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PLASMA LIPID ALTERATIONS IN MALIGNANT LYMPHOMA

THESIS

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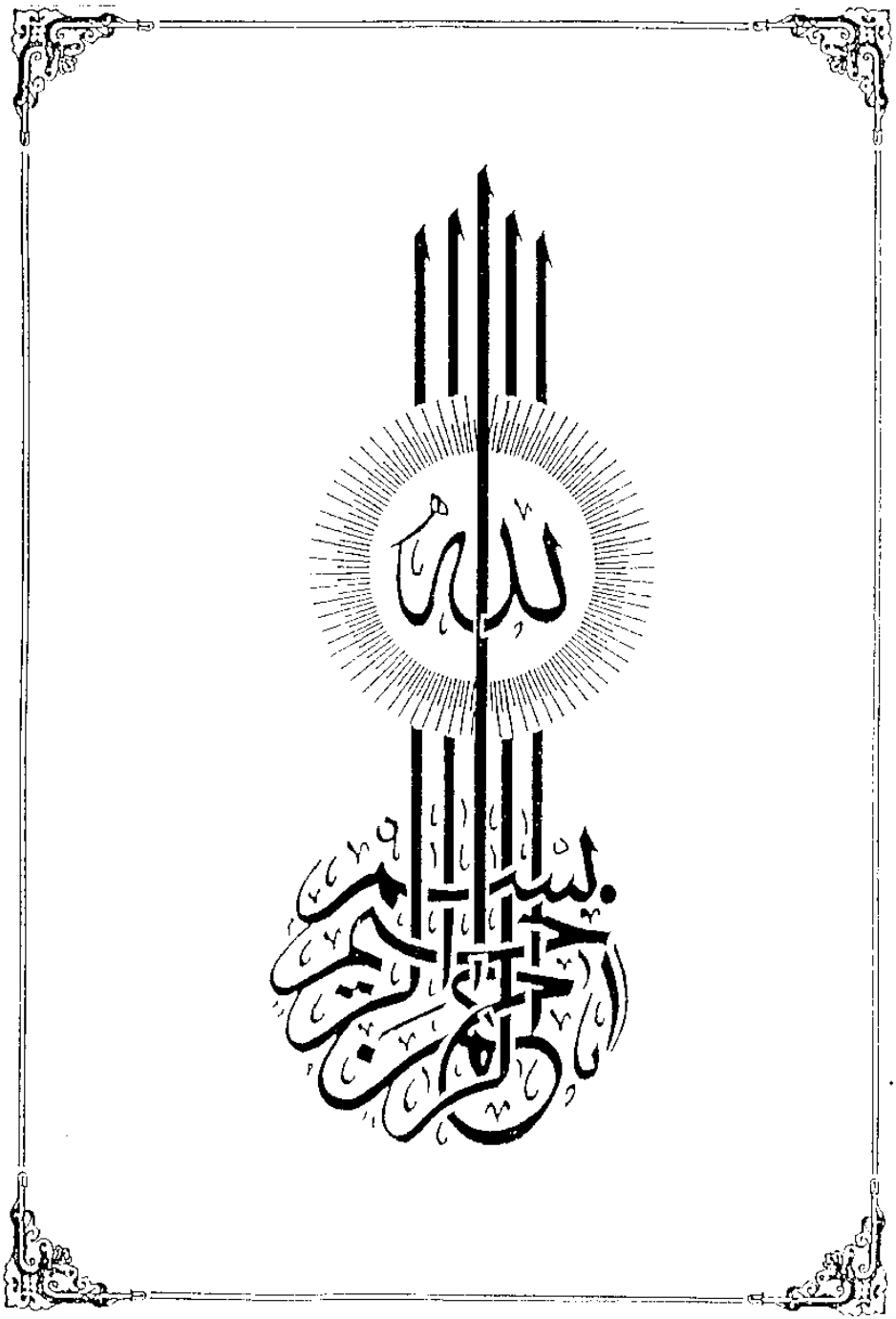

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INTRODUCTION AND AIM OF THE WORK

Malignant lymphoma pose challenging problems in basic and therapeutic fields. Despite the great advance that has been achieved in the treatment of malignant lymphoma, there is still much to do for solving the problem of increasing incidence rate of this malignancy. Only perpetual work and extensive studies can help solving these problems.

