INTESTINAL LYMPHOMA

ESSAY

Submitted in Partial Fulfillment of

MASTER DEGREE

IN

GENERAL SURGERY

BY

HISHAM HASSAN H. WAGDY

M.B.B.Ch.

Under Supervision of

Prof. Dr. M. SAMIR ABOU-ZEID

Head of General Surgery Department

Prof. of General Surgery

Faculty of Medicine

Ain Shams University

Dr. ALAA ABD ALLAH

Assistant Prof. of General Surgery

Faculty of Medicine

Ain Shams University

FACULTY OF MEDICINE

AIN SHAMS UNIVERSITY

1990

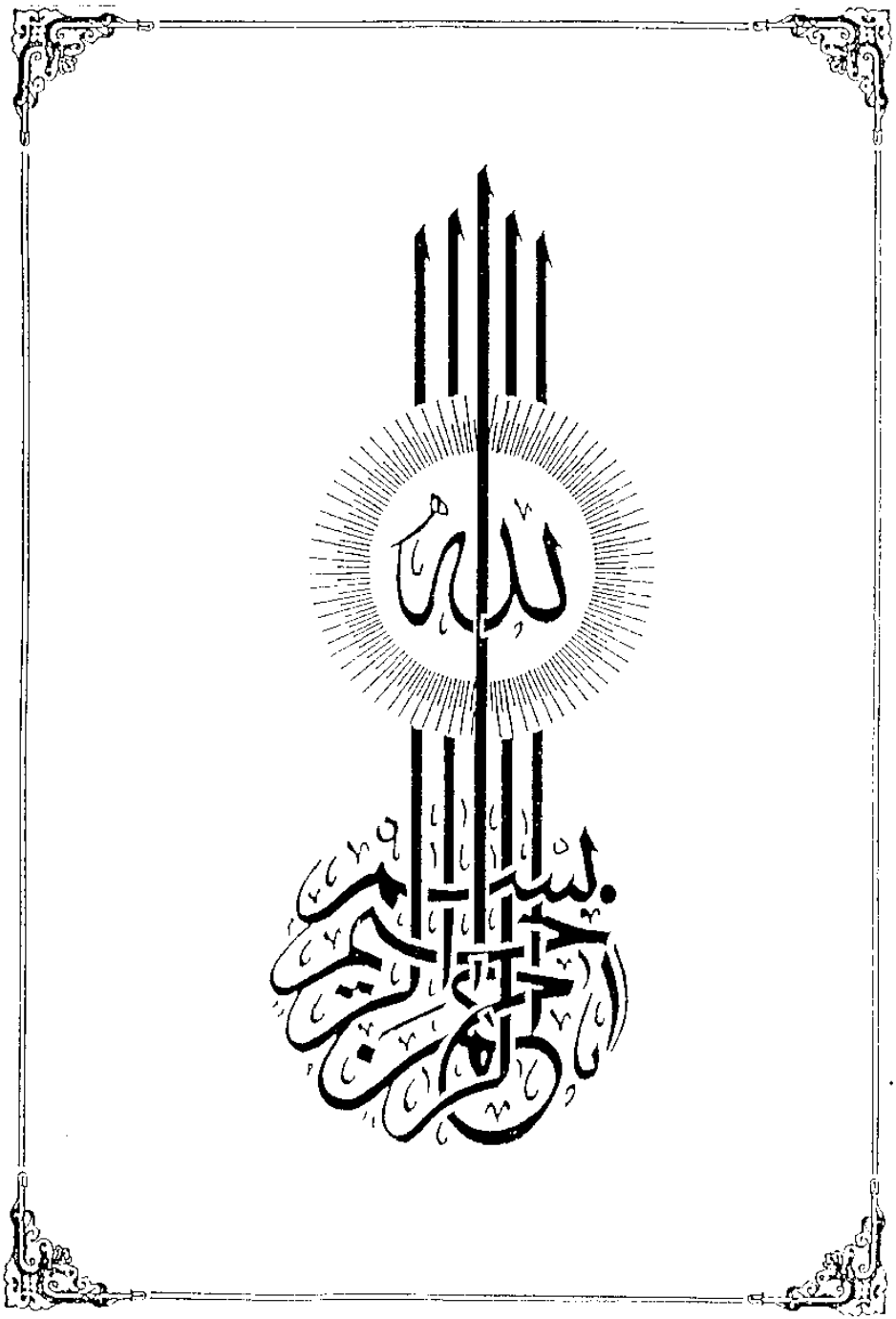
ACKNOWLEDGEMENT

I find great pleasure to express my sincere gratitude towards our great Professor Dr. *M. SAMIR ABOU-ZEID* for his helpful guidance and supervision.

