Role of Surveillance CT in Detection of Pre-Clinical Relapse in Patients with B-Cell lymphoma: A Retrospective Study

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NHL	Non-Hodgkin lymphoma
DLBCL	Diffuse large B-Cell lymphoma
HL	Hodgkin lymphoma
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
WHO	World Health Organization
NHL	Non-Hodgkin lymphoma
FDG	Fludeoxyglucose
MIP	Maximum Intinsity Projection
IWG	International Working Group
RECIST	Response Evaluation Criteria In Solid Tumors
SUV	Standardized Uptake Values
WB-MRI	Whole-body MRI
FL	Follicular Lymphoma
CR	Complete Remission
CRu	Complete Resmission Unconfirmed
PR	Partial respose
SD	Stationary Disease

Non-Hodgkin lymphoma is a fairly common tumor according to Surveillance, Epidemiology, and End Results (SEER), which states that NHL accounts for 4.3% of all new cancer cases per year in USA. Its incidence is almost doubling annually ***(SEER database, 2013)***. In Egypt, lymphoma is the fourth most common tumor in adults, with B-Cell lymphoma being the commonest subtype of NHL accounting for about 49% of all NHL cases presenting to NCI ***(Allah HG et.al., 2014)*.**

With such a disease burden, and about one third relapsed NHL patients after complete remission, on-going research on new methods of detection, staging and response assessment is always making the highlights, with relapse detection being of major concern, especially with the new curative methods made available for relapsed cases. The high risk of radiation induced malignancies associated with frequent radiological follow-up scans for those long term survivors also raised the red flag for re-establishing a risk-benefit oriented follow-up plan for those patients ***(Lalit et. al., 2014).***

Careful history taking, thorough physical examination and good clinical judgment are the cornerstones of an appropriate follow-up. Many recommendations have been published for formulating follow-up plans according to histology; curable versus non-curable. For curable conditions (HL, DLBCL) the likelihood of relapse decreases with time, so the frequency of follow-up decreases accordingly, and the contrary goes for non-curable conditions (mantle cell lymphoma and follicular lymphoma) ***(Bruce et.al, 2014)***.

Although most guidelines do not recommend whole body CT scan as part of routine follow-up for patients who went through complete remission, it is still adopted by many clinicians as part of their patients' follow-up visits. However, its value for assessment of early asymptomatic relapse is questionable, let alone its influence on the overall outcome compared to other modalities of relapse detection ***(Tung-Liang Lin et. al., 2012)***.

- **Aim and objectives:**

  I. To clarify whether surveillance CT scan has a significant role in early detection of asymptomatic relapse in B-Cell lymphoma patients.

  II. To assess the contribution of image-based relapse detection to the overall survival of B-Cell lymphoma patients.

o Patients and methods:

This is a retrospective cohort study in which 50 Patients with B-Cell lymphoma diagnosed between 2014-2016 were selected from the PACS of radiology department at Ain Shams University Hospitals. Age ranges between 20-70 year-old. All diagnoses were confirmed by histopathology studies. all patients underwent treatment and follow-up strategy as planned by their treating oncologist/hematologist, after which they entered CR or SD according to IWG Cheson criteria of treatment response.

Baseline clinical, laboratory and treatment data were abstracted from medical records. State progression was retrospectively reviewed over a period of 6 months up to 2 years. Surveillance CT scan was performed on the neck, chest abdomen and pelvis on each of the planned follow-up visits. Relapses were defined as “asymptomatic” if there were no reported symptoms and a normal examination was recorded.

- **Statistical methodology:**

Overall survival (OS) after relapse was calculated from the date of relapse to the date of death for any cause or the last date of follow-up. Continuous variables were compared using *t*-test. Categorical variables were compared using Chi-Sq test. All comparisons were considered significant at p value < 0.05.

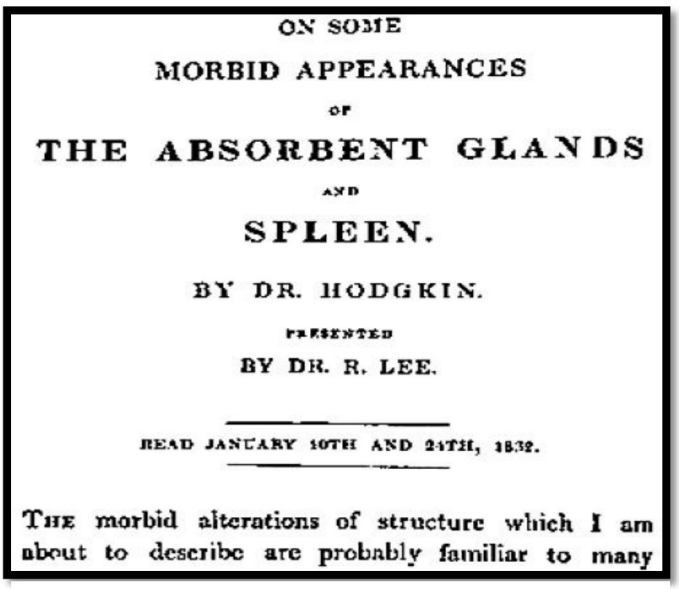
CLASSIFICATION OF LYMPHOID NEOPLASMS

Chapter I

Classification of Lymphoid neoplasms

Malignant transformation of lymphocytes at different stages of differentiation gives rise to lymphoid neoplasms which include lymphoma, myeloma and lymphoid leukaemia, all together compromise the sixth commonest malignancy worldwide. (Morton et al., 2007)

Having heterogeneous aetiologies, morphologies, genetic and molecular basis, lymphoma has had a very long history of classification systems since 1832 when Hodgkin reported the first description of lymphoma in his manuscript entitled "on some morbid appearances of the absorbent glands and spleen" (Hodgkin, 1832) *Figure 1*, till the most recent updated WHO classification system in 2016 (Swerdlow et



ON SOME

MORBID APPEARANCES

OF

THE ABSORBENT GLANDS

AND

SPLEEN.

