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ORIGINAL ARTICLE

Lymphoma in Taiwan: Review of 1347 neoplasms from a single institution according to the 2016 Revision of the World Health Organization Classification

Shih-Sung Chuang [a,b,c,*], Shang-Wen Chen [d], Sheng-Tsung Chang [a,e], Yu-Ting Kuo [f]

[a] *Department of Pathology, Chi-Mei Medical Center, Tainan, Taiwan*
[b] *Department of Pathology, Taipei Medical University, Taipei, Taiwan*
[c] *Department of Pathology, National Taiwan University, Taipei, Taiwan*
[d] *Division of Hemato-Oncology, Department of Internal Medicine, Chi-Mei Medical Center, Liouying, Tainan, Taiwan*
[e] *Department of Nursing, National Tainan Institute of Nursing, Tainan, Taiwan*
[f] *Department of Radiology, Chi-Mei Medical Center, Tainan, Taiwan*

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Background/Purpose: Lymphoid neoplasms are heterogeneous and types of lymphoma vary in different geographic regions. In this study, we aimed at classifying the lymphoid neoplasms at our institution in Taiwan and to compare the relative frequency of various types of lymphoma in different countries.
Methods: We retrospectively searched the files of patients diagnosed with lymphoma at our institution from 2000 to 2015 based on the 2016 Revision of the World Health Organization classification.
Results: We identified 1339 patients with lymphoid neoplasms; among them, eight had two distinct types of lymphoid neoplasms. Of the 1347 neoplasms, 6.09% were Hodgkin lymphomas (HLs) and 93.31%, non-HL (NHLs). Among the 1257 NHLs, 82.66% were of B-cell lineage and 17.34% of T-cell lineage. The most common B-cell lymphoma types were diffuse large B-cell lymphoma, follicular lymphoma, and mucosa-associated lymphoid tissue lymphoma. Among T-cell neoplasms, 37% cases were of nodal origin and 63% cases arose in extranodal sites. The most common nodal and extranodal T-cell neoplasms were angioimmunoblastic T-cell lymphoma and extranodal natural killer/T-cell lymphoma, nasal type, respectively.
Conclusion: We analyzed the largest series of lymphomas to date from Taiwan and concluded that HL was rare and T-cell neoplasms comprised around 17% of all NHLs in Taiwan. The

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* Corresponding author. Department of Pathology, Chi-Mei Medical Centre, 901 Chung-Hwa Road, Yong-Kang District, Tainan 71004, Taiwan.
E-mail address: cmh5301@mail.chimei.org.tw (S.-S. Chuang).

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relative frequency of the major lymphoma types is similar in East Asian countries, with only a minor difference, but the overall pattern in the East is quite different from that in the West, with the latter showing a higher frequency of HL and a lower rate of T-cell neoplasms.

Introduction

Lymphoid neoplasms are clonal lymphoproliferations and are heterogeneous in clinical presentation, histopathology, immunophenotype, and prognosis. Characterization and classification of lymphoid neoplasms are challenging and evolve with advances in technology. Currently, the 2008 World Health Organization classification is the gold standard in diagnosis and classification of lymphoid neoplasms.[1] Lymphoma types vary across geographic regions, reflecting the impact of ethnicity, socioeconomic status, and various environmental factors on lymphomagenesis.[2]

In our prior studies with smaller numbers of cases, we showed that the frequency of T and natural killer (NK)/T-cell lymphoma in Taiwan was higher than that in the Western countries and there was an increase in the frequency of follicular lymphoma (FL) in the early years of the 21st century in Taiwan.[3,4] In this study, we aimed to systematically review the cases of lymphoma at our institution in the first 16 years of the 21st century and to compare our data with those from different geographical regions.

