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| 原文題目(出處)： | Lymphoma in Taiwan: Review of 1374 neoplasms from a single institution according to the 2016 Revision of the World Health Organization Classification J Formosan Med Association 2017;116:620-5 |
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| 報告日期： | 2017.08.08 |

內文：

A. Main Objectives :

- a. Aimed at classifying lymphoid neoplasms in Taiwan
- b. Compare the Frequency of different types among other nations.

B. Intro :

- a. Studying 1347 cases from 2000~2016 from 奇美醫院
- b. Characterization of Lymphoid neoplasm is hard and differs with technological advancement
- c. 2008 WHO classification is standard now
- d. Lymphoma types differs across nations and regions; reflects, race, social status, and environment factors.
- e. In prior study :
 - i. T cell & NK T cell lymphoma is higher than western countries
 - ii. Frequency of Follicular Lymphoma (FL) Increases in 2000's in Taiwan

C. Materials & Methods

- a. Diagnosed with 2008 WHO classification & 2016 revision
- b. Diagnosed with immunohistochemistry & flow cytometric immunophenotyping
- c. Divide into B cell type & T cell type with Clonality Assay
- d. B/T cell receptor rearrangement for 排除型態 mimics
- e. In situ EBV mRNA 混合法用在 Peripheral T-cell lymphoma , 排除 extranodal NK/T-cell lymphoma, nasal type
- f. 使用 Fluorescence in situ 混合法 , 來鑑別 lymphoma 相關染色體 translocation , 其主要用於鑑別 Burkitt Lymphoma (BL)& High Grade B-cell Lymphoma, NOS(B-cell lymphoma, unclassifiable)
- g. Primary Splenic Lymphomas :

Main: flow cytometric immunophenotyping & morphological appearance. Also:

- i. Without surgical / biopsy 樣本 : Splenic B-cell lymphoma, unclassifiable
- ii. Splenic Marginal Zone Lymphoma(MZL), Hairy cell leukemia 等地切片中若沒有 Splenic 組織都會被分類至此
- h. 在 lymphocytosis 的 case 中，卻沒有器官肥大(organomegaly)/未達 Chronic Lymphocytic Leukemia 的標準者，分類至 Unclassifiable Small B-cell Leukemia
- i. Flow cytometric immunophenotyping and/or bone marrow 抽液診斷為 Mature Small B-cell Leukemia，用以下方式再細分：
 - i. 區分 Plasmacytoid Lymphocytes:
 1. 骨髓抹片中， plasmacytoid lymphocyte, plasma cell, small lymphocytes 型態
 2. Plasmacytoid lymphocyte, plasma cell 的 Flow cytometric immunophenotyping，與 Mature B-cell lymphoma 不同
 3. 有 IgM, monoclonal Gamma-globulin
 - j. 轉變型 lymphoma 以最初的診斷為主；同時有兩種並存者，視為兩種 lymphoma

D. Results

- a. Hodgkin Lymphoma(HL) : 6.09%(82 case)
- b. Non-HL : 93.31 % (1257)
- c. Other diseases : 0.59% (8)
 - i. Composite lymphoma : 3 cases
 - ii. Mediastinal lymphoblastic lymphoma(2)
 - iii. Mediastinal gray zone lymphoma(1)
 - iv. Follicular dendritic cell sarcoma (1)
 - v. Langerhans cell neoplasm (1)
- d. HL is 6 % (4~8% in Asia, greatly lower than west) 15~30%
- e. 1 only of 82 nodular lymphocyte-predominant HL
 - i. 99 % of HL are Classic HL(CHL)
- f. Of 1257 cases:
 - i. B-cell : 82.66% (1039 cases)
 1. No.1 : DLBCL(diffuse large B-cell lymphoma), FL(Follicular Lymphoma), MALT(Mucosa-associated lymphoid tissue) lymphoma
 2. Account DLBCL+FL+MALT + MZL(marginal zone