I am also grateful and I wish to express my thanks and utmost gratitude to Assistant Professor Dr. *ALAA ABD-ALLAH* for his kind assistance, constructive discussions and unlimited patience in supervising this work and for his guidance and encouragement.

I would like also to thank every person gave me a hand in this work particularly my father.

HISHAM WAGDY



CONTENTS

INTRODUCTION

INTRODUCTION

The lymphomas are a group of malignant diseases of lymphoreticular origin. Although there are similarities among the various lymphomas, they include a wide spectrum of clinical and pathological pictures.

The problem of AIDS-related tumors especially extranodal non-Hodgkin's lymphomas deserves attention, not only from a clinical point of view but also in consideration of the possible progress achievable in understanding the aetiology and pathogenesis of the malignant lymphomas (Ultmann and DeVita, 1987).

The increased incidence of primary gastrointestinal lymphomas noticed in the last decade is difficult to explain but it must be recognized by surgeons and endoscopists (Hayes and Dunn, 1989).

Although the majority of non-Hodgkin's lymphomas arise in lymph nodes, up to 50% of all patients with non-Hodgkin's lymphomas have disease which arises in an extranodal site. Of the extranodal non-Hodgkin's lymphoma, the gastrointestinal tract and Waldayer's ring usually predominate as primary sites. The gastrointestinal tract is the first recognized site of involvement in 12-25% of cases (Ibrahim *et al.*, 1986).

Primary small intestinal lymphoma (PSIL) or the "Western" type arises focally from lymphoid tissues, the remaining small bowel is uninvolved. The "Mediterranean" type of small intestinal lymphoma is a manifestation of immuno-proliferative small intestinal disease (IPSID) and is characterized by proliferation of gut-associated B-lymphoid cells affecting virtually the whole length of the small intestine (Cooper and Read, 1985).

It is sometimes difficult to know whether patients with advanced lymphoma have primary or secondary gut involvement. Hermann *et al.* (1980), have suggested that primary gut lymphomas are those with predominant gut lesion or that presented initially with symptoms related to gastrointestinal tract involvement (Hermann *et al.*, 1980).

A higher incidence of small bowel tumors was noticed most notable in the Middle East and Southern Mediterranean areas (Khojasteh *et al.*, 1983).

Intestinal lymphoma remains a matter of growing interest because of:

- It is still an incompletely studied field especially for surgeons and so many cases might have misdiagnosed or inadequately managed.
- Gastrointestinal involvement symptoms are common in our country and so, the diagnosis of early small intestinal

lymphoma could be missed easily. Also, infectious diarrhea which is common in our country and other parasitic infestation may predispose to small intestinal lymphoma.

- Our country is located geographically in the epidemic region for the immuno-proliferative small intestinal disease (IPSID), or what is called "Mediterranean Abdominal Lymphoma".

Therefore, this assay was planned to review the subject of intestinal lymphoma and throw a light on its different pathological and clinical aspects.

AETIOLOGY

OF

LYMPHOMA

AETIOLOGY OF LYMPHOMA

The aetiology of lymphomas is unknown. However, there has been considerable epidemiologic evidence that suggest an infectious aetiology, particularly a virus. There have been a number of studies addressing the possibility of increased risk with infectious mononucleosis "Epstein-Barr Virus" especially in Burkitt lymphoma (Rosdahl *et al.*, 1974).

Order and Hellmann (1972), suggested that T-lymphocytes may be infected by either a single or a number of viruses that alter their antigenicity. Uninvolved T-cells react against these altered cells, resulting in an anti-immune response similar to graft versus host disease.

The most convincing evidence for viral aetiology of human malignant lymphoma has come from recent studies of a distinct clinicopathologic entity, adult T-cell leukaemia-lymphoma (ATL). The convincing proof has come from the work of Gallo *et al.* (1978), who identified a unique type c-RNA tumor virus in certain patients with mature T-cell malignancies. This virus was termed "Human T-Cell Leukaemia-Lymphoma Virus, HTLV) (Gallo and Gelman, 1981).

The epidemiologic evidence implicating malaria as contributory factor in the aetiology of Burkitt lymphoma has

increased. It has been suggested that continuous stimulation of the lymphoid system in chronic malaria makes it more susceptible to neoplastic transformation in the presence of EB virus (Plorde, 1987).

Other predisposing factors will share in aetiology of lymphoma. A hereditary influence on the incidence of lymphoma is suggested by their higher incidence in patients with inherited immunologic deficiency disease and by a small increase in the incidence in families of patients with immunologic disorders. Investigations of the association of histo-compatibility antigens with lymphoma, report an association with HLA-B_{12} antigen (DeVita *et al.*, 1985).

In many patients with B-cell lymphoma, additional material at the end of the number of 14 chromosome, "$14q^{+}$" can be demonstrated. This abnormality has been reported in adults with lymphomas and multiple myeloma and also in children with African Burkitt lymphoma (Ultmann and DeVita, 1987).