Materials and methods

We retrospectively searched the files of patients diagnosed with lymphoma at our institution from January 2000 to December 2015. Diagnoses were made according to the 2008 World Health Organization classification of lymphoid neoplasms and the 2016 revision.[5] Plasma cell neoplasms were not included. This study was approved by the Internal Review Board of Chi-Mei Medical Center, Tainan, Taiwan and conducted in accordance with the Helsinki Declaration.

Diagnosis was based on detailed histopathological examination with the aid of immunohistochemistry and/or flow cytometric immunophenotyping. Clonality assay for B-cell and T-cell receptor gene rearrangement was performed for confirmation of clonality and exclusion of morphological mimics of lymphoma/leukemia. *In situ* hybridization for Epstein—Barr virus (EBV) encoded mRNA was applied for cases of peripheral T-cell lymphoma to exclude extranodal NK/T-cell lymphoma (ENKTL), nasal type as previously described.[6] Fluorescence *in situ* hybridization for common lymphoma-associated chromosomal translocation (*IGH*, *BCL2*, *BCL6*, *MYC*, and *CCND1*) was performed mainly for the identification of Burkitt lymphoma (BL) and high-grade B-cell lymphoma, NOS (previously called B-cell lymphoma, unclassifiable, with features between diffuse large B-cell lymphoma (DLBCL) and BL), and the differential diagnoses between cyclin D1-positive DLBCL versus mantle cell lymphoma as previously described.[7—9]

For primary splenic lymphomas, diagnoses were made based on morphological and flow cytometric immunophenotyping of the leukemic cells when present and histological evaluation plus immunohistochemistry of the splenectomy specimens. For those cases of primary splenic lymphoma with leukemic change (confirmed by flow cytometric immunophenotyping) but devoid of surgical or biopsy specimens, "splenic B-cell lymphoma/leukemia, unclassifiable" was diagnosed, since splenic marginal zone lymphoma (MZL), splenic diffuse red pulp small B-cell lymphoma, and even hairy cell leukemia variant may fall into this category if no splenic tissue can be obtained for histopathological examination.[10—12] Patients with lymphocytosis but devoid of organomegaly and not fulfilling the phenotypic criteria of chronic lymphocytic leukemia (CLL; dim CD20 expression and positivity for CD5, CD23, and CD43) were diagnosed with "unclassifiable small B-cell leukemia"; its neoplastic nature was confirmed by flow cytometric immunophenotyping and/or bone marrow aspiration biopsy as mature small B-cell leukemia. We separated lymphoplasmacytic lymphoma from other mature low-grade B-cell leukemia including "unclassifiable small B-cell leukemia" by: (1) morphological identification of plasmacytoid lymphocytes and plasma cells in addition to small lymphocytes in the marrow aspirate smears; (2) flow cytometric immunophenotyping of these plasmacytoid lymphocytes and plasma cells, which was distinct from the mature B-cell leukemic cells; and (3) presence of immunoglobulin M monoclonal gammaglobulin.

Transformed lymphoma, either at disease presentation or at relapse, was counted only once at initial diagnosis. For example, Grade 3A FL and DLBCL at the same site was diagnosed as FL. By contrast, coexistence of two distinct lymphomas, either synchronously or metachronously, is defined as two lymphomas. For example, one patient with primary cutaneous peripheral T-cell lymphoma not otherwise specified (PTCL-NOS) and subsequent development of DLBCL during the disease course was diagnosed as two kinds of lymphoma accordingly.

Results

A total of 1347 cases of lymphoid neoplasms were identified among 1339 patients, including eight with two distinct types of lymphoid neoplasms (1 synchronously and 7 metachronously). Among the 1347 cases, 6.09% (82 neoplasms) were Hodgkin lymphoma (HL), 93.31% (1257) were non-HL (NHL), and 0.59% (8) was other diseases [3 composite lymphomas, 2 mediastinal lymphoblastic lymphoma of ambiguous phenotypes (1 mixed T and myeloid and 1 mixed B, T, and myeloid lineages), 1 mediastinal gray zone lymphoma,