- lymphoma)
most common :
- #1. DLBCL(50.62%)
 - #2. FL (16.27%),
 - #3. MZL (12.70%)
3. 2nd tier most common:
- #1. CLL(small lymphocytic lymphoma)(7.31%)
 - #2. unclassifiable small B-cell(3.27%)
 - #3. Mantle cell lymphoma (2.5%)
 - #4. BL (2.41 %)
- ii. T-cell: 17.34 % (218 cases)
- #1. Angioimmunoblastic T-cell lymphoma(AITL;18.3%)
 - #2. ENKTL(), nasal type(16.5%)
 - #3. PTCL-NOS(15.1%)
 - #4. Systemic anaplastic large cell lymphoma(ALCL,10.5%)
 - a. Anaplastic lymphoma kinase (ALK+; 5.0%)
 - b. ALK- ; 5.5%
- 2nd Tier most common T-cell lymphoma:
- #1. T-cell large granular lymphocytic leukemia(T-GL leukemia; 7.3%)
 - #2. Adult T-cell Leukemia(4.1%)
 - #3. Mycosis Fungoides (4.1%)
 - #4. Primary cutaneous CD30+ T-cell lymphoproliferative disorder(4.1%)
 - a. Primary cutaneous ALCL(1.4%)
 - b. Lymphomatoid papulosis(2.8%)
- iii. 10 cases of 218 TL 被剷除，因沒有確切來源(nodal & extranodal 並存)
剩餘 208 case 中:
1. Nodal (37%; 76cases)
 - a. AITL most common (53%; 40 cases)
 - b. PTCL-NOS(21%, 16 cases)
 - c. Systemic ALCL[17%; 9% ALK(+) & 8% ALK(-)]
 2. Extranodal (63%, 132 cases)
 - a. ENKTL(26.5%; 35 cases)

- b. T lymphoblastic Leukemia (13.6%; 18 cases)
- c. T-LGL leukemia (12.1%; 16 cases)
- d. PTCL-NOS (7.6%; 10 cases)

E. Discussion :

B-cell lymphoma:

Table 4 Relative frequencies of the common B-cell lymphoma types among all B-cell non-Hodgkin lymphoma (NHL) in various countries/geographic regions.

| Countries/region (case no.) | DLBCL (case no.) | FL (case no.) | MALT lymphoma (case no.) | CLL/SLL (case no.) | MCL (case no.) | BL (case no.) | Reference |
|-------------------------------|------------------|------------------|--------------------------|-------------------------|----------------|---------------|---------------|
| USA (n = 498,057) | 38.92% (193,855) | 20.48% (101,997) | 9.94% (49,508) | 22.28% (110,944) | 4.91% (24,456) | 1.92% (9543) | [22] |
| CSA (n = 809) | 45.8% (371) | 23.4% (189) | 7.9% (64) | 4.3% (35) | 5.7% (46) | 3.3% (27) | [20] |
| UK (n = 5488) | 43.24% (2373) | 16.82% (923) | 17.91% (983) | Not included | 4.50% (247) | 1.88% (103) | [16] |
| Japan (n = 1166) | 51.37% (599) | 24.10% (281) | 7.89% (92) | 1.29% (15) ^b | 3.00% (35) | 0.60% (7) | [15] |
| Korea (n = 3399) ^a | 47.75% (1623) | 2.68% (91) | 19.45% (661) | 2.85% (97) | 2.88% (98) | 3.27% (111) | [14] |
| China (n = 3012) | 55.78% (1680) | 4.48% (135) | 11.78% (355) | 5.74% (173) | 3.75% (113) | 1.56% (47) | [13] |
| Taiwan (n = 1039) | 48.03% (499) | 16.27% (169) | 7.89% (82) | 7.31% (76) | 2.50% (26) | 2.41% (25) | Current study |

BL = Burkitt lymphoma; CLL = chronic lymphocytic leukemia; CSA = Central and South America; DLBCL = diffuse large B-cell lymphoma; FL = follicular lymphoma; MALT = mucosa-associated lymphoid tissue; MCL = mantle cell lymphoma; SLL = small lymphocytic lymphoma; UK = United Kingdom; USA = United States of America.

^a In this Korean study, plasma cell neoplasms (762 among a total of 4161 cases) were included. In the current table, plasma cell neoplasms were excluded for the purpose of comparison.

^b In this Japanese study, only small lymphocytic lymphoma SLL but not CLL was included.

- a. 1347 cases of 16 years (2000~2016)
- b. 跟過去研究資料一起看，跟西方比較起來：
 - i. HL 機率較低(%6)
 - ii. T-cell neoplasms 較高 (所有淋巴病變中 16%，所有 NHL 中 17%)
- c. 1347 cases 中，有 8 cases (0.60%)同時有兩種並存
- d. 西方主要的淋巴病變中，HL 佔了 15~30%，其中的 90~95% Classic HL(CHL)，其餘為 Nodular lymphocyte predominant Hodgkin lymphoma(NLPHL; 3~8%)
- e. CHL 在工業化國家較開發中國家多
- f. HL 頻率在東亞國家較西方低很多
- g. NLPHL 頻率比起西方是極低(1.2~3.7%)
- h. NLPHL 佔所有 HL 的比率也是在東方較低
- i. DLBCL 最多，10 個 case 中會有 4~5 個 case
- j. 東亞國家中，FL 在台灣(16%)，日本(24%)是第二多
- k. 根據一篇 1993~2012 台灣癌症登記資料庫的統計研究，FL 近期在台灣出現頻率有變高，且有很強的 birth-cohort effect,原因未知
- l. FL 在韓國(%3)，中國(4%)很低，在兩國是 MALT lymphoma 第二多 B-cell lymphoma type，可能與兩國有較高的 Helicobacter pylori 感染 gastric MALT lymphoma，胃癌胃鏡檢驗補助計畫有關
- m. 在台灣，MZL 較低可能與腸胃科醫師在早期就幫病患消滅 H.plori 感染有關，而間接減少 gastric MALT lymphoma 的出現頻率