The possibility has been raised that lipid alterations and in some cases lipid accumulation, may be intrinsic to cell proliferation or malignant transformation. Secondary hyperlipidaemia is seen in lympho-proliferative malignancy and is likely to be both a precursor and response to the cancer process.

The aim of this work is to document the occurance of plasma lipid abnormalities in those patients having malignant lymphoma and its relation to their ages, sexs and stage of the disease, but not pathogenesis which will need further investigations.

Review of Literature

MALIGNANT LYMPHOMA

INTRODUCTION

Malignant lymphomas are tumors (neoplasms) of the immune system (Donald et al., 1985). The term encompasses a spectrum of disease processes which range in aggressiveness from very indolent cellular proliferations which appear to be lesions of slow accumulation and which may take years to become noticeable to the afflicted individual, to highly aggressive and rapidly proliferating process which may become rapidly fatal in a few weeks if left untreated (Barbara and Tindle, 1984).

The two major categories of malignant lymphoma are Hodgkin's disease and non-Hodgkin's lymphomas. Hodgkin's disease is an easily classifiable lesion (four major subtypes) which is associated with a generally predictable good response to therapy, and is a lesion of which the pathogenesis is poorly understood.

Non-Hodgkin's lymphoma includes a large number of lesions which are classified with difficultly, treated with variable success, and which have a fairly clear (at least superficially apparent) pathogenesis.

EPIDEMIOLOGY

Malignant lymphomas constituted 2.7% of all malignant tumors and the seventh commonest causes of death from cancer in the United States. For unexplained reasons the incidence of lymphomas is increasing each year (Cole et al., 1968).

In United States, non-Hodgkin's Lymphomas are more common in males (8.1:100,000) than in females (5.7:100,000) (Cantor et al., 1980).

There is bimodal incidence curve of Hodgkin's disease in economically developed countries, one mode at ages 15 to 35 years and another after the age of 50 years, in underdevloped countries the incidence prior to the age of 15 years is higher than in developed countries (Correa et al., 1973).

ETIOLOGY

The etiology of lymphoid neoplasia is as clear as that for most neoplasms, that is, the precise cause of these lesions is not known. Etiologies evoked in carcinogenesis generally, as well as lymphomas, include viruses, toxins, especially chemicals, hereditary or genetic factors and abnormal immune states.

VIRALINFECTION:

Burkitt's lymphoma, observed first in African children, seems clearly related to the incidence of the Epstein-Barr virus in certain areas of that countary. It is still unclear whether the virus has a direct etiologic relationship to that lymphoma, despite the evidence that Epstein-Barr virus does infect B-Lymphocytes and that components of the virus have been found in Burkitt's lymphoma cells (Barbara and Tindle, 1984).

There have been a number of studies addressing the question of the increased risk of Hodgkin's disease in infectious mononucleosis (Rosdahl et al., 1974).

CHEMICAL FACTORS:

Individuals who have suffered reactions to drugs and chemicals of various types have developed generalised abnormal lymphoid proliferations. Wheather the drugs are

directly responsible or related to the immune states of the individual host, is not clear. Lymphoma like syndroms associated with lymphadenopthy have been found in patients receving phenytoin. Although in most cases the disease regress with drug discontinuation, a small fraction proceeds to develop malignant lymphoma of several different varieties, including Hodgkin's disease (Hyman and Sommers, 1966).

ABNORMAL IMMUNE LESIONS:

Patients who are chronically immunosupressed by drugs, particularly those who have recieved renal transplants, have a higher incidence of diffuse histocytic lymphoma and immunoblastic sarcoms, often in the brain (Matas et al., 1976).

