomata. In fact they are composed of columns and masses of epithelia which have tendency to infiltrate the sourronding structures. Their usual small size earned for them the name of "little carcinomata" by ***Lubarch in 1888***. Then carcinoids by ***Oberndorfer in 1907*** under which name they are commonly described ***[Masson et al., 1928]***. Carcinoids are found in the gastrointestinal tract, biliary tract, pancreas, ovary, lung, bronchi, genitourinary tract, breast, thymas and skin.

In the small intestine and appendix they are the most common tumors, since over 80 percent of carcinoids develop in the wall of the hollow organs of the gastrointestinal tract. *[Godwin, 1975]*. When carcinoid tumor is found in the liver, and no other primary tumor can be traced, it is presumed that the neoplasm has arisen from cells in the wall of the bile ducts which may show argentaffin properties *[Ashly, 1980]*.

Carcinoid tumors have attracted much interst because of their characteristic histology and electron microscopic findings and their endocrine functions in producing amines and peptide hormones. *[Hirose et al., 1986]*.

In this study the carcinoid tumors of the gastrointestinal tract will be discussed in more detail including their aetiology, pathology, pathogenesis, presentation, investigation, treatment and prognosis.

REVIEW OF LITERATURE

CARCINOID TUMORS OF THE GASTROINTESTINAL TRACT

Carcinoid tumors are APUDomas which arise from the entero-chromaffin cell precursors of the submucosa [E.C.]. The term APUDomas is used to describe collectivelly the tumors of the gastro entero pancreatic endocrine cells that are widely dispersed through the GIT. Neuroendocrine tumors of GIT are composed of carcanoids and paragangliomas.

The formers are presumed to be derived from endocrine mucosal cells, where is the latter are said to be derived from the vagus, associated E.C. cells of the intramural autonomic ganglia in the intestinal wall *[Someren et al., 1985]*.

Carcinoid tumors may arise any where in the GIT from mouth to the anal region.

Most of those in the midgut and its dervatives are argentaffin and secrete 5-Ht [5-hydroxy-tryptamine] while those in the forgut and its dervatives [including the bronchi] are argyrophil *[Rubbin et al., 1985]*.

They are multiple and may be associated with malignant gastrointestinal tumors of other microscopic types. The overlying mucosa is often intact. At times, the tumors might grow to a large size to involve the full thickness of the bowel wall with characteristic associated fibrosis and bulking of the wall *[Someren, 1985]*.

[Thorson et al., 1954] drew a precise correlation between the carcinoid tumors and clinical manifestations of vasomotor changes, hypermotility of the intestine, right sided valvular heart disease and bronchospasm *[Thompson et al., 1985]*.

The first discription of the malignant carcinoid syndrome date to *"Cassidy's"* reprot in 1934. In the early 1950, *"Lembeck"* isolated serotonin from a carcinoid tumor and demonstrated the presence of a large amount of 5-hydroxy-indolacetic acid [5-HIAA]; a serotonin metabolite, in the urine of patiens with malignant carcinoid syndrome *[Thompson et al., 1985]*.

There is no evidence of herditary transmission of carcinoids from diseased parents to the offsprings. Also carcinoids never have been found as a congenital findings.

Incidence and natural course :

Carcinoid tumors of the small intestine are found in about one of 150 autopsis and in the appendix in one of 300 appendectomies. Rectal carcinoids are found in about one of 2500 proctoscopic biopsies.

In the stomach and duodenum, carcinoids are described through routine endoscopic and x-ray investigations ***[Robert and Oat, 1985]***.

Gastrointestinal carcinoids are usually found incidentally during laparotomy for other resones, endoscopic or x-ray investigations and as an autopsy findings. However, the majority of carcinoids are localized tumors with less evidence of metastasis.

Rectal and appendiceal carcinoids have a low malignant potential and rarely metastasize ***[Robert et al., 1985]***. The incidence of metastasis from small bowel carcinoids has been correlated directly with the size of the tumor.

2% of primary lesions less than 1cm in diameter had metastasized.

Conversly, nearly 50% of tumors from 1-2cm in diameter, and 80% of those larger than 2cm were associated with metastasis *[Strodel, 1983]*. Carcinoid tumors spread to give metastasis to submucosa, musculosa and serosa of the gut by direct invasion, then spread to regional lymph nodes, mesentery through lymphatic or blood circulation and organs and liver. *[Dawes et al., 1984]*. Metastasis have also been reported to skin, bone, brain, heart, kidney, adrenal, spleen and orbit. Cases of midgut carcinoids with breast metastasis were reported *[Ahlman et al., 1986]*.

The incidence of metastatic disease is less in hindgut carcinoids than in either midgut or forgut e.g. [Rectum 18%, Jejuno-ileal 34% , stomach 23% and colon 6%] *[Nauheim et al., 1983]*.

The histological distinction between benign and malignant carcinoids is frequently impossible to make. Carcinoids smaller than 2 cm are benign, but may be considered potentially malignant particularly if they manifest evidence of endocrine activity. Such activity persists until the source has been completely removed *[Gencsi et al., 1986]*.

The malignant potentiality of any carcinoid tumor is known to depend upon three factors : site, size and depth of invasion.

Distribution of carcioid tumors :

The distribution of carcinoid tumors according to site varies widely. It is dependant on whether the study is clinical or at autopsy.

Clinical carcinoids of the appendix are much more common than those discovered at autopsy *[Devita et al., 1984]*.

In comparison with the number of cases analysed by *["Greenberg et al., 1987"; "Strodel et al., 1983"; "Zeitels et al., 1982" and "Thompson et al., 1985"]*. It shows the primary sites in decreasing order of frequency, where the appendix, ileum, rectum, colon, stomach, duodenum, biliary system, Meckel's diverticulum, pancreas and oesophagus. About forty-five percent arise from the appendix and 28% from the small intestine . The rectum is the third most common site for these tumors.

Males predominated slightly for the intestine and females for other sites.

Men and women have similar incidence rates for carcinoid detected by appendectomy, but more appendectomies are performed in women, so more carcinoids are detected in