BY DR. HODGKIN.

PRESENTED

BY DR. R. LEE.

READ JANUARY 10TH AND 24TH, 1832.

THE morbid alterations of structure which I am about to describe are probably familiar to many

Figure 1 1832 publication on the first seven lymphoma cases (Hodgkin, 1832)

al., 2016)

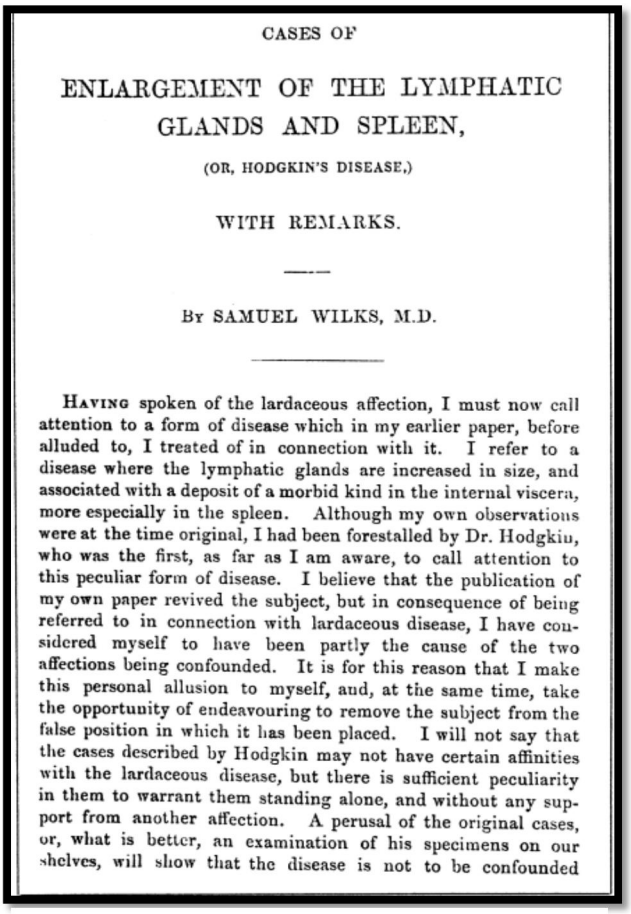
In this early description by Thomas Hodgkin, he described autopsy findings of seven cases who had multiple lymphadenopathy *Figure 2*. He was the first to conclude that it is a disease primarily arising from lymphoid tissue and spleen. He recognized the disease grossly, and noted the orderly spread of disease through multiple lymph nodes and

Figure 2 autopsy of Hodgkin's case number two. Abdominal lymph nodes (Stone, 2005)

the late involvement of the spleen (Stone, 2005).

When this was first published in the Medical and Chirurgical Society in London, UK, it almost passed unnoticed, until Samuel Wilks described the same disease findings on 1865 and first called it "Hodgkin's Disease" *Figure 3*. So, it wasn't until three decades later that Hodgkin was given the eponym for his work on describing lymphoma (Bonadonna, 2000).

Nevertheless, none of Hodgkin or Samuel had related their gross autopsy findings to histological appearance of the disease which is together with morphological appearance, immunohistochemistry as well as molecular basis now compromise indispensable parts in recognizing and diagnosing lymphoma.



CASES OF

ENLARGEMENT OF THE LYMPHATIC GLANDS AND SPLEEN,

(OR, HODGKIN'S DISEASE,)

WITH REMARKS.

By SAMUEL WILKS, M.D.

Having spoken of the lardaceous affection, I must now call attention to a form of disease which in my earlier paper, before alluded to, I treated of in connection with it. I refer to a disease where the lymphatic glands are increased in size, and associated with a deposit of a morbid kind in the internal viscera, more especially in the spleen. Although my own observations were at the time original, I had been forestalled by Dr. Hodgkin, who was the first, as far as I am aware, to call attention to this peculiar form of disease. I believe that the publication of my own paper revived the subject, but in consequence of being referred to in connection with lardaceous disease, I have considered myself to have been partly the cause of the two affections being confounded. It is for this reason that I make this personal allusion to myself, and, at the same time, take the opportunity of endeavouring to remove the subject from the false position in which it has been placed. I will not say that the cases described by Hodgkin may not have certain affinities with the lardaceous disease, but there is sufficient peculiarity in them to warrant them standing alone, and without any support from another affection. A perusal of the original cases, or, what is better, an examination of his specimens on our shelves, will show that the disease is not to be confounded

Figure 3 Cover page of the 1865 paper by Sir Samuel Wilks (Bonadonna, 2000).

Histological typing of HL using the concept of Reed-Strenberg (R-S) cell was identified as late as 1902 by Dorothy Reed when she first depicted what she saw under microscopy, and later on was referred to as (R-S) cells *figure 4*. Since then, scientists started hunting those large cells and their variants to further classify the disease, they were described as "owel-eye", "mirror image", "lacunar" or "mummified" based on nuclear configuration. However, such descriptions are now liable to extinction as immuno-histo-chemical and molecular based typing is dominating over microscopic description in disease classification