HEREDITY AND GENETIC FACTORS:

Heredity has been considered an important factor in the development of certain cancers. Patients with both African and American Burkitt's lymphoma have been found to have an abnormally long arm of chromosome 14 (Manolove, 1972.). Changes in chromosome 14 have also been reported in patients with diffuse histocytic lymphoma (Fukuhara, et al. 1978).

COLLAGEN DISEASES AND SJOGRAN'S SYNDROME:

A slight increase in the incidence of lymphomas has been noted in large series of patients with collagen diseases,

systemic lupus erythematosis and rheumatoid arthritis (Miller, 1967.). This increased incidence approached 10% in patients with long-standing Sjogran's syndrome who tend to develop diffuse lymphomas or immunoblastic sarcomas (Kassan et al, 1978.).

PATHOLOGY OF HODGKIN'S DISEASE

The minimum requirement for the pathologic diagnosis of Hodgkin's disease is the presence of characteristic giant cells of the Reed-Sternberg type in an appropriate histologic setting. The Sternberg-Reed cell is a large cell with two or more mirror image nuclei, each containing a single prominent nucleolus (Kadin et al, 1978.).

The Sternberg-Reed cells are characteristic but not pathognomonic of Hodgkin's disease. Cells simulating the Sternberg-Reed cells have been found in tissue of patients with infectious mononucleosis and cancer breast (Lukes et al, 1969.).

In the first clinically usefull subclassification of Hodgkin's disease, developed by Jackson and Parker, cases were divided into three groups: Paragranuloma, granuloma and sarcoma (Jackson and Parker, 1944). This classification proved of little value in clinical practice because nearly 90% of all cases were found to fall in the granuloma category. This and other refinements have permitted the development of Rye histopathologic classification, which is now widely accepted and employed by both pathologists and clinicians. In the Rye classification, Hodgkin's disease is classified into the following four categories:

1- Lymphocyte predominant type

2- Nodular sclerosis.

3- Mixed cellularity type.

4- Lymphocytic depleted type.

1- LYMPHOCYTE PREDOMINANT TYPE. "LPHD"

This subtype is more in men than women and often occurs in younger age groups "less than 35 years of age (Anderson et al, 1970). The lymph node architecture may be partially or completely destroyed and lymphocytes are the predominant cells. Sternberg-Reed cells are scanty, fibrosis is usually not seen. The majority of cases have clinically localized disease and are a symptomatic, and the prognosis is usually favourable.

2- NODULAR SCLEROSIS (NSHD)

Nodular sclerosis is the only form of Hodgkin's disease that is more common in females than males and most frequently occurs in adolescents and young adults (Butler, 1971). Histologically, there is a particular variant of the sternberg-Reed cell, the so called lacunar cell (Anagnostou et al, 1977). Another histologic feature seen in most, but not all, cases is a thickened capsule with a proliferation of orderly collagenous bands dividing the lymphoid tissue into circumscribed nodules. Patients with nodular sclerosis, particularly those with localized tumours usually have a good

prognosis (Axtell et al, 1972).

3- MIXED CELLULARITY TYPE (MCHD):

This type is slightly more common in males than females and often is associated with systemic symptoms (Keller et al, 1968).

Histologically Sternberg-Reed cells are usually quite plentiful (5-15) per high power field. The lymph node is usually diffusely affected, but occusionally focal involvement is observed. Broad bands of fibrosis are not seen and focal necrosis is minimal. It occupies an intermediate position between lymphocyte predominant and lymphocyte depleted varities with respect to both proportion of neoplastic cells and prognosis.

4- LYMPHOCYTIC DEPLETED TYPE (LDHD):

Most patients are older and symptomatic and the disease usually is disseminated at the time of diagnosis (Neirman et al, 1973).

Histologically, Sternberg-Reed cells are abundant usually more than 15 per high-power field and relative paucity of lymphocytes is apparent, fibrosis and necrosis are common but not diffuse.