There is immunophenotypic heterogeneity in DHL cases compared to DLBCL. DHL had more frequent expression of immunophenotypic features, with a variety of rearrangements involving MYC, IGH/BCL2, and BCL6. Our THL, 67 lymphomas double hit lymphomas were compared to DLBCL/DHL groups. Compared to DLBCL, DHL had more frequent expression of CD10 (83% vs. 40%), BCL6 (92% vs. 80%) and less frequent expression of MUM1 (42% vs. 59%) and LMO2 (33% vs. 62%). Half of all DHL (50%) had >90% expression of MYC. THL (5/54) showed comparable immunohistochemical findings to DHL. In DHL, 86% (31/36) were of GCB origin by Hans’ method and 14% (5/36) were of NGC origin. Using the tally method, 38% (5/13) were of GCB origin and 62% (8/13) were of NGC center origin.

We identified 15 cases of BCL2/BCL6 lymphomas. These are included in the WHO 2008 BLU category, but most authorities agree that these are not equivalent to DHL. Of these cases, there were 6 males and 9 females, with an average age of 75.7 years (range 59-90). There were 10 extranodal cases and 5 cases were nodal.

In general, these cases did not differ significantly immunophenotypically from the larger group of DLBCL. In these lymphomas, 54% (7/13) were of GCB origin by Hans’ method and 46% (6/13) were of NGC origin. Using the tally method, 67% (2/3) were of GCB origin and 33% (1/3) were of NGC center origin. In one discordant case, a Hans’ method GCB case was switched to NGC by the tally method.

Diffuse large B-cell lymphoma (DLBCL) is the most commonly diagnosed subtype of lymphoma worldwide. The current World Health Organization (WHO) classification includes several subtypes which are based on combination of clinical, immunohistochemical, and genetic features. One aggressive variant of B-cell lymphomas include diffuse large hit lymphomas (DHL). The WHO classification describes DHL as a subset of aggressive B-cell lymphomas containing a MYC rearrangement in combination with either BCL2 and/or BCL6 (DHL-MYC) or a combination of BCL2 and BCL6 rearrangements.

The presence of a variety of immunohistochemical, genetic and clinical features have an impact on prognosis of these patients. The goal of this study is to further characterize distinctive immunophenotypic and genetic findings of this subgroup.

**TYPE # Mean age M:F N:E (%) CD20 (%) CD10 (%) BCL6 (%) MUM1 (%) BCL2 (avg) (%) GCE1 (avg) (%) FOXP1 (%) LMO2 (%) CD30 (%)**

**DHL**

+THL 39 (44-91) 24:15 (1.6:1) 14:20 (1.1:1) 100% 93% 93% 86% 86.2% 33% 100% 100% 100% 33% 100% 100% 33% 5% 1/19

THL 5 64 (22-83) 1:1 100% 100% 100% 75.5% 67% 100% 100% 100% 7/3 100% 100% 100% 100% 0/3

**BCL2/BCL6**

15 75 (59-90) 6:9 5:1 100% 100% 100% 93% 100% 100% 100% 100% 100% 100% 100% 0/3

**Results**

We considered cases of DHL to have two or more identified driver mutations of lymphomas associated genes (IGH/BCL2, BCL6 or MYC). We subdivided these into DHL with MYC translocations (DHL-MYC), with a subset of these cases with three mutations, or THL (e.g. MYC, and IGH/BCL2 and BCL6). We identified 39 cases of DHL; 24 were male and 15 were female and ages ranged from 44 to 91 years old with an average age of 67 years. 25 cases were extranodal and 14 were nodal. Expression of CD10, BCL2, and MUM1 were comparable in DHL and DLBCL groups. Compared to DLBCL, DHL had more frequent expression of CD10 (83% vs. 40%), BCL6 (92% vs. 80%) and less frequent expression of MUM1 (42% vs. 59%) and LMO2 (33% vs. 62%). Half of all DHL (50%) had >90% expression of MYC. THL (5/54) showed comparable immunohistochemical findings to DHL. In DHL, 86% (31/36) were of GCB origin by Hans’ method and 14% (5/36) were of NGC origin. Using the tally method, 38% (5/13) were of GCB origin and 62% (8/13) were of NGC center origin.

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**Discussion**

- There is immunophenotypic heterogeneity in DHL cases
- DHL associated MYC gene abnormalities had similar immunophenotypic features to those with IGH/BCL2 and BCL6 translocations
- Compared to DLBCL, DHL had more frequent expression of CD10, BCL2, and less frequent expression of MUM1 and LMO2