T-cell lymphoma:

Table 5 Relative frequencies of the common mature T-cell lymphoma types among all T-cell non-Hodgkin lymphomas (NHLs) in various countries/geographic regions.

| Countries/region (case no.) | AITL (case no.) | PTCL-NOS (case no.) | ENKTL (case no.) | ALCL, ALK+ and ALK- (case no.) | ATLL (case no.) | Reference |
|-------------------------------|-----------------|---------------------|------------------|--------------------------------|-----------------|---------------|
| USA (n = 6228) | 2.83% (176) | 16.55% (1031) | NA | 13.87% (864) | NA | [21] |
| CSA (n = 104) | Not specified | 60.6% (63) | 26.0% (27) | Not specified | 9.6% (10) | [20] |
| UK (n = 308) | 17.9% (55) | 29.5% (91) | Not specified | 14.9% (46) | Not specified | [16] |
| Japan (n = 287) | 14.6% (42) | 29.6% (85) | 7.0% (20) | 5.2% (15) | 14.3% (41) | [15] |
| Korea (n = 667) | 6.4% (43) | 31.6% (211) | 30.9% (206) | 15.6% (104) | 0.1% (1) | [14] |
| China (n = 1082) | 6.28% (68) | 16.82% (182) | 47.04% (509) | 10.26% (111) | 0.09% (1) | [13] |
| Taiwan (n = 197) ^a | 20.3% (40) | 19.8% (39) | 18.3% (36) | 11.7% (23) | 4.6% (9) | Current study |

AITL = angioimmunoblastic T-cell lymphoma; ALCL = anaplastic large cell lymphoma; ALK = anaplastic lymphoma kinase; ATLL = adult T-cell leukemia/lymphoma; CSA = Central and South America; ENKTL = extranodal natural killer/T-cell lymphoma; NA = not available; PTCL-NOS = peripheral T-cell lymphoma, not otherwise specified; UK = United Kingdom; USA = United States of America.

^a Twenty-one cases of T lymphoblastic leukemia/lymphomas in the current study were excluded for comparison of mature T-cell neoplasms.

- n. ENKTL(Extranodal NK/T-cell Lymphoma) 在中國意外的很常見，幾乎佔所有 T-cell lymphoma 一半，在韓國也很常見(佔 1/3 的案例)，原因不明，但可能跟生活方式，環境因子有關(務農，接觸殺蟲劑；住在焚化爐附近等)
- o. EBV mRNA 混合法的成果，強烈顯示種族的相關性，代表了對 EBVmRNA 免疫反應有 defect 是由基因表現缺失造成
- p. 在東亞國家，AITL 較 PTCL-NOS 少，但參考此次資料，AITL 近年在台灣增多
- q. 在法國為例，AITL 是目前最多的，原因可能為對疾病有較多認識，進而將其診斷為 AITL，而非誤診為不尋常免疫反應而已

F. 這篇研究的缺點:

- a. 單一病理中心(奇美醫院)的 16 年的資料，可能無法反映全國的真實分布狀態
- b. 其中一位研究員在座 flow cytometric immunophenotyping 時可能取了較多的 Mature lymphoid leukemia 的 case

G. 這篇研究的優點:

- a. 有長期追蹤的資料，其中一位 case 追蹤期長達 20 年，因而得以幫助區分並存 lymphoid neoplasm 的 case

H. 結論:

- a. 分析了全台灣最大的 lymphoma series
- b. 導論出 HL 是很稀有的(佔總體 6%)
- c. T-cell neoplasms 佔所有 NHL 的 17%，與其他東亞國家相近
- d. 整體來說，在東方，西方比較下可觀察到，東方的 HL 頻率較高，T-cell neoplasms 較低

| 題號 | 題目 |
|-------------|---|
| 1 | Which of the following lymphoma is the most common type ? (A) Hodgkin Lymphoma(HL) (B) Non-Hodgkin Lymphoma(NHL) (C) Burkitt Lymphoma (D) Follicular Lymphoma |
| 答案 (B) | 出處 : Oral Pathology : Clinical Pathologic Correlations, 7 th edition p. 228, 229 |
| 題號 | 題目 |
| 2 | What are the NOT likely reasons for different percentage of certain lymphomas between geographical regions? (A) Life style (B) Environmental factors (C) Religion (D) More understanding to the disease |
| 答案 (C) | 出處 : Oral Pathology : Clinical Pathologic Correlations, 7 th edition, p.238, 239 |