Patients who are chronically immuno-suppressed by drugs particularly those who have received renal transplants have a higher incidence of diffuse histiocytic lymphomas and immunoblastic sarcomas, often involving the brain. Although it appears that ionizing radiation can cause malignant lymphoma in humans, the mechanism of neoplastic transformation and the

condition under which it occurs have been clearly delineated. There are unexplained observations such as the increased risk of acquiring Hodgkin's disease among wood workers and the relationship between development of Hodgkin's disease and tonsillectomy and appendicectomy (DeVita *et al.*, 1985).

MALIGNANT LYMPHOMA AND AIDS:

The increased incidence of malignancies associated with AIDS has been the subject of several reports. Besides Kaposi's sarcoma and other tumors such as squamous carcinoma of the tongue and cloacogenic carcinoma of the ano-rectum, malignant lymphomas have been demonstrated as one of the major problems among the neoplastic complications of AIDS. It was confirmed that in contrast to what was observed in the general population of the median age, non-Hodgkin's lymphomas seem to be more common than Hodgkin's disease in persons with immunodeficiency virus "HIV" infection, i.e., patients with, or at risk, of AIDS. Non-Hodgkin's lymphomas are concentrated in extranodal and often unusual locations with frequent CNS involvement. These lymphomas are predominantly high-grade B-cell neoplasms, classified as immunoblastic and Burkitt's-like lymphomas. Patients with Hodgkin's disease had an increased incidence of mixed cellularity and lymphocytic depletion subtypes. It is now established that non-Hodgkin's lymphoma of Burkitt's type is one of the earliest recognized manifestations of AIDS. According to the CDC "Center for Disease Control", definition, non-Hodgkin's lymphomas of high

grade histology or of CNS origin occurring in HIV-seropositive patients are diagnostic of AIDS even in absence of opportunistic infections or Kaposi's sarcoma, while Hodgkin's disease is not considered *per se* to be diagnostic of AIDS (Italian Co-operative Group, 1988).

In young homosexual men, gastrointestinal complaints may not always be related to "gay bowel" syndrome, or other infectious diseases in patients with acquired immunodeficiency syndrome "AIDS", but small intestinal lymphoma should be added to the list of neoplasms to which this group is susceptible (Steinberg *et al.*, 1985).

MICROSCOPIC ANATOMY OF NORMAL LYMPHOID TISSUES:

The principal cellular component of lymphoid tissue is the lymphocytes. The lymphoid cells are distributed as normally inconspicuous interstitial elements in essentially all tissues except the CNS. Other cells of lympho-reticular system include reticular supporting cells "dendritic and interdigitating reticulum cells" and cells of the monocyte-macrophage series (DeVita *et al.*, 1985).

Normally, both the lymphoid and monocytic cells of the lymphoreticular system originate in the bone marrow and from there migrate by way of the blood and lymphatic vessels to populate other lymphoreticular tissues. The lymphocytes processed

through the thymus gland are called T-cells. Other lymphocytes are thymus independent and are processed through the mammalian equivalent of the avian bursa of Fabricious, probably the foetal liver and they are termed B-cells (Mann *et al.*, 1979).

Monocytes also migrate in the bone marrow and circulate and eventually populate extramedullary tissues as cells of the monocyte-histiocyte series (DeVita *et al.*, 1985).

CELLULAR ORIGIN OF LYMPHOMAS:

Depending on the primary site of proliferation, the lymphoreticular cancers initially may become manifest either in the bone marrow and peripheral blood "where the disease is classified as acute or chronic lymphocytic or less frequently monocytic leukaemia" or in one of the centers of aggregations of lymphoreticular cells, most commonly lymph nodes "where is referred to as malignant lymphoma" (DeVita *et al.*, 1985).

The precise cellular origin of Hodgkin's disease is not yet firmly established, but popular theories have included derivation from either a T-lymphocyte or a macrophage/reticulum cell line. However, the lymphomas can now in most cases be classified by their cell of origin. Most non-Hodgkin's lymphomas in adults are derived from a monoclonal population of B-lymphocytes (Figure 1). Lymphoid malignancies of T-cell origin are less common. Approximately, 15-35% of diffuse lymphomas in adults are of

peripheral T-cell origin "mature or peripheral T-cell lymphoma". Lymphoreticular malignancies of true macrophage histiocytic origin are exceedingly uncommon. Most large cell lymphomas that Rappaport had termed "histiocytic" because of their morphologic resemblance to histiocytes have been shown to be derived from transformed lymphoid cells. Fewer than 5% of such tumours have the phenotypic and functional characteristics of histiocytes (DeVita *et al.*, 1985).