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Study of

Clinico-pathological correlation of Lymphoma

THESIS

Submitted For The Partial Fulfillment of the

M.Sc. Degree In General Medicine



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1984



TO MY FAMILY

ACKNOWLEDGMENT

My grateful thanks are given to Professor Dr. Mohamed S. Sabbour Professor of General Medicine who has been a great encouragement throughout this work with his supervision, continuous guidances, marvellous support, objective criticism and valuable directions.

Also, my acknowledgements to Professor Dr. Lilly A. El-Malek Solomon Professor of Pathology who was extremely helpful with suggestions and comments.

Particular thanks are to my colleagues of surgery for their valuable and fruitful cooperation.

MISTAKES

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FORWARD

Lymphomas are one of the neoplastic disorders of the haematopoietic system as the leukemias, polycythemia vera and idiopathic myelofibrosis as well as the myelomas.

The causes of neoplastic diseases of the haematopoietic system are unknown. All are characterized by abnormalities in the growth of haematopoietic cells. All of these diseases appear to be clonal in origin and produce a tumour which, in some of these conditions, overgrows the normal haematopoietic system. In certain instances the diseases are curable, in others they are not till now, although therapy will ameliorate symptoms and in some patients will prolong life.

Lymphomas by definition are tumours arising from peripheral lymphoreticular tissue and thus exclude neoplastic proliferations of bone marrow- the leukemias - and the primary epithelial tumours of thymus- thymomas.

Lymphomas are conveniently separated into two broad categories, Hodgkin's disease (H.D.) and Non Hodgkin's Lymphomas (N.H.L.). Hodgkin's disease has been further subdivided according to histologic patterns because these have prognostic significance. The distinctive geographic distribution and exquisite sensitivity to therapy of Burkitt's (African) lymphoma justify its consideration as separate entity, whereas Histiocytic Medullary Reticulosis, ' Hairy Cell Leukemia'

and certain other illdefined diseases often regarded as lymphoma is debatable.

Lymphomas represent solid tumours of the immune system and immunologic abnormalities are common.

Lymphomas are all malignant: since they vary considerably in their clinical course, many attempts have been made to classify them so that behaviour may be correlated with the histologic type.

There is still no agreed classification and the nomenclature is confusing; hence it is often impossible to compare the results of treatment in one centre with those in another.

It can be extremely difficult to interpret the histological features of some lymph nodes, and clinicopathological correlation is necessary by the detailed follow up of these cases so that our knowledge of the natural history of these diseases becomes broadened.

REVIEW OF LITERATURE

One of the reasons for the confusion surrounding the Non-Hodgkin's Lymphomas is that there has until fairly recently been a failure to keep pace with, or take into account advances in our knowledge of lymphoreticular tissue and its importance in immunological function. Therefore, before embarking on a discussion of classifications of Non-Hodgkin's Lymphomas a brief account will first be given about the lymphoreticular system.

THE RETICULO-ENDOTHELIAL SYSTEM

The term reticulo-endothelial system was coined by Aschoff in 1924, to delineate a large collection of cells that shared a common origin, morphology, and phagocytic function. The cells that have been included in Aschoff's reticulo-endothelial system are the "reticulum cells" of the spleen and lymph nodes, the cells lining the lymphatic and blood sinuses, e.g. of the lymph nodes, spleen, and liver (where they are called Kupffer cells), the monocytes of the blood, and the tissue histiocytes. The name reticulo-endothelium was derived from the close relationship of some of these cells to the reticulin framework that intersects the lymph nodes and spleen, and their endothelium-like appearance when lining sinuses in these organs. But the cells of the system are very different both morphologically and functionally from both endothelial cells and reticular cells, and the name reticulo-endothelial (RE) system is inappropriate although it is in general use by pathologists.

At a conference held in Leiden in 1969 a group of workers proposed a new classification of this system of cells, which they call the mononuclear phagocyte system.⁽²⁰⁵⁾ They proposed that the following cells form part of this system :

- Precursor cells from the bone marrow.
- Promonocytes from the bone marrow.
- Monocytes from the bone marrow and from the blood.
- Macrophages, which include the connective-tissue histiocytes, the liver Kupffer cells, the alveolar macrophages of the lung, the sinus-lining cells and free macrophages of the spleen and lymph nodes, the pleural and peritoneal macrophages and those of the bone marrow, and probably also the osteoclast which is believed to arise by coalescence of monocytes. The microglial cell of the central nervous system is also regarded as a probable candidate for membership of this system.

While the RE (or mononuclear phagocyte) system is widely dispersed throughout the tissues of the body, most of its content is present in the liver, bone marrow, lymph nodes, and spleen.

They are sometimes called the reticuloendothelial organs on this account. They are also sometimes described as the lymphoreticular tissues because of their reticulin frame work and the predominance of lymphocytes, though in the marrow the granulocytic and normoblastic elements far outnumber the lymphocytic ones.

The lymphoreticular system is now divided into :

1. The stem cell compartment as exemplified by the bone marrow.
2. The primary or central lymphoid organs such as the thymus and the human analogue of the bursa of Fabricius, whatever this may ultimately prove to be, but of which at the moment bone marrow itself is the favoured candidate.
3. The secondary or peripheral lymphoreticular tissue which incorporates lymph nodes, spleen, bronchial and gut associated lymphoid tissue (BALT and GALT respectively) and other extra nodal sites such as skin (SALT).⁽¹¹⁵⁾

In practice most lymphomas arise in lymph nodes in the first instance. Therefore a brief account will be given of some of the normal lymph node structures with their component cells since these are potential sites of neoplastic transformation, or may show reactive changes misinterpreted as a malignant process.