UNIVERSITI TEKNOLOGI MARA

THE PREVALENCE OF GERMINAL CENTRE B-CELL AND NON-GERMINAL CENTRE B-CELL SUBTYPES OF DIFFUSE LARGE B-CELL LYMPHOMAS (HANS ALGORITHM) IN HOSPITAL SULTANAH BAHIYAH: A COMPARISON WITH MODIFIED HANS AND MURIS ALGORITHMS

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ABSTRACT

Diffuse large B-cell lymphoma (DLBCL) is the most common Non-Hodgkin lymphoma worldwide. It can be classified into two prognostic subgroups, germinal centre B-cell (GCB) and non-GCB (NGCB) subtypes using an immunohistochemistry (IHC) panel comprising of CD10, BCL6, and MUM1 according to Hans Algorithm (HA) while Muris algorithm (MA) incorporate BCL2 as a prognostic marker. Modified Hans (MH) used only CD10 and MUM1 in the algorithm. We had analysed 97 cases extracted from laboratory information system and review of IHC according to HA, MH and MA to determine the prevalence of DLBCL subtypes and agreement between the three and its prognostic significance. NGCB subtype predominates in HA and MH by 60.8% (59 cases) and 68.04% (66 cases) respectively but was reversed to GCB subtype, 53.61% (52 cases) when MA applied. Kappa agreement was strong, moderate, and weak for HA versus MH, HA versus MA and MH versus MA, respectively. BCL6 and MUM1 showed significant result in term of survival status (p= 0.038 and 0.002, respectively) and BCL2+ patient who did not received chemotherapy showed higher number of deaths (p=0.000). MA showed patients with NGCB subtype had inferior outcome with greater number of death (p=0.039). High agreement between HA and MH may suggest the possibility of using MH in the future but correlation with molecular profiling is recommended in the future. BCL2 had proved its prognostic significance in this study that patients may be benefited for anti-BCL2 targeted therapy.

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CHAPTER ONE
INTRODUCTION

1.1 Background of the study

Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (NOS) is the most frequent type of Non-Hodgkin Lymphomas encountered, encompasses up to 40% of all types of lymphomas [1]. DLBCL is a high-grade mature B-cell lymphoma and had been recognized to have an aggressive course but curable disease.

DLBCL, NOS is a heterogenous entity pertaining to its histomorphology, molecular profiles and patients' survival. Based on World Health Organization (WHO) classification of hematopoietic and lymphoid malignancies, DLBCL can be divided into two groups based on the cell of origin of either germinal centre B-cell (GCB) and non-GCB or activated B-cell (ABC) subtypes. This classification was established by genetic expression profiling (GEP) of each DLBCL case studied before adopted into immunohistochemistry (IHC) by tissue microarray. The widely used IHC panel is created by Hans et al which was developed in 2004. In addition, this study also showed each subtype had prognostic significance in which GCB patients had favourable outcome in contrast to NGCB patients [2].

In Hospital Sultanah Bahiyah, pathologists started to report the DLBCL cases with inclusion of these subtypes by Hans et al as per request by clinicians starting around end of 2013. However, limitation of samples such as poor fixation, markedly crushed tissues and minimal diagnostic material hampered further IHC staining for subtyping of DLBCL. The diagnosis of DLBCL might not be straight forward when the morphology can be mistaken as poorly differentiated carcinomas, sarcomas and the great mimicker of malignant melanomas. The list of IHC needed to diagnose DLBCL can be exhausting and those limited biopsies mentioned earlier were impossible to make a definitive subtyping.

1.2 Problem statement

According to Malaysian National Cancer Registry Report 2007 to